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La prise en charge du cancer chez les personnes souffrant de troubles psychiques sévères

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Sommaire

En guise d'introduction

Les individus suivis pour des troubles psychiques font face à une mortalité prématurée, quelle que soit la cause de décès. Ce phénomène, marqueur d'inégalité de santé, questionne le suivi et l'accès aux soins somatiques des personnes vivant avec un trouble psychique sévère. Les données du Système national des données de santé (SNDS) permettent de caractériser leur recours aux soins courants à l'échelle nationale en comparaison aux principaux bénéficiaires de l'Assurance maladie. Leur exploitation démontre un moindre recours aux soins de prévention et aux soins de spécialistes courants chez les individus suivis pour un trouble psychique sévère, malgré une prévalence plus élevée des principales pathologies chroniques qu'en population générale, et une fréquence plus importante des hospitalisations évitables, malgré des contacts plus fréquents en médecine générale. Ces résultats soulignent les difficultés du système de santé à répondre de manière satisfaisante aux besoins spécifiques des personnes vivant avec un trouble psychique et soutiennent le développement de mesures dédiées pour améliorer l'accès et la prise en charge somatique de cette population aux multiples vulnérabilités.[1]

Réalisée dans le cadre du projet Canopée[2] dont l'objectif est d'étudier les potentiels défauts de prise en charge du cancer chez les personnes souffrant de troubles psychiques sévères, cette bibliographie rassemble de la littérature scientifique identifiée à partir de l'interrogation des bases de données et portails suivants : Medline, Irdes, Cairn, Science direct, Web of science, Googlescholar. Après un focus sur la surmortalité et les difficultés dans l'accès aux soins somatiques, les aspects principalement documentés sont : la prévalence, l'incidence et le parcours de soins pour cancer des personnes souffrant de troubles psychiques sévères (schizophrénie, troubles bipolaires) sous l'angle à la fois qualitatif et quantitatif.

Surmortalité et difficultés dans l'accès aux soins somatiques

ÉTUDES DE L'IRDES

Coldefy, M. et Gandré, C. (2018). "Personnes suivies pour des troubles psychiques sévères : une espérance de vie fortement réduite et une mortalité prématurée quadruplée." Questions D'economie De La Sante (Irdes)(237): 1-8.
http://www.irdes.fr/recherche/questions-d-economie-de-la-sante/237-personnes-suivies-pour-des-troubles-psychiques-severes-une-esperance-de-vie-fortement-reduite.pdf

> La mortalité des individus suivis pour des troubles psychiques sévères n'avait été étudiée que de façon parcellaire en France. La mise à disposition de données relatives aux causes médicales de décès appariées aux données de consommation de soins dans le Système national des données de santé (SNDS) en a permis l'étude à l'échelle nationale chez les principaux bénéficiaires de l'Assurance maladie. La réduction de l'espérance de vie des individus suivis pour des troubles psychiques atteint en moyenne 16 ans chez les hommes et 13 ans chez les femmes avec des variations en fonction des troubles considérés. Ces individus ont des taux de mortalité deux à cinq fois supérieurs à ceux de la population générale, quelle que soit la cause de décès, et un taux de mortalité prématurée quadruplé. Ces premiers résultats encouragent à développer des travaux visant à expliquer cette surmortalité ainsi qu'à mener en parallèle des actions ciblées pour réduire les inégalités de santé dont sont victimes les personnes vivant avec un trouble psychique.

Coldefy, M. et Gandre, C. (2019). "Troubles psychiques et surmortalité." Sante Mentale(238): 1-4.
https://www.santementale.fr/boutique/acheter-article/troubles-psychiques-et-surmortalite.html

> La mortalité des individus suivis pour des troubles psychiques sévères n'avait été étudiée que de façon parcellaire en France. La mise à disposition de données relatives aux causes médicales de décès appariées aux données de consommation de soins dans le Système national des données de santé (SNDS) en a permis l'étude à l'échelle nationale chez les principaux bénéficiaires de l'Assurance

[1] Gandré, C. et Coldefy, M. (2020). "Le recours aux soins somatiques des personnes suivies pour des troubles psychiques sévères en France : comparaison avec la population générale." Revue D'epidemiologie Et De Sante Publique **68**: S31
[2] Irdes. Programme de recherche 2021-2023. Page 76.

maladie. Les résultats montrent une réduction de l'espérance de vie des individus suivis pour des troubles psychiques en moyenne de 16 ans chez les hommes et 13 ans chez les femmes avec des variations en fonction des troubles considérés. Ces individus ont des taux de mortalité deux à cinq fois supérieurs à ceux de la population générale, quelle que soit la cause de décès, et un taux de mortalité prématurée quadruplé.

Gandré C., Beauguitte, L., Lolivier, A., et al. (2020). "Care Coordination for Severe Mental Health Disorders: an Analysis of Healthcare Provider Patient-Sharing Networks and their Association with Quality of Care in a French Region." BMC Health Services Research **20**(548): 1-15.
https://http://bmchealthservres.biomedcentral.com/articles/10.1186/s12913-020-05173-x

For patients with multiple and complex health needs, such as those suffering from mental health disorders, outcomes are determined by the combined actions of the care providers they visit and their interactions. Care coordination is therefore essential. However, little is known on links between hospitals providing psychiatric care and community-based care providers which could serve as a basis for the creation of formal mental care networks supported by recent policies. In this context, we first aimed to identify and characterize existing types of healthcare provider patient-sharing networks for severe mental health disorders in one French region. Second, we aimed to analyse the association between their characteristics and the quality of the care they provide.

Gandré, C. et Coldefy, M. (2020). "Disparities in the Use of General Somatic Care among Individuals Treated for Severe Mental Disorders and the General Population in France." International Journal of Environmental Research and Public Health **17**(10): 1-17.
https://www.mdpi.com/1660-4601/17/10/3367#cite

Individuals with severe mental illnesses (SMI) face a striking excess and premature mortality which has been demonstrated in several national contexts. This phenomenon, which constitutes a red-flag indicator of public health inequities, can be hypothesized to result from healthcare access issues which have been insufficiently documented so far. In this context, our objective was to explore patterns of general somatic healthcare use of individuals treated for SMI in comparison to those of the general population in France using national health administrative data and a matched case-control study. Differences in the use of general and specific somatic preventive care services, primary care, routine specialized somatic care and admissions to non-psychiatric hospital departments for somatic causes were described between cases and controls after adjustment on differing clinical needs, socio-economic status, and living environment. Our results show a lower use of general preventive care services and of routine specialized somatic care in the SMI population, despite more frequent comorbidities, and a higher occurrence of avoidable hospitalizations, despite higher contacts with primary care physicians. These findings suggest that the health system fails to address the specific needs of this vulnerable population and support the development of measures aimed at reducing this gap.

Gandré, C. et Coldefy, M. (2020). "Moins de soins de prévention, de recours aux spécialistes et plus d'hospitalisations évitables chez les personnes suivies pour un trouble psychique sévère." Questions D'economie De La Sante (Irdes)(250): 8.
https://www.irdes.fr/recherche/questions-d-economie-de-la-sante/250-moins-de-soins-de-prevention-plus-d-hospitalisations-evitables-chez-personnes-suivies-pour-trouble-psychique-severe.pdf

Les individus suivis pour des troubles psychiques font face à une mortalité prématurée, quelle que soit la cause de décès. Ce phénomène, marqueur d'inégalité de santé, questionne le suivi et l'accès aux soins somatiques des personnes vivant avec un trouble psychique sévère. Les données du Système national des données de santé (SNDS) permettent de caractériser leur recours aux soins courants à l'échelle nationale en comparaison aux principaux bénéficiaires de l'Assurance maladie. Leur exploitation démontre un moindre recours aux soins de prévention et aux soins de spécialistes courants chez les individus suivis pour un trouble psychique sévère, malgré une prévalence plus élevée des principales pathologies chroniques qu'en population générale, et une fréquence plus importante des hospitalisations évitables, malgré des contacts plus fréquents en médecine générale. Ces résultats soulignent les difficultés du système de santé à répondre de manière satisfaisante aux besoins

spécifiques des personnes vivant avec un trouble psychique et soutiennent le développement de mesures dédiées pour améliorer l'accès et la prise en charge somatique de cette population aux multiples vulnérabilités.

Gandré, C. et Coldefy, M. (2020). "Le recours aux soins somatiques des personnes suivies pour des troubles psychiques sévères en France : comparaison avec la population générale." Revue D'epidemiologie Et De Sante Publique **68**: S31.
http://www.sciencedirect.com/science/article/pii/S0398762020300778

Introduction La surmortalité des individus suivis pour des troubles psychiques a été récemment objectivée en France, appelant des éléments explicatifs et suggérant que cette population est confrontée à des inégalités de santé. Dans ce contexte, notre objectif est d'identifier d'éventuels défauts dans les parcours de soins somatiques des personnes suivies pour des troubles psychiques sévères. Méthodes Nous mobilisons le Système national des données de santé (SNDS) pour décrire et comparer le recours aux soins somatiques entre les individus suivis pour des troubles psychiques sévères (identifiés via la cartographie médicalisée de la Caisse nationale d'assurance maladie pour l'année 2014) et la population générale. Plusieurs aspects des parcours de soins sont étudiés sur une période allant jusqu'à deux ans (2015 et 2016) : notamment le recours aux soins préventifs, aux soins somatiques courants, aux soins en urgence et aux hospitalisations évitables. Résultats La part des personnes ayant recours à la vaccination et au dépistage du cancer du sein et/ou de l'utérus est moindre chez les personnes suivies pour des troubles psychiques en comparaison avec la population générale (ratios de 0,91 et 0,76 respectivement). Ce moindre recours est également observé pour les soins dentaires, gynécologiques et ophtalmologiques (ratios compris entre 0,66 et 0,94). Les individus suivis pour des troubles psychiques présentent un nombre moyen de passage aux urgences annuelles 2,4 fois plus élevé que la population générale. Les disparités sont particulièrement marquées pour les hospitalisations évitables qui sont 3,4 fois plus fréquentes chez les personnes avec des troubles psychiques. Discussion/Conclusion Ces premiers résultats mettent en évidence des disparités dans le recours aux soins somatiques courants des individus suivis pour des troubles psychiques sévères, dont la persistance après ajustement sur les caractéristiques individuelles (notamment socio-économiques) devra être explorée. Ils soutiennent le développement d'approches qualitatives visant à mieux comprendre les difficultés et obstacles dans les parcours de soins somatiques des patients suivis pour des troubles psychiques.

Gandré, C., Rosenberg, S., Coldefy, M., et al. (2019). "Experimenting locally with a stepped-care approach for the treatment of mild to moderate mental disorders in France: Challenges and opportunities." Health Policy **123**(11): 1021-1027.
https://www.sciencedirect.com/science/article/pii/S0168851019301903

In France, publicly funded mental care services are mostly hospital-based and focused on treating severe illnesses. Mild to moderate mental disorders are typically managed by general practitioners (GP) who often lack specific training to treat these conditions. Antidepressant prescribing levels for mild to moderate conditions are inadequately high. Public reimbursement for psychotherapies provided by psychologists is generally not available. This paper presents a local experiment with a stepped-care approach for the treatment of mild to moderate mental disorders in four French départements launched in 2018. The experiment includes the introduction of a standardized assessment protocol for GPs, clear referral guidelines, and full reimbursement of visits to psychologists upon GP referral. Seemingly simple, the policy raises several issues related to the regulation, training and reimbursement of psychologists, and illustrates the need for careful preparation and workforce planning to ensure success and stakeholder support. An independent evaluation of the local experiments is planned, which provides the opportunity to fine-tune the policy before any broader rollout. The issues raised in France and the on-going debate is relevant for other countries preparing similar policies for improving mental care.

ÉTUDES FRANÇAISES

Anastasi, A. (2021). "Psychiatrie et soins somatiques « C'est pas le tout d'y dire, faut aussi y faire »." L'information psychiatrique **97**(6): 465-475.
https://www.cairn.info/revue-l-information-psychiatrique-2021-6-page-465.htm

Les patients psychiatriques ont une espérance de vie réduite du fait d'une morbi-mortalité somatique augmentée. Les difficultés d'accès aux soins en sont les causes essentielles malgré une évolution de la prise en compte de ces problématiques au cours des dernières années. La prise en charge des patients psychiatriques doit être globale et s'appuyer sur des dispositifs allant du droit commun à des structures hospitalières spécialisées comme les unités médico-psychiatriques, en capacité d'appréhender simultanément des situations somato-psychiatriques complexes. L'unité de médecine du centre hospitalier Le Vinatier illustre ce type de prises en charge. La temporalité nécessaire au soin de ces patients est un paramètre incontournable de ce type de situations complexes. Les unités médico-psychiatriques sont complémentaires dans le parcours de soins global pensé autour du sujet psychiatrique et restent concurrentielles au vu du service médical rendu à une population de patients vulnérables.

Bendjema, Z. (2021). "Construction et évaluation d'un parcours de prévention somatique destiné aux patients psychotiques et bipolaires suivis par un secteur de santé mentale." L'information psychiatrique **98**(8): 727-728.
https://www.cairn.info/revue-l-information-psychiatrique-2021-8-page-727.htm

Les patients souffrant de troubles mentaux sévères ont un excès de mortalité imputable au risque cardiovasculaire, métabolique et de cancer réduisant leur espérance de vie de 20 %. Ces facteurs de risque sont similaires à ceux de la population générale dans leur nature, mais sont surreprésentés. Les pathologies qui en découlent sont accessibles à la prévention et au dépistage. Néanmoins les études suggèrent un défaut de prévention et de suivi.

Bougerol, C., Charles, R., Bally, J. N., et al. (2020). "Discrimination et stigmatisation des patients psychotiques dans les soins somatiques." Medecine : De La Medecine Factuelle a Nos Pratiques **16**(7): 305-308.

Les patients psychotiques souffrent de discrimination dans la société, mais également auprès des professionnels de santé. Cette stigmatisation peut conduire à un biais de raisonnement diagnostique et à des soins sub-optimaux. Pour lutter contre cette discrimination, certains centres mettent en place des adaptations du système de soins, notamment ambulatoires

Cnam (2018). Santé mentale. Rapport sur les charges et produits de l'assurance maladie pour 2019 : Améliorer la qualité du système de santé et maîtriser les dépenses : propositions de l'Assurance Maladie pour 2019. Paris Cnam**:** 262 , tabl.
www.ameli.fr/l-assurance-maladie/statistiques-et-publications/rapports-et-periodiques/rapports-charges-produits-de-l-assurance-maladie/rapports-charges-et-produits-pour-2018-et-2019/rapport-charges-et-produits-pour-l-annee-2018.php

Chaque année, l'Assurance Maladie présente au Gouvernement et au Parlement ses propositions relatives à l'évolution des charges et produits au titre de l'année suivante et aux mesures nécessaires pour atteindre l'équilibre prévu par le cadrage financier pluriannuel des dépenses d'assurance maladie. À partir d'analyses réalisées sur l'évolution des dépenses et des pratiques, et en s'appuyant sur les recommandations françaises et internationales, le rapport Charges et produits pour l'année 2019 présente des propositions et des pistes de réflexion visant à améliorer la qualité et l'efficience des soins, et à optimiser les dépenses de santé.

Ha, Chan Che, C. et Decool, E. (2017). "Mortalité des personnes souffrant de troubles mentaux. Analyse en causes multiples des certificats de décès en France, 2000-2013." Bulletin Epidemiologique Hebdomadaire(23): 500-508.

[BDSP. Notice produite par SANTE-PUBLIQUE-FRANCE nR0xGk97. Diffusion soumise à autorisation]. Introduction : l'objectif était de décrire la mortalité associée à l'existence de troubles mentaux (TM) en France. Méthodes : notre analyse, dite en causes multiples, porte à la fois sur les causes initiales (CI) et

sur les causes associées des décès survenus en France de 2000 à 2013, extraits de la base nationale du CépiDc-Inserm. L'ensemble des TM du chapitre F de la Classification internationale des maladies (CIM-10, codes F00 à F99) ainsi que des sous-groupes ont été considérés. Résultats : de 2000 à 2013,783 403 décès avec mention de TM ont été enregistrés, représentant en moyenne 55 957 décès annuels et 10,3% de l'ensemble des décès survenus sur cette période. Les taux de décès avec TM standardisés sur l'âge ont baissé globalement (-15,1%) sur l'ensemble de la période. Pour les hommes comme pour les femmes, l'âge moyen au décès était particulièrement bas pour la schizophrénie (respectivement 55,9 ans et 67,6 ans) et pour les TM liés à l'alcool (respectivement 59,4 et 60,7 ans). Les CI de décès se répartissaient ainsi : pour les décès avec mention de TM, le suicide (11,1%) se situait en 3e position, derrière les causes cardiovasculaires (27,3%) et les cancers (18,1%), alors que pour les décès sans mention de TM, le suicide (1,3%) se plaçait loin derrière les cancers (31,0%) et le cardiovasculaire (28,9%). Conclusion : ce travail souligne l'importance de prendre soin aussi bien de la santé mentale que physique des personnes souffrant de TM, ainsi que de la nécessité de développer auprès d'elles des actions de prévention, notamment du suicide mais portant aussi sur les facteurs de risque cardiovasculaire, respiratoire et métabolique.

ÉTUDES ETRANGERES

Bradford, D. W. et Cunningham, N. (2016). "Psychotic disorders cause the greatest mortality disparity among mental disorders, though more deaths are attributable overall to mood and anxiety disorders." Evid Based Ment Health **19**(2): 58.

Chang, C. K. (2012). "Improving the life expectancy of people with serious mental illness." Br J Hosp Med (Lond) **73**(3): 126-127.

De Hert, M., Cohen, D., Bobes, J., et al. (2011). "Physical illness in patients with severe mental disorders. II. Barriers to care, monitoring and treatment guidelines, plus recommendations at the system and individual level." World Psychiatry **10**(2): 138-151.
https://onlinelibrary.wiley.com/doi/abs/10.1002/j.2051-5545.2011.tb00036.x

Druss, B. G., Zhao, L., Von Esenwein, S., et al. (2011). "Understanding excess mortality in persons with mental illness: 17-year follow up of a nationally representative US survey." Med Care **49**(6): 599-604.

BACKGROUND: Although growing concern has been expressed about premature medical mortality in persons with mental illness, limited data are available quantifying the extent and correlates of this problem using population-based, nationally representative samples. METHODS: The study used data from the 1989 National Health Interview Survey mental health supplement, with mortality data through 2006 linked through the National Death Index (80,850 participants, 16,435 deaths). Multivariable models adjusting for demographic factors assessed the increased hazard of mortality adding socioeconomic status, healthcare variables, clinical factors first separately, and then together. RESULTS: Persons with mental disorders died an average of 8.2 years younger than the rest of the population (P < 0.001). Adjusting for demographic factors, presence of a mental illness was associated with a significant risk of excess mortality, (hazard ratio=2.06, 95% confidence interval=1.71-2.40), with 95.4% of deaths owing to medical rather than unnatural causes. Adding socioeconomic variables to the model, the hazard ratio was 1.77 (P < 0.001); adding health system factors, it was 1.80 (P < 0.001)); adding baseline clinical characteristics, the hazard ratio was 1.32 (P < 0.001). After adding all the 3 groups of variables simultaneously, the association was reduced by 82% from baseline and became statistically nonsignificant (hazard ratio=1.19, P=0.053). CONCLUSIONS: The results of the study underscore the complex causes and high burden of medical mortality among persons with mental disorders in the United States. Efforts to address this public health problem will need to address the socioeconomic, healthcare, and clinical risk factors that underlie it.

Dutta, R., Murray, R. M., Allardyce, J., et al. (2012). "Mortality in first-contact psychosis patients in the U.K.: a cohort study." Psychol Med **42**(8): 1649-1661.

https://www.cambridge.org/core/journals/psychological-medicine/article/abs/mortality-in-firstcontact-psychosis-patients-in-the-uk-a-cohort-study/7472B10ED0B451E9D247ED7A566BF9FB

BACKGROUND: The excess mortality following first-contact psychosis is well recognized. However, the causes of death in a complete incidence cohort and mortality patterns over time compared with the general population are unknown. METHOD: All 2723 patients who presented for the first time with psychosis in three defined catchment areas of the U.K. in London (1965-2004, n=2056), Nottingham (1997-1999, n=203) and Dumfries and Galloway (1979-1998, n=464) were traced after a mean of 11.5 years follow-up and death certificates were obtained. Data analysis was by indirect standardization. RESULTS: The overall standardized mortality ratio (SMR) for first-contact psychosis was 184 [95% confidence interval (CI) 167-202]. Most deaths (84.2%, 374/444) were from natural causes, although suicide had the highest SMR (1165, 95% CI 873-1524). Diseases of the respiratory system and infectious diseases had the highest SMR of the natural causes of death (232, 95% CI 183-291). The risk of death from diseases of the circulatory system was also elevated compared with the general population (SMR 139, 95% CI 117-164) whereas there was no such difference for neoplasms (SMR 111, 95% CI 86-141). There was strong evidence that the mortality gap compared with the general population for all causes of death ($p<0.001$) and all natural causes ($p=0.01$) increased over the four decades of the study. There was weak evidence that cardiovascular deaths may be increasing relative to the general population ($p=0.07$). CONCLUSIONS: People with first-contact psychosis have an overall mortality risk that is nearly double that of the general population. Most excess deaths are from natural causes. The widening of the mortality gap over the last four decades should be of concern to all clinicians involved in delivering healthcare.

Gatov, E., Rosella, L., Chiu, M., et al. (2017). "Trends in standardized mortality among individuals with schizophrenia, 1993-2012: a population-based, repeated cross-sectional study." Cmaj **189**(37): E1177-e1187.

BACKGROUND: We examined mortality time trends and premature mortality among individuals with and without schizophrenia over a 20-year period. METHODS: In this population-based, repeated cross-sectional study, we identified all individual deaths that occurred in Ontario between 1993 and 2012 in persons aged 15 and over. We plotted overall and cause-specific age- and sex-standardized mortality rates (ASMRs), stratified all-cause ASMR trends by sociodemographic characteristics, and analyzed premature mortality using years of potential life lost. Additionally, we calculated mortality rate ratios (MRRs) using negative binomial regression with adjustment for age, sex, income, rurality and year of death. RESULTS: We identified 31 349 deaths among persons with schizophrenia, and 1 589 902 deaths among those without schizophrenia. Mortality rates among people with schizophrenia were 3 times higher than among those without schizophrenia (adjusted MRR 3.12, 95% confidence interval 3.06-3.17). All-cause ASMRs in both groups declined in parallel over the study period, by about 35%, and were higher for men, for those with low income and for rural dwellers. The absolute ASMR difference also declined throughout the study period (from 16.15 to 10.49 deaths per 1000 persons). Cause-specific ASMRs were greater among those with schizophrenia, with circulatory conditions accounting for most deaths between 1993 and 2012, whereas neoplasms became the leading cause of death for those without schizophrenia after 2005. Individuals with schizophrenia also died, on average, 8 years younger than those without schizophrenia, losing more potential years of life. INTERPRETATION: Although mortality rates among people with schizophrenia have declined over the past 2 decades, specialized approaches may be required to close the persistent 3-fold relative mortality gap with the general population.

Kisely, S., Preston, N., Xiao, J., et al. (2013). "Reducing all-cause mortality among patients with psychiatric disorders: a population-based study." Cmaj **185**(1): E50-56.

BACKGROUND: Among patients with psychiatric disorders, there are 10 times as many preventable deaths from physical disorders as there are from suicide. We investigated whether compulsory community treatment, such as community treatment orders, could reduce all-cause mortality among patients with psychiatric disorders. METHODS: We conducted a population-based survival analysis of an inception cohort using record linking. The study period extended from November 1997 to December 2008. The cohort included patients from all community-based and inpatient psychiatric services in Western Australia (state population 1.8 million). We used a 2-stage design of matching and

Cox regression to adjust for demographic characteristics, previous use of health services, diagnosis and length of psychiatric history. We collected data on successive cohorts for each year for which community treatment orders were used to measure changes in numbers of patients, their characteristics and outcomes. Our primary outcome was 2-year all-cause mortality. Our secondary outcomes were 1-and 3-year all-cause mortality. RESULTS: The study population included 2958 patients with community treatment orders (cases) and 2958 matched controls (i.e., patients with psychiatric disorders who had not received a community treatment order). The average age for cases and controls was 36.7 years, and 63.7% (3771) of participants were men. Schizophrenia and other nonaffective psychoses were the most common diagnoses (73.4%) among participants. A total of 492 patients (8.3%) died during the study. Cox regression showed that, compared with controls, patients with community treatment orders had significantly lower all-cause mortality at 1, 2 and 3 years, with an adjusted hazard ratio of 0.62 (95% confidence interval 0.45-0.86) at 2 years. The greatest effect was on death from physical illnesses such as cancer, cardiovascular disease or diseases of the central nervous system. This association disappeared when we adjusted for increased outpatient and community contacts with psychiatric services. INTERPRETATION: Community treatment orders might reduce mortality among patients with psychiatric disorders. This may be partly explained by increased contact with health services in the community. However, the effects of uncontrolled confounders cannot be excluded.

Kredentser, M. S., Martens, P. J., Chochinov, H. M., et al. (2014). "Cause and rate of death in people with schizophrenia across the lifespan: a population-based study in Manitoba, Canada." J Clin Psychiatry **75**(2): 154-161.

OBJECTIVE: To compare the causes and rates of death for people with and without schizophrenia in Manitoba, Canada. METHOD: Using de-identified administrative databases at the Manitoba Centre for Health Policy, a population-based analysis was performed to compare age- and sex-adjusted 10-year (1999-2008) mortality rates, overall and by specific cause, of decedents aged 10 years or older who had 1 diagnosis of schizophrenia (ICD-9-CM code 295, ICD-10-CA codes F20, F21, F23.2, F25) over a 12-year period (N = 9,038) to the rest of the population (N = 969,090). RESULTS: The mortality rate for those with schizophrenia was double that of the rest of the population (20.00% vs. 9.37%). The all-cause mortality rate was higher for people with schizophrenia compared to all others (168.9 vs. 99.1 per thousand; relative risk [RR] = 1.70, P < .0001); rates of death due to suicide (RR = 8.67, P < .0001), injury (RR = 2.35, P < .0001), respiratory illness (RR = 2.00, P < .0001), and circulatory illness (RR = 1.64, P < .0001) were also significantly higher in people with schizophrenia. Overall cancer deaths were similar (28.6 vs. 27.3 per thousand, P = .42, NS) except in the middle-aged group (40-59), in which cancer death rates were significantly higher for those with schizophrenia (28.7 vs. 11.6 per thousand; RR = 2.48, P < .01). Mortality rates due to lung cancer were significantly higher in people with schizophrenia (9.4 vs. 6.4 per thousand, RR = 1.45, P < .001). CONCLUSIONS: People with schizophrenia are at increased risk of death compared to the general population, and the majority of these deaths are occurring in older age from physical disease processes. Risk of cancer mortality is significantly higher in middle-aged but not younger or older patients with schizophrenia. Understanding these patients' vulnerabilities to physical illness has important public health implications for prevention, screening, and treatment as the population ages.

Lawrence, D., Hancock, K. J. et Kisely, S. (2013). "The gap in life expectancy from preventable physical illness in psychiatric patients in Western Australia: retrospective analysis of population based registers." Bmj **346**: f2539.

OBJECTIVE: To examine the mortality experience of psychiatric patients in Western Australia compared with the general population. DESIGN: Population based study. SETTING: Western Australia, 1985-2005. PARTICIPANTS: Psychiatric patients (292,585) registered with mental health services in Western Australia. MAIN OUTCOME MEASURES: Trends in life expectancy for psychiatric patients compared with the Western Australian population and causes of excess mortality, including physical health conditions and unnatural causes of death. RESULTS: When using active prevalence of disorder (contact with services in previous five years), the life expectancy gap increased from 13.5 to 15.9 years for males and from 10.4 to 12.0 years for females between 1985 and 2005. Additionally, 77.7% of excess deaths were attributed to physical health conditions, including cardiovascular disease (29.9%) and cancer (13.5%). Suicide was the cause of 13.9% of excess deaths. CONCLUSIONS: Despite

knowledge about excess mortality in people with mental illness, the gap in their life expectancy compared with the general population has widened since 1985. With most excess deaths being due to physical health conditions, public efforts should be directed towards improving physical health to reduce mortality in people with mental illness, in addition to ongoing efforts to prevent suicide.

Lemogne, C., Nabi, H., Melchior, M., et al. (2013). "Mortality associated with depression as compared with other severe mental disorders: a 20-year follow-up study of the GAZEL cohort." J Psychiatr Res **47**(7): 851-857.

Individuals with severe mental disorders (SMD) have an increased risk of mortality from somatic diseases. This study examined whether this risk is different in persons with depressive disorders compared to those with other SMD (i.e. schizophrenia and bipolar disorder). In 1989, 20,625 employees of the French national gas and electricity company (15,011 men and 5614 women, aged 35-50) agreed to participate in the GAZEL cohort study. Three diagnosis groups were created based on sick leave spells from 1978 onwards: 1) no SMD, 2) depressive disorders and 3) other SMD. Dates and causes of death were available from January 1, 1990 to December 31, 2010. The association of diagnosis groups with mortality was estimated with hazard ratios (HR) and 95% confidence intervals (CI) computed using Cox regression. During a mean follow-up of 19.8 years, 1544 participants died, including 1343 from a natural cause, of which 258 died from cardiovascular diseases. After adjustment for age, gender, occupational status, alcohol consumption, smoking and body-mass index, participants with a history of sickness absence for SMD had a greater risk of natural mortality (HR: 1.24, CI: 1.08-1.43), cardiovascular mortality (HR: 1.49, CI: 1.08-2.05) and non-cardiovascular natural mortality (HR: 1.19, CI: 1.02-1.39). Compared to depressive disorders, other SMD were associated with an increased risk of natural mortality (HR: 1.94, CI: 1.17-3.22) and cardiovascular mortality (HR: 3.58, CI: 1.53-8.39). Job security and systematic medical follow-up may fall short of preventing premature death among workers with sickness absence due to SMD.

Lesage, A., Rochette, L., Emond, V., et al. (2015). "A Surveillance System to Monitor Excess Mortality of People With Mental Illness in Canada." Can J Psychiatry **60**(12): 571-579.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4679166/pdf/cjp-2015-vol60-dec2015-571-579.pdf

OBJECTIVE: Outcome measures are rarely available for surveillance and system performance monitoring for mental disorders and addictions. Our study aims to demonstrate the feasibility and face validity of routinely measuring the mortality gap in the Canadian context at the provincial and regional levels using the methods and data available to the Canadian Chronic Disease Surveillance System (CCDSS) of the Public Health Agency of Canada. METHODS: We used longitudinal data from the Quebec Integrated Chronic Disease Surveillance System, which also provides aggregated data to the CCDSS. This includes data from the health insurance registry physician claims and the hospital discharge abstract for all mental disorder diagnoses (International Classification of Diseases [ICD]-9 290-319 or ICD-10 F00-F99). Patients were defined as having had received a mental disorder diagnosis at least once during the year. Life expectancy was measured using Chiang's method for abridged life tables, complemented by the Hsieh method for adjustment of the last age interval. RESULTS: We found a lower life expectancy among psychiatric patients of 8 years for men and 5 years for women. For patients with schizophrenia, life expectancy was lowered by 12 years for men and 8 years for women. Cardiovascular disease and cancer were the most common causes of premature death. Findings were consistent across time and regions of the province. Lower estimates of the mortality gap, compared with literature, could be explained by the inclusion of primary care patients and methods. CONCLUSIONS: Our study demonstrates the feasibility of using administrative data to measure the impact of current and future mental health plans in Canada provided the techniques can be replicated in other Canadian provinces.

Liu, N. H., Daumit, G. L., Dua, T., et al. (2017). "Excess mortality in persons with severe mental disorders: a multilevel intervention framework and priorities for clinical practice, policy and research agendas." World Psychiatry **16**(1): 30-40.

Excess mortality in persons with severe mental disorders (SMD) is a major public health challenge that warrants action. The number and scope of truly tested interventions in this area remain limited, and strategies for implementation and scaling up of programmes with a strong evidence base are scarce. Furthermore, the majority of available interventions focus on a single or an otherwise limited number

of risk factors. Here we present a multilevel model highlighting risk factors for excess mortality in persons with SMD at the individual, health system and socio-environmental levels. Informed by that model, we describe a comprehensive framework that may be useful for designing, implementing and evaluating interventions and programmes to reduce excess mortality in persons with SMD. This framework includes individual-focused, health system-focused, and community level and policy-focused interventions. Incorporating lessons learned from the multilevel model of risk and the comprehensive intervention framework, we identify priorities for clinical practice, policy and research agendas.

Martens, P. J., Chochinov, H. M. et Prior, H. J. (2013). "Where and how people with schizophrenia die: a population-based, matched cohort study in Manitoba, Canada." J Clin Psychiatry **74**(6): e551-557.

OBJECTIVE: To compare place and cause of death for people with and without schizophrenia in Manitoba, Canada. METHOD: By using deidentified administrative databases at the Manitoba Centre for Health Policy, a 1:3 matched cohort of decedents aged >/= 10 years in fiscal years April 1995-March 2008 (n = 3,943 with schizophrenia; n = 11,827 without schizophrenia) was selected and matched on age, sex, geography, and date of death +/- 2 months. Schizophrenia was defined as ICD-9-CM code 295 or ICD-10-CA codes F20, F21, F23.2, or F25 in hospital/physician files at least once within 12 years of death. RESULTS: The median age at death was 77 years. The attributable percentage of deaths was higher for respiratory illnesses (all ages) and suicide (age 10-59 years only), similar for circulatory illnesses, and lower for cancer in decedents with schizophrenia compared to matched controls. For cancer deaths, decedents with schizophrenia were equally likely to die of gastrointestinal, breast, or prostate cancer, but more likely to die of lung cancer at ages 10-59 (32.5% versus 20.6%, P < .004). Place of death was more likely a nursing home (29.7% vs 13.9%) and less likely a hospital (55.5% vs 70.5%) (P < .0001) for decedents with schizophrenia overall and by specific cause, with the exception of suicide deaths showing no difference by place. Except for those who died in nursing homes, decedents with schizophrenia had higher general practitioner but lower specialist rates and inpatient hospital separations. CONCLUSIONS: Generally, patients with schizophrenia were more likely to die in nursing homes but less likely to die in hospitals. Understanding where these patients die is critical for improving access to quality palliative end-of-life care.

Moreno-Küstner, B., Guzman-Parra, J., Pardo, Y., et al. (2021). "Excess mortality in patients with schizophrenia spectrum disorders in Malaga (Spain): A cohort study." Epidemiol Psychiatr Sci **30**: e11. https://www.cambridge.org/core/services/aop-cambridge-core/content/view/72BF70346141AE84A5935779E58D04EB/S2045796020001146a.pdf/div-class-title-excess-mortality-in-patients-with-schizophrenia-spectrum-disorders-in-malaga-spain-a-cohort-study-div.pdf

AIMS: There is evidence that patients with schizophrenia spectrum disorders present higher mortality in comparison with the general population. The aim of this study was to analyse the causes of mortality and sociodemographic factors associated with mortality, standardised mortality ratios (SMRs), life expectancy and potential years of life lost (YLL) in patients with schizophrenia spectrum disorders in Spain. METHODS: The study included a cohort of patients from the Malaga Schizophrenia Case Register (1418 patients; 907 males; average age 42.31 years) who were followed up for a minimum of 10 years (median = 13.43). The factors associated with mortality were analysed with a survival analysis using Cox's proportional hazards regression model. RESULTS: The main causes of mortality in the cohort were circulatory disease (21.45%), cancer (17.09%) and suicide (13.09%). The SMR of the cohort was more than threefold that of the population of Malaga (3.19). The life expectancy at birth was 67.11 years old, which is more than 13 years shorter than that of the population of Malaga. The YLL was 20.74. The variables associated with a higher risk of mortality were age [adjusted hazard ratio (AHR) = 1.069, p < 0.001], male gender (AHR = 1.751, p < 0.001) and type of area of residence (p = 0.028; deprived urban zone v. non-deprived urban area, AHR = 1.460, p = 0.028). In addition, receiving welfare benefit status in comparison with employed status (AHR = 1.940, p = 0.008) was associated with increased mortality. CONCLUSIONS: There is excess mortality in patients with schizophrenia spectrum disorders and also an association with age, gender, socioeconomic inequalities and receiving welfare benefits. Efforts directed towards improved living conditions could have a positive effect on reducing mortality.

Olfson, M., Gerhard, T., Huang, C., et al. (2015). "Premature Mortality Among Adults With Schizophrenia in the United States." JAMA Psychiatry **72**(12): 1172-1181.

IMPORTANCE: Although adults with schizophrenia have a significantly increased risk of premature mortality, sample size limitations of previous research have hindered the identification of the underlying causes. OBJECTIVE: To describe overall and cause-specific mortality rates and standardized mortality ratios (SMRs) for adults with schizophrenia compared with the US general population. DESIGN, SETTING, AND PARTICIPANTS: We identified a national retrospective longitudinal cohort of patients with schizophrenia 20 to 64 years old in the Medicaid program (January 1, 2001, to December 31, 2007). The cohort included 1,138,853 individuals, 4,807,121 years of follow-up, and 74,003 deaths, of which 65,553 had a known cause. MAIN OUTCOMES AND MEASURES: Mortality ratios for the schizophrenia cohort standardized to the general population with respect to age, sex, race/ethnicity, and geographic region were estimated for all-cause and cause-specific mortality. Mortality rates per 100,000 person-years and the mean years of potential life lost per death were also determined. Death record information was obtained from the National Death Index. RESULTS: Adults with schizophrenia were more than 3.5 times (all-cause SMR, 3.7; 95% CI, 3.7-3.7) as likely to die in the follow-up period as were adults in the general population. Cardiovascular disease had the highest mortality rate (403.2 per 100,000 person-years) and an SMR of 3.6 (95% CI, 3.5-3.6). Among 6 selected cancers, lung cancer had the highest mortality rate (74.8 per 100,000 person-years) and an SMR of 2.4 (95% CI, 2.4-2.5). Particularly elevated SMRs were observed for chronic obstructive pulmonary disease (9.9; 95% CI, 9.6-10.2) and influenza and pneumonia (7.0; 95% CI, 6.7-7.4). Accidental deaths (119.7 per 100,000 person-years) accounted for more than twice as many deaths as suicide (52.0 per 100,000 person-years). Nonsuicidal substance-induced death, mostly from alcohol or other drugs, was also a leading cause of death (95.2 per 100,000 person-years). CONCLUSIONS AND RELEVANCE: In a US national cohort of adults with schizophrenia, excess deaths from cardiovascular and respiratory diseases implicate modifiable cardiovascular risk factors, including especially tobacco use. Excess deaths directly attributable to alcohol or other drugs highlight threats posed by substance abuse. More aggressive identification and management of cardiovascular risk factors, as well as reducing tobacco use and substance abuse, should be leading priorities in the medical care of adults with schizophrenia.

Polednak, A. P. (2014). "Trend in rates for deaths with mention of schizophrenia on death certificates of US residents, 1999-2010." Soc Psychiatry Psychiatr Epidemiol **49**(7): 1083-1091.

BACKGROUND: Trends in mortality rates for schizophrenia using multiple causes of death (including contributory causes) coded on death certificates in the US resident population apparently have not been reported. METHODS: Age-standardized rates for deaths per 100,000 in 1999-2010 at age 15+ years (and for 15-64 and 65+ years) with mention of schizophrenia were examined for the US resident population, including variation by age, gender, race (blacks/African Americans and whites) and region. RESULTS: Deaths at age 15+ years coded with schizophrenia as underlying cause were only 12 % of all deaths with mention of schizophrenia, for which the rate declined from 1.58 in 1999 (3,407 deaths) to 1.32 in 2010 (3,422 deaths) (percentage change or PC = -16 %). Declines were larger in females than males, in whites than blacks, and occurred in the Northeast, Midwest and South but not the West. The rate increased for age 15-64 years (PC = +28 %) (mainly in males), however, while declining for age 65+ years (PC = -35 %). For deaths at age 15-64 years with schizophrenia coded as other than the underlying cause, the largest continuous increase was for endocrine-metabolic diseases (predominantly diabetes mellitus) as underlying cause, with smaller increases in males for cardiovascular diseases, external causes and neoplasms. CONCLUSION: Trends in the US rate for deaths with mention of schizophrenia varied among the sociodemographic groups examined. The lack of decline for age 15-64 years requires further study especially with regard to mediators (e.g., obesity) of excess mortality in schizophrenia identified from cohort studies.

Saha, S., Whiteford, H. et McGrath, J. (2014). "Modelling the incidence and mortality of psychotic disorders: data from the second Australian national survey of psychosis." Aust N Z J Psychiatry **48**(4): 352-359.

OBJECTIVES: The aim of this study was to model estimates related to (a) the incidence of psychotic disorders and (b) the mortality associated with these disorders based on a large, population-based prevalence study. METHODS: Data were drawn from the second national survey of adults with

psychotic disorders conducted in seven Australian catchment areas during March to December 2010. To generate incidence rate estimates, we identified recent onset cases recruited as part of the prevalence study and then imputed population-based incidence rates using a set of conservative assumptions. Similarly, for mortality rates, we identified individuals who had died after being identified as 'screen-positive' for psychosis, but prior to full clinical assessment. Using a set of conservative assumptions, we then used these estimates to infer population-based mortality rates. RESULTS: Based on our models, we estimated that the incidence rate for psychotic disorders was 28 cases per 100,000 population. The rate estimates were significantly higher in males than females, with an overall male:female ratio of 1.57:1. Incidence rate estimates peaked in the youngest age group (18-24 years). The adjusted mortality rate estimated during the whole period of observation was 12.5 per 1000 persons, with a standardised mortality ratio of 5.5. CONCLUSIONS: Using treated prevalence data and observed deaths with appropriate algorithms, we were able to impute incidence and mortality rates for psychotic disorders consistent with the published literature. While the second national survey of psychotic disorders was not designed to identify mortality, our estimates provide a stark reminder of the increased mortality associated with these disorders.

Thornicroft, G. (2011). "Physical health disparities and mental illness: the scandal of premature mortality." Br J Psychiatry **199**(6): 441-442.

A 20-year mortality gap for men, and 15 years for women, is still experienced by people with mental illness in high-income countries. The combination of lifestyle risk factors, higher rates of unnatural deaths and poorer physical healthcare contribute to this scandal of premature mortality that contravenes international conventions for the 'right to health.'

Wahlbeck, K., Westman, J., Nordentoft, M., et al. (2011). "Outcomes of Nordic mental health systems: life expectancy of patients with mental disorders." Br J Psychiatry **199**(6): 453-458.

BACKGROUND: People with mental disorders evince excess mortality due to natural and unnatural deaths. The relative life expectancy of people with mental disorders is a proxy measure of effectiveness of social policy and health service provision. AIMS: To evaluate trends in health outcomes of people with serious mental disorders. METHOD: We examined nationwide 5-year consecutive cohorts of people admitted to hospital for mental disorders in Denmark, Finland and Sweden in 1987-2006. In each country the risk population was identified from hospital discharge registers and mortality data were retrieved from cause-of-death registers. The main outcome measure was life expectancy at age 15 years. RESULTS: People admitted to hospital for a mental disorder had a two- to threefold higher mortality than the general population in all three countries studied. This gap in life expectancy was more pronounced for men than for women. The gap decreased between 1987 and 2006 in these countries, especially for women. The notable exception was Swedish men with mental disorders. In spite of the positive general trend, men with mental disorders still live 20 years less, and women 15 years less, than the general population. CONCLUSIONS: During the era of deinstitutionalisation the life expectancy gap for people with mental disorders has somewhat diminished in the three Nordic countries. Our results support further development of the Nordic welfare state model, i.e. tax-funded community-based public services and social protection. Health promotion actions, improved access to healthcare and prevention of suicides and violence are needed to further reduce the life expectancy gap.

Woodhead, C., Ashworth, M., Schofield, P., et al. (2014). "Patterns of physical co-/multi-morbidity among patients with serious mental illness: a London borough-based cross-sectional study." BMC Fam Pract **15**: 117. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4062514/pdf/1471-2296-15-117.pdf

BACKGROUND: Serious mental illness (SMI) is associated with elevated mortality compared to the general population; the majority of this excess is attributable to co-occurring common physical health conditions. There may be variation within the SMI group in the distribution of physical co/multi-morbidity. This study aims to a) compare the pattern of physical co- and multi-morbidity between patients with and without SMI within a South London primary care population; and, b) to explore socio-demographic and health risk factors associated with excess physical morbidity among the SMI group. METHODS: Data were obtained from Lambeth DataNet, a database of electronic patient

records derived from general practices in the London borough of Lambeth. The pattern of 12 co-morbid common physical conditions was compared by SMI status. Multivariate ordinal and logistic regression analyses were conducted to assess the strength of association between each condition and SMI status; adjustments were made for potentially confounding socio-demographic characteristics and for potentially mediating health risk factors. RESULTS: While SMI patients were more frequently recorded with all 12 physical conditions than non-SMI patients, the pattern of co-/multi-morbidity was similar between the two groups. Adjustment for socio-demographic characteristics - in particular age and, to a lesser extent ethnicity, considerably reduced effect sizes and accounted for some of the associations, though several conditions remained strongly associated with SMI status. Evidence for mediation by health risk factors, in particular BMI, was supported. CONCLUSIONS: SMI patients are at an elevated risk of a range of physical health conditions than non-SMI patients but they do not appear to experience a different pattern of co-/multimorbidity among those conditions considered. Socio-demographic differences between the two groups account for some of the excess in morbidity and known health risk factors are likely to mediate the association. Further work to examine a wider range of conditions and health risk factors would help determine the extent of excess mortality attributable to these factors.

Cancers et troubles psychiques sévères : Études globales

ÉTUDES FRANÇAISES

Fond, G., Pauly, V., Duba, A., et al. (2021). "End of life breast cancer care in women with severe mental illnesses." Sci Rep **11**(1): 10167.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8119688/pdf/41598_2021_Article_89726.pdf

Little is known on the end-of-life (EOL) care of terminal breast cancer in women with severe psychiatric disorder (SPD). The objective was to determine if women with SPD and terminal breast cancer received the same palliative and high-intensity care during their end-of-life than women without SPD. Study design, setting, participants. This population-based cohort study included all women aged 15 and older who died from breast cancer in hospitals in France (2014-2018). Key measurements/outcomes. Indicators of palliative care and high-intensity EOL care. Multivariable models were performed, adjusted for age at death, year of death, social deprivation, duration between cancer diagnosis and death, metastases, comorbidity, smoking addiction and hospital category. The analysis included 1742 women with SPD (287 with bipolar disorder, 1075 with major depression and 380 with schizophrenia) and 36,870 women without SPD. In multivariate analyses, women with SPD had more palliative care (adjusted odd ratio aOR 1.320, 95%CI [1.153-1.511], $p < 0.001$), longer palliative care follow-up before death (adjusted beta = 1.456, 95%CI (1.357-1.555), $p < 0.001$), less chemotherapy, surgery, imaging/endoscopy, and admission in emergency department and intensive care unit. Among women with SPD, women with bipolar disorders and schizophrenia died 5 years younger than those with recurrent major depression. The survival time was also shortened in women with schizophrenia. Despite more palliative care and less high-intensity care in women with SPD, our findings also suggest the existence of health disparities in women with bipolar disorders and schizophrenia compared to women with recurrent major depression and without SPD. Targeted interventions may be needed for women with bipolar disorders and schizophrenia to prevent these health disparities.

Schraub, S., Sancho-Garnier, H. et Velten, M. (2009). "Existe-t-il un lien entre un événement psychique et le risque de survenue d'un cancer ?" Revue D'epidemiologie Et De Sante Publique **57**(2): 113-123.

[BDSP. Notice produite par ORSLR AnR0xCkG. Diffusion soumise à autorisation]. L'idée d'un lien causal entre un événement psychique et le déclenchement d'un cancer est largement répandue dans le public et parmi les médecins. Une revue des publications récentes concernant les études épidémiologiques consacrées à ce sujet a été effectuée, avec une analyse des différents types d'études (méta-analyses, cas-témoins, cohortes) sur le rôle des événements difficiles de la vie (stress), des troubles de la personnalité et de la dépression dans l'apparition des cancers du sein et d'autres

types de cancers. Il existe une grande hétérogénéité dans les études qui comportent des biais pouvant expliquer des résultats divergents. Nous n'avons retenu dans cette analyse que les 32 études dont la méthodologie permet l'interprétation la moins biaisée possible. Au total, 18 études sur les 32 retenues ne montrent pas de lien entre facteurs psychologiques et risque de cancer, six travaux ne montrent une association que dans certains sous-groupes et quatre enquêtes, dont trois du même auteur, montrent une liaison inverse pour des cancers féminins. En ce qui concerne les éléments stressants de la vie et les cancers du sein, les résultats sont légèrement en faveur d'une augmentation du risque pour quatre études, mais sont contrebalancés par quatre autres études dont les résultats sont non significatifs et une qui montre une association en sens inverse. Pour les événements stressants de la vie en relation avec les autres cancers, les diverses analyses sont plutôt en faveur d'une absence de lien à l'exception, peut-être, des cancers en rapport avec l'environnement oestrogénique chez les femmes (cancer du côlon et de l'endomètre), où le stress apparaît protecteur. Aucune des études ne montre de lien significatif entre un trouble de la personnalité et le risque de cancer. Enfin, en ce qui concerne le lien entre dépression et risque de cancer, aucune conclusion ne peut être tirée. Dans l'état actuel des connaissances, il paraît difficile de conclure à la responsabilité des événements stressants de la vie, d'un type de personnalité particulier ou d'une dépression dans l'apparition de certains cancers. (R.A.).

ÉTUDES ETRANGERES

Abedin, Y., Gabrilovich, S., Govindarajan, P., et al. (2021). "Mental illness is associated with advanced-stage cervical cancer in a vulnerable patient population." Gynecologic Oncology **162**: S205-S205.

Ahlgrén-Rimpiläinen, A. J., Arffman, M., Suvisaari, J., et al. (2020). "Excess mortality from breast cancer in female breast cancer patients with severe mental illness." Psychiatry Res **286**: 112801.

Women with a history of severe mental illness (SMI) have elevated breast cancer mortality. Few studies have compared cancer-specific mortality in women with breast cancer with or without SMI to reveal gaps in breast cancer treatment outcomes. We compared breast-cancer specific mortality in women with or without SMI and investigated effects of stage at presentation, comorbidity, and differences in cancer treatment. Women with their first breast cancer diagnosis in 1990-2013 (n = 80,671) were identified from the Finnish Cancer Registry, their preceding hospital admissions due to SMI (n = 4,837) from the Hospital Discharge Register and deaths from the Causes of Death Statistics. Competing risk models were used in statistical analysis. When controlling for age, year of cancer diagnosis, and comorbidity, breast cancer mortality was significantly elevated in patients with SMI. Relative mortality was highest in breast cancer patients with non-affective psychosis, partly explained by stage at presentation. Mortality was also significantly elevated in breast cancer patients with a substance use disorder and mood disorder. Patients with SMI received radiotherapy significantly less often than patients without SMI. Our findings emphasize the need to improve early detection of breast cancer in women with SMI and the collaboration between mental health care and oncological teams.

Arffman, M., Manderbacka, K., Suvisaari, J., et al. (2019). "The impact of severe mental illness on lung cancer mortality of patients with lung cancer in Finland in 1990-2013: a register-based cohort study." Eur J Cancer **118**: 105-111.
https://www.ejcancer.com/article/S0959-8049(19)30386-7/fulltext

BACKGROUND: Although the link between severe mental illness (SMI) and elevated cancer mortality is well established, few studies have examined lung cancer survival and SMI in detail. Our study compared cancer-specific mortality in patients with lung cancer with and without a history of SMI and analysed whether mortality differences could be explained by cancer stage at presentation, comorbidity or differences in cancer treatment. METHODS: We identified patients with their first lung cancer diagnosis in 1990-2013 from the Finnish Cancer Registry, their preceding hospital admissions due to SMI from the Hospital Discharge Register and deaths from the Causes of Death statistics. Competing risk analyses were used to estimate hazard ratios (HRs) for the impact of SMI on mortality.

RESULTS: Of the 37,852 lung cancer cases, 12% had a history of SMI. Cancer-specific mortality differences were found between patient groups in some cancer types after controlling for stage at representation and treatment. Men with a history of psychosis had excess mortality risk (HR = 1.24, 1.06-1.45) in squamous cell carcinoma. Similar excess risk was found among women with psychosis in small-cell carcinoma (HR = 1.76, 1.41-2.19) and in squamous cell carcinoma (HR = 1.67, 1.26-2.20) and among women with mood disorders in adenocarcinoma (HR = 1.37, 1.08-1.74). Patient group differences in HRs in five-year mortality did not markedly change from the 1990s. CONCLUSIONS: We found elevated cancer-specific mortality among persons with a history of SMI. Collaboration between patients, mental healthcare professionals and oncological teams is needed to reduce the mortality gap between patients with cancer with and without SMI.

Barak, Y., Levy, T., Achiron, A., et al. (2008). "Breast cancer in women suffering from serious mental illness." Schizophr Res **102**(1-3): 249-253.

BACKGROUND: Breast cancer is a major public health concern and the most common cause of cancer-related mortality among women. Compared with the general population, schizophrenia patients have been reported to have lower or similar rates of breast cancer despite several risk factors such as excess smoking, obesity and hyperprolactinemia. However, it has been argued that psychiatric morbidity itself may be the confounding factor that affects cancer incidence and not particularly schizophrenia. OBJECTIVE: To evaluate the frequency of breast cancer in a large cohort of female schizophrenia patients utilizing tertiary psychiatric care and to compare it with that of female inpatients with other serious mental illness (SMI). METHOD: Data were analyzed from a cohort of 2011 female schizophrenia patients and 6243 female SMI patients. All patient's records in the database were meshed with records of the Israeli National Cancer Registry to identify pathologically confirmed cancer co-morbidity. Cancer incidence rates among patients were compared with the expected incidence in age matched general population for the same time interval. RESULTS: Among 2011 female schizophrenia patients, 51 (2.5%) developed breast cancer vs. 83 (1.3%) breast cancer cases amongst SMI patients. The standardized incidence ratios (SIR) for breast cancer were low for both patient groups; 0.63 (95% CI, 0.47-0.83) and 0.54 (95% CI, 0.43-0.67) (schizophrenia and SMI respectively). CONCLUSIONS: The findings emphasize that reduced risk of breast cancer is found in a tertiary care cohort of female schizophrenia patients. Yet, breast and ovarian cancer screening for all women who are on long term drugs that induce weight gain or hyperprolactinemia should not be neglected. Our study emphasizes the probable contribution of environmental factors to the mechanisms responsible for this lower risk.

Barley, E., Borschmann, R., Walters, P., et al. (2013). "Interventions to encourage uptake of cancer screening for people with severe mental illness." Cochrane Database Syst Rev(7): Cd009641.

BACKGROUND: Adults with severe mental illness (i.e. schizophrenia or other related psychotic disorders and bipolar disorder) can be at greater risk of cancer than those without severe mental illness (SMI). Early detection of cancer through screening is effective in improving patient outcomes including death. However, people with SMI are less likely than others to take up available cancer screening. OBJECTIVES: To determine the effectiveness of interventions targeted at adults with SMI, or their carers or health professionals, and aimed at increasing the uptake of cancer screening tests for which the adults with SMI are eligible. SEARCH METHODS: We searched electronically the Cochrane Schizophrenia Group's Register (25th October 2012). SELECTION CRITERIA: All randomised controlled trials (RCTs) of interventions, targeted towards adults with SMI or their carers or health professionals, to encourage uptake of cancer screening tests for which the adults with SMI were eligible. DATA COLLECTION AND ANALYSIS: Two review authors independently screened titles and abstracts and assessed these against the inclusion criteria. MAIN RESULTS: We did not find any trials that met the inclusion criteria. AUTHORS' CONCLUSIONS: A comprehensive search showed that currently there is no RCT evidence for any method of encouraging cancer screening uptake in people with SMI. No specific approach can therefore be recommended. High-quality, large-scale RCTs are needed urgently to help address the disparity between people with SMI and others in cancer screening uptake.

Bellman, V., Russell, N., Depala, K., et al. (2021). "Challenges in Treating Cancer Patients With Unstable Psychiatric Disorder." World Journal of Oncology **12**(5): 137-148.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8577605/pdf/wjon-12-137.pdf

> In this review, we first present a case of chronic myeloid leukemia with acute psychosis, and then we will discuss the incidence of cancer in patients with psychotic disorders, the manifestations of new-onset psychosis, and the prevalence of preexisting psychosis in cancer patients, coupled with their impact on the treatment, diagnosis, and prognosis of cancer. This was a case that presented with acute psychosis and was found to have an elevated white blood cell count upon admission to an inpatient psychiatric unit. He was diagnosed with chronic myeloid leukemia and successfully managed with imatinib/dasatinib therapy. Psychiatrically, he was stabilized on two long-acting injectable medications to help maintain adherence. We were able to eliminate his active psychotic symptoms and return him to normal functioning in affect and thinking, achieving sustained compliance with treatment. We identified multiple inconsistencies in screening for cancer of all types in these patients, masking of signs and symptoms that would typically clue physicians to the presence of cancers, underreporting of symptoms, and disparate access to healthcare resources in patients with mental disorders when compared to the general population. Treatment of cancer in these patients as compared to the general population has also been shown to be incongruent, which will be elaborated upon. Psychiatric interventions, as well as supportive measures, for treating patients who are facing challenges during active cancer treatment will be discussed.

Binder, R. L. (1983). "Neurologically silent brain tumors in psychiatric hospital admissions: three cases and a review." J Clin Psychiatry **44**(3): 94-97.

> Three cases are described of patients with brain tumors who presented to a psychiatric hospital with disturbances in behavior or thinking. Neurologic signs and symptoms were absent or minimal in all cases, and psychiatric signs and symptoms were intermittent in two cases. The literature is reviewed and it is noted that tumors cannot be localized definitively by their psychiatric presentation. Further, patients with psychiatric symptoms secondary to brain tumors may respond to treatment with psychotropic medications. One of these cases is the fourth patient reported in the English language literature who meets the criteria for secondary mania due to a brain tumor.

Bisseling, E. M., Compen, F. R., Schellekens, M. P. J., et al. (2021). "Exploring Fear of Cancer Recurrence in a Sample of Heterogeneous Distressed Cancer Patients with and Without a Psychiatric Disorder." Journal of Clinical Psychology in Medical Settings **28**(3): 419-426.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8458175/pdf/10880_2021_Article_9776.pdf

> Fear of Cancer Recurrence (FCR) is a concern among cancer patients. Recent insights suggest that FCR should be viewed as a distinct syndrome. However, few studies have explored its overlap with psychiatric morbidity. We examined this overlap in a sample of distressed cancer patients. Self-referred patients (n = 245) were assessed with the Structured Clinical Interview for DSM-IV-TR Axis-I disorders and the Fear of Cancer Recurrence Inventory-Short Form. Proportions of patients with and without a psychiatric disorder meeting validated cut-offs for screening and clinically relevant FCR were compared. The prevalence of psychiatric disorders was 36%. Clinically relevant FCR was found in 198 patients (81%). Patients with a current psychiatric disorder reported clinically relevant FCR more frequently (89%) compared to those with no disorder (77%). Of patients reporting clinically relevant FCR, the majority (61%) did not additionally meet the criteria for a psychiatric disorder. These findings suggest that there should be particular attention for patients with elevated levels of FCR, warranting FCR-specific treatment. Trial registry number Clinicaltrials.gov NCT02138513

Borrull-Guardeno, J., Dominguez, A., Merizalde-Torres, M. H., et al. (2019). "Cervical Cancer Screening in Women With Severe Mental Disorders: An Approach to the Spanish Context." Cancer Nurs **42**(4): E31-e35.

> BACKGROUND: The incidence of invasive cervical cancer and its mortality have been reduced through primary and secondary prevention. Screening rates tend to be lower in vulnerable groups, such as people with severe mental disorders, who have a later detection of cancer and a higher mortality. The access of these women to cervical cancer screening is uncertain in our context. OBJECTIVE: The aim of this study was to determine the cervical cancer screening rates in women with severe mental disorders. METHODS: This was a descriptive cross-sectional study. Women 25 to 65 years old who

were admitted during 2016 to the psychiatric unit of a public hospital in Spain were included in the study, and it was determined if they had had cervical cancer screening. RESULTS: A total of 103 eligible women, with a mean age of 45.6 years, were enrolled. Only 28 of the participants (27.2%) had had a cervical cancer screening done in the last 5 years. By age groups, statistically significant differences were found, with women between 35 and 44 years of age having higher rates of cervical cancer screening (41.9%) and the oldest, between 55 and 65 years of age, having the lowest (5%). CONCLUSIONS: Women with severe mental health disorders who were admitted to acute psychiatric care units had much lower cervical cancer screening rates compared with the general population. IMPLICATIONS FOR PRACTICE: Mental health nurses could be the optimum professionals to promote cancer primary and secondary prevention in women with mental disorders.

Branecka-Wozniak, D. et Cymbaluk-Ploska, A. (2021). "The influence of support and medical data on the level of illness acceptance, the way of coping with a stressful situation, and mental adjustment to the disease among cancer patients." European Review for Medical and Pharmacological Sciences **25**(18): 5584-5596.

OBJECTIVE: The aim of this study was to analyze the behavior of cancer patients. PATIENTS AND METHODS: This survey-based study involved 145 oncological patients and was conducted from July to November 2018. It was performed using an author's questionnaire and three standardized tools: the mini-Mental Adjustment to Cancer Scale, the Acceptance of Illness Scale, and the Coping Inventory for Stressful Situations. RESULTS: The acceptance of illness was at a medium level. Patients who had been ill for longer time periods coped with stress better ($p < 0.071$) and showed better mental adjustment ($p < 0.05$ for Positive Redefinition, and $p < 0.08$ for Fighting Spirit). Patients with benign tumors focused on emotions ($p < 0.001$) and avoidance ($p < 0.005$) and were preoccupied with anxiety ($p < 0.05$). Longer treatment time was associated with a higher ability to cope with stress ($p < 0.05$). Patients receiving support were characterized by Anxious Preoccupation attitude ($p < 0.1$), and those who had not got it by Fighting Spirit ($p < 01$). CONCLUSIONS: Cancer patients have problems coping with new circumstances. They need support and help to understand and accept their situation.

Callaway, C. A., Corveleyn, A. E., Barry, M. J., et al. (2021). "Lessons learned: Building a coalition to advance equity in cancer and mental health care." Psychooncology **30**(12): 2087-2091.
https://onlinelibrary.wiley.com/doi/10.1002/pon.5852

Catala-Lopez, F., Hutton, B., Driver, J. A., et al. (2017). "Cancer and central nervous system disorders: protocol for an umbrella review of systematic reviews and updated meta-analyses of observational studies." Syst Rev **6**(1): 69.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5379758/pdf/13643_2017_Article_466.pdf

BACKGROUND: The objective of this study will be to synthesize the epidemiological evidence and evaluate the validity of the associations between central nervous system disorders and the risk of developing or dying from cancer. METHODS/DESIGN: We will perform an umbrella review of systematic reviews and conduct updated meta-analyses of observational studies (cohort and case-control) investigating the association between central nervous system disorders and the risk of developing or dying from any cancer or specific types of cancer. Searches involving PubMed/MEDLINE, EMBASE, SCOPUS and Web of Science will be used to identify systematic reviews and meta-analyses of observational studies. In addition, online databases will be checked for observational studies published outside the time frames of previous reviews. Eligible central nervous system disorders will be Alzheimer's disease, anorexia nervosa, amyotrophic lateral sclerosis, autism spectrum disorders, bipolar disorder, depression, Down's syndrome, epilepsy, Huntington's disease, multiple sclerosis, Parkinson's disease and schizophrenia. The primary outcomes will be cancer incidence and cancer mortality in association with a central nervous system disorder. Secondary outcome measures will be site-specific cancer incidence and mortality, respectively. Two reviewers will independently screen references identified by the literature search, as well as potentially relevant full-text articles. Data will be abstracted, and study quality/risk of bias will be appraised by two reviewers independently. Conflicts at all levels of screening and abstraction will be resolved through discussion. Random-effects meta-analyses of primary observational studies will be conducted where appropriate. Parameters for exploring statistical heterogeneity are pre-specified. The World Cancer Research Fund (WCRF)/American Institute for Cancer Research (AICR) criteria and the Grading of Recommendations

Assessment, Development and Evaluation (GRADE) approach will be used for determining the quality of evidence for cancer outcomes. DISCUSSION: Our study will establish the extent of the epidemiological evidence underlying the associations between central nervous system disorders and cancer and will provide a rigorous and updated synthesis of a range of important site-specific cancer outcomes. SYSTEMATIC REVIEW REGISTRATION: PROSPERO CRD42016052762.

Catala-Lopez, F., Suarez-Pinilla, M., Suarez-Pinilla, P., et al. (2014). "Inverse and direct cancer comorbidity in people with central nervous system disorders: a meta-analysis of cancer incidence in 577,013 participants of 50 observational studies." Psychother Psychosom **83**(2): 89-105.
https://www.karger.com/Article/Abstract/356498

BACKGROUND: There is a lack of scientific consensus about cancer comorbidity in people with central nervous system (CNS) disorders. This study assesses the co-occurrence of cancers in patients with CNS disorders, including Alzheimer's disease (AD), amyotrophic lateral sclerosis (ALS), autism spectrum disorders, Down's syndrome (DS), Huntington's disease (HD), multiple sclerosis (MS), Parkinson's disease (PD) and schizophrenia (SCZ). METHOD: Comprehensive search in PubMed/MEDLINE, Scopus and ISI Web of Knowledge of the literature published before March 2013. We identified 51 relevant articles from 2,229 discrete references, 50 of which contained data suitable for quantitative synthesis (577,013 participants). Pooled effect sizes (ES) were calculated using multiple random-effects meta-analyses. Sources of heterogeneity and uncertainty were explored by means of subgroup and sensitivity analyses, respectively. RESULTS: The presence of CNS disorders was associated with a reduced co-occurrence of cancer (ES = 0.92; 95% confidence interval, CI: 0.87-0.98; I(2) = 94.5%). A consistently lower overall co-occurrence of cancer was detected in patients with neurodegenerative disorders (ES = 0.80; 95% CI: 0.75- 0.86; I(2) = 82.8%), and in those with AD (ES = 0.32; 95% CI: 0.22-0.46; I(2) = 0.0%), PD (ES = 0.83; 95% CI: 0.76-0.91; I(2) = 80.0%), MS (ES = 0.91; 95% CI: 0.87-0.95; I(2) = 30.3%) and HD (ES = 0.53; 95% CI: 0.42-0.67; I(2) = 56.4%). Patients with DS had a higher overall co-occurrence of cancer (ES = 1.46; 95% CI: 1.08-1.96; I(2) = 87.9%). No association was observed between cancer and ALS (ES = 0.97; 95% CI: 0.76-1.25; I(2) = 0.0%) or SCZ (ES = 0.98; 95% CI: 0.90-1.07; I(2) = 96.3%). Patients with PD, MS and SCZ showed (a) higher co-occurrence of some specific cancers (e.g. PD with melanoma, MS with brain cancers and SCZ with breast cancer), and (b) lower co-occurrence of other specific cancers (e.g. lung, prostate and colorectal cancers in PD; lung and prostate cancers in MS; and melanoma and prostate cancer in SCZ). CONCLUSION: Increased and decreased co-occurrence of cancer in patients with CNS disorders represents an opportunity to discover biological and non-biological connections between these complex disorders.

Céspedes, P., Sánchez-Martínez, V., Lera-Calatayud, G., et al. (2020). "Delay in the Diagnosis of Breast and Colorectal Cancer in People With Severe Mental Disorders." Cancer Nurs **43**(6): E356-e362.

BACKGROUND: People with severe mental disorders have a worse cancer prognosis, with higher mortality rates than the general population, and this could be partially attributed to a later detection. Breast cancer and colorectal cancer have mass population screenings in Spain, but the influence in early diagnosis is unknown in persons with severe mental disorders. OBJECTIVE: To compare the severity of breast and colorectal cancers at diagnosis in people with and without mental disorders. METHODS: This was an observational, retrospective, case-control study with 1:2 matching performed in Eastern Spain. Data were retrieved for analysis from electronic medical records. RESULTS: The study included 111 oncology patients (75 with breast cancer and 36 with colorectal cancer). Individuals with mental disorders had a significantly higher (P = .002) relative risk (odds ratio [OR], 3.93; 95% confidence interval [CI], 1.60-9.65) to be diagnosed with an advanced tumor stage (clinical stages IIIA, IIIB, IIIC, and IV), for both breast and colorectal cancers when analyzed separately. The variables associated with advanced cancer at the time of diagnosis were the presence of a previous mental disorder (OR, 4.67; 95% CI, 1.73-12.61) and older age (OR, 1.08; 95% CI, 1.02-1.14). CONCLUSIONS: Individuals with severe mental disorders showed a higher risk of being diagnosed with breast and colorectal cancers at advanced stages. IMPLICATIONS FOR PRACTICE: Cancer screening for earlier detection and intervention in people with severe mental disorders needs improvement. Mental health nurses, screening nurses, and oncology nurses could serve an essential role in increasing the screening adherence of this group of individuals.

Chang, T. S., Hou, S. J., Su, Y. C., et al. (2013). "Disparities in oral cancer survival among mentally ill patients." PLoS One **8**(8): e70883.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3737269/pdf/pone.0070883.pdf

BACKGROUND: Many studies have reported excess cancer mortality in patients with mental illness. However, scant studies evaluated the differences in cancer treatment and its impact on survival rates among mentally ill patients. Oral cancer is one of the ten most common cancers in the world. We investigated differences in treatment type and survival rates between oral cancer patients with mental illness and without mental illness. METHODS: Using the National Health Insurance (NHI) database, we compared the type of treatment and survival rates in 16687 oral cancer patients from 2002 to 2006. The utilization rate of surgery for oral cancer was compared between patients with mental illness and without mental illness using logistic regression. The Cox proportional hazards model was used for survival analysis. RESULTS: Oral cancer patients with mental disorder conferred a grave prognosis, compared with patients without mental illness (hazard ratios [HR] = 1.58; 95% confidence interval [CI] = 1.30-1.93; P<0.001). After adjusting for patients' characteristics and hospital characteristics, patients with mental illness were less likely to receive surgery with or without adjuvant therapy (odds ratio [OR] = 0.47; 95% CI = 0.34-0.65; P<0.001). In multivariate analysis, oral cancer patients with mental illness carried a 1.58-times risk of death (95% CI = 1.30-1.93; P<0.001). CONCLUSIONS: Oral cancer patients with mental illness were less likely to undergo surgery with or without adjuvant therapy than those without mental illness. Patients with mental illness have a poor prognosis compared to those without mental illness. To reduce disparities in physical health, public health strategies and welfare policies must continue to focus on this vulnerable group.

Chang, W. H. et Lai, A. G. "Cumulative burden of psychiatric disorders and self-harm across 26 adult cancers." Nature Medicine: 17.
https://www.nature.com/articles/s41591-022-01740-3.pdf

Cancer is a life-altering event causing considerable psychological distress. However, information on the total burden of psychiatric disorders across all common adult cancers and therapy exposures has remained scarce. Here, we estimated the risk of self-harm after incident psychiatric disorder diagnosis in patients with cancer and the risk of unnatural deaths after self-harm in 459,542 individuals. Depression was the most common psychiatric disorder in patients with cancer. Patients who received chemotherapy, radiotherapy and surgery had the highest cumulative burden of psychiatric disorders. Patients treated with alkylating agent chemotherapeutics had the highest burden of psychiatric disorders, whereas those treated with kinase inhibitors had the lowest burden. All mental illnesses were associated with an increased risk of subsequent self-harm, where the highest risk was observed within 12 months of the mental illness diagnosis. Patients who harmed themselves were 6.8 times more likely to die of unnatural causes of death compared with controls within 12 months of self-harm (hazard ratio (HR), 6.8; 95% confidence interval (CI), 4.3-10.7). The risk of unnatural death after 12 months was markedly lower (HR, 2.0; 95% CI, 1.5-2.7). We provide an extensive knowledge base to help inform collaborative cancer-psychiatric care initiatives by prioritizing patients who are most at risk. A large-scale population analysis quantifies the burden of mental illness and self-harm events in patients diagnosed with the most common adult cancers and highlights opportunities for advancing patient care.

Chen, P. M., Chen, S. C., Liu, C. J., et al. (2015). "The association between prostate cancer and mood disorders: a nationwide population-based study in Taiwan." Int Psychogeriatr **27**(3): 481-490.
https://www.cambridge.org/core/journals/international-psychogeriatrics/article/abs/association-between-prostate-cancer-and-mood-disorders-a-nationwide-populationbased-study-in-taiwan/46AAA5CDDD4A8394848901C336917684

BACKGROUND: This study identified possible risk factors for newly diagnosed mood disorders, including depressive and bipolar disorders, in prostate cancer patients. METHODS: From 2000 to 2006, two cohorts were evaluated on the occurrence of mood disorder diagnosis and treatment. For the first cohort, data of patients diagnosed with prostate cancer was obtained from the Taiwan National Health Insurance (NHI) Research Database. As the second cohort, a cancer-free comparison group was matched for age, comorbidities, geographic region, and socioeconomic status. RESULTS: Final analyses

involved 12,872 men with prostate cancer and 12,872 matched patients. Increased incidence of both depressive (IRR 1.52, 95% CI 1.30-1.79, P <0.001) and bipolar disorder (IRR 1.84, 95% CI 1.25-2.74, P = 0.001) was observed among patients diagnosed with prostate cancer. Multivariate matched regression models show that cerebrovascular disease (CVD) and radiotherapy treatment could be independent risk factors for developing subsequent depressive and bipolar disorders. CONCLUSION: We observed that the risk of developing newly diagnosed depressive and bipolar disorders is higher among Taiwanese prostate cancer patients. Clinicians should be aware of the possibility of increased depressive and bipolar disorders among prostate cancer patients in Taiwan. A prospective study is necessary to confirm these findings.

Chen, W.-Y., Huang, S.-J., Chang, C.-K., et al. (2021). "Excess mortality and risk factors for mortality among patients with severe mental disorders receiving home care case management." Nordic Journal of Psychiatry **75**(2): 109-117.
https://doi.org/10.1080/08039488.2020.1799431

AbstractAim Home care case management (CM) is the main intervention for patients with severe mental disorders (SMDs) requiring outreach care. This study investigated the long-term mortality outcome and associated risk factors in patients who received home care CM.Methods This nationwide study enrolled patients who received home care CM (n?=?10,255) between 1 January 1999 and 31 December 2010. Each patient was followed up from the baseline (when patients underwent home case CM for the first time during the study period) to the censor (i.e. mortality or the end of the study). We calculated the standardized mortality ratio (SMR) and presented by age and diagnosis. Multivariate regression was performed to assess independent risk factors for mortality.Results Among 10,255 patients who received home care CM, 1409 died during the study period; the overall SMR was 3.13. Specifically, patients with organic mental disorder had the highest SMR (4.98), followed by those with schizophrenia (3.89), major depression (2.98), and bipolar disorder (1.97). In the multivariate analysis, patients with organic mental disorder or dementia had the highest risk, whereas the mortality risk in patients with schizophrenia was comparable to that in patients with bipolar disorder or major depression. Deceased patients had a significantly higher proportion of acute or chronic physical illnesses, including cancer, chronic hepatic disease, pneumonia, diabetes mellitus, cardiovascular disease, and asthma.Conclusion This study presented the gap of mortality in patients with SMDs receiving home care CM in Taiwan. We highlight the need for effective strategies to improve medical care for this specified population.

Clifton, A., Burgess, C., Clement, S., et al. (2016). "Influences on uptake of cancer screening in mental health service users: a qualitative study." BMC Health Services Research **16**(1).
https://bmchealthservres.biomedcentral.com/track/pdf/10.1186/s12913-016-1505-4.pdf

Cooke, I. J., Patil, D., Bobrek, K., et al. (2021). "Longitudinal impact of bladder cancer diagnosis on common psychiatric disorders." Cancer Med **10**(23): 8412-8420.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8633250/pdf/CAM4-10-8412.pdf

Background The presence of psychiatric disorders in patients with cancer is associated with increased morbidity and poorer outcomes. We sought to determine the impact of a new bladder cancer diagnosis on the incidence of depression and anxiety. Methods We used a database of billing claims (MarketScan (R)) to identify patients newly diagnosed with bladder cancer between 2009 and 2018. Patients with preexisting psychiatric disorders or use of anxiolytics/antidepressants were excluded. We matched cases to patients without a bladder cancer or psychiatric diagnosis. Our primary outcome was a new diagnosis of depression, anxiety, or use of anxiolytics/antidepressants. Other exposures of interest included gender and treatment received. We used multivariable regression to estimate odds ratios for these exposures. Results We identified 65,846 cases with a new diagnosis of bladder cancer (31,367 privately insured; 34,479 Medicare-eligible). Compared to controls, bladder cancer patients were more likely to develop new-onset depression/anxiety at 6 months (privately insured: 6.9% vs. 3.4%, p < 0.001; Medicare-eligible: 5.7% vs. 3.4%, p < 0.001) and 36 months (privately insured: 19.2% vs. 13.5%, p < 0.001; Medicare-eligible: 19.3% vs. 16.0%, p < 0.001). Women (vs. men, privately insured: OR 1.65, 95%CI 1.53-1.78; Medicare-eligible: OR 1.63, 95%CI 1.50-1.76) and those receiving cystectomy and chemotherapy (vs. no treatment, privately insured: OR 4.94, 95%CI 4.13-5.90;

Medicare-eligible: OR 2.35, 95%CI 1.88-2.94) were more likely to develop significant depression/anxiety. Conclusion A new diagnosis of bladder cancer was associated with increased burden of significant depression/anxiety compared with matched controls. Women and patients receiving more radical treatments had higher rates of depression and anxiety.

Cunningham, R., Sarfati, D., Stanley, J., et al. (2015). "Cancer survival in the context of mental illness: a national cohort study." Gen Hosp Psychiatry **37**(6): 501-506.
https://www.sciencedirect.com/science/article/pii/S0163834315001401?via%3Dihub

OBJECTIVE: To explore the reasons for worse cancer survival in people with experience of mental illness, including differences by cancer type and psychiatric diagnosis. METHOD: New Zealand breast and colorectal cancer registrations (2006-2010) were linked to psychiatric hospitalization records for adults (18-64 years). Cancer-specific survival was compared for recent psychiatric service users and nonusers using Cox regression. The contributions of deprivation, comorbidity and stage at diagnosis were assessed for those with schizophrenia or bipolar affective disorder (Group A) and others using mental health services (Group B). RESULTS: Of 8762 and 4022 people with breast and colorectal cancer respectively, 440 (breast) and 190 (colorectal) had recent contact with psychiatric services. After adjusting for confounding, risk of death from breast cancer was increased for Group A [Hazard Ratio (HR) 2.55 (95% confidence interval 1.49-4.35)] and B [HR 1.62 (1.09-2.39)] and from colorectal cancer for Group A [HR 2.92 (1.75-4.87)]. Later stage at diagnosis contributed to survival differences for Group A, and comorbidity contributed for both groups. Fully adjusted HR estimates were breast: Group A 1.65 (0.96-2.84), B 1.41 (0.95-2.09); colorectal: Group A 1.89 (1.12-3.17), B 1.25 (0.89-1.75)]. CONCLUSIONS: The high burden of physical disease and delayed cancer diagnosis in those with psychotic disorders contributes to worse cancer survival in New Zealand psychiatric service users.

Etoh, T., Fujiwara, M., Yamada, Y., et al. (2021). "Cancer care for people with mental disorders: A qualitative survey among cancer care and psychiatric care professionals in Japan." Psychooncology **30**(12): 2060-2066.
https://onlinelibrary.wiley.com/doi/abs/10.1002/pon.5780

Abstract Objective It is widely assumed that there are multiple levels (from individual to policy level) of problems involving disparities in cancer care for people with mental disorders. However, few studies have comprehensively investigated issues as perceived by medical professionals. The purpose of the present study was to identify a wide range of issues in cancer care for people with mental disorders and offer corresponding solutions for both cancer care professionals and psychiatric care professionals. Methods We distributed open-ended questionnaires to 754 healthcare professionals in various medical facilities, including designated cancer hospitals, psychiatric hospitals, and other local healthcare/welfare facilities. Participants were asked to describe issues in cancer care for people with mental disorders. Results Of the 754 recruited professionals, 439 (58.2%) responded to the questionnaire. Sixty-one issues were extracted and categorized into 10 categories: patient factors; isolation and lack of support; obstacles to transport; socioeconomic factors; attitudes of psychiatric professionals; medical system of psychiatric hospitals; attitudes of cancer care professionals; medical system of designated cancer hospitals; regional cancer medical systems; and lack of coordination among multidisciplinary healthcare professionals. Forty-eight specific solutions were summarized into 12 goals. Conclusions The present study widely identified issues causing disparities in cancer care for patients with mental disorders. We found that the issues extended from the patient level to the public-policy level. Our findings suggest the need for a multidisciplinary approach that includes both cancer and psychiatric care professionals to address the gap in cancer care for people with mental disorders.

Flores, E. J., Neil, J. M., Tiersma, K. M., et al. (2021). "Feasibility and Acceptability of a Collaborative Lung Cancer Screening Educational Intervention Tailored for Individuals With Serious Mental Illness." J Am Coll Radiol **18**(12): 1624-1634.
https://www.jacr.org/article/S1546-1440(21)00575-5/pdf

PURPOSE: Individuals with serious mental illness (SMI) experience disparities in lung cancer mortality. Using a two-phase, mixed-methods approach, we developed a person-centered lung cancer screening (LCS) educational intervention (phase 1) for individuals with SMI (schizophrenia and bipolar disorder)

and evaluated acceptability, feasibility, and changes in attitudes toward LCS (phase 2). METHODS: Phase 1: We conducted three focus groups with mental health, primary care, and radiology clinicians and utilized rapid qualitative analysis to adapt the LCS intervention (LCS walk-through video and smoking cessation handouts) tailored for individuals with SMI. Phase 2: We enrolled LCS-eligible patients with SMI (n = 15) and assessed the feasibility (>50% enrollment; >75% completion) and acceptability (>75% overall satisfaction) of an LCS educational intervention delivered by a radiologist and a mental health clinician at a community mental health clinic. We explored changes in participant attitudes about lung cancer, LCS, and smoking before and after the intervention. RESULTS: Phase 1: Focus groups with primary care (n = 5), radiologists (n = 9), and mental health clinicians (n = 6) recommended person-centered language and adapting a video demonstrating the process of LCS to address concerns specific to SMI, including paranoia and concrete thinking. Phase 2: Fifty percent (15 of 30) of eligible patients enrolled in the LCS intervention, 100% (15 of 15) completed the intervention, and 93% (14 of 15) were satisfied with the intervention. Participants reported a significantly greater worry about developing lung cancer postintervention, but there were no other significant differences. CONCLUSIONS: Radiologists can partner with primary care and community mental health clinics to lead equity efforts in LCS among individuals with SMI.

Grassi, L., Caruso, R., Biancosino, B., et al. (2021). "Knowledge about risk factors for cancer and cancer risk behavior among patients with severe mental illness." Psychooncology **30**(12): 2077-2081. https://onlinelibrary.wiley.com/doi/pdfdirect/10.1002/pon.5822?download=true

OBJECTIVE: To examine knowledge about, perception of and current risk factors for cancer, among patients with severe mental illness (SMI) and to compare these variables with patients without SMI. METHODS: A series of patients affected by SMI (i.e., schizophrenia spectrum disorders, bipolar disorders and severe personality disorders) and a matched (gender, age) control group of primary care attenders were assessed, by using an ad hoc semi-structured interview and a short true/false 17-item questionnaire, about family history of cancer, cancer risk-related lifestyles, personal perception and knowledge of risk for cancer. RESULTS: Patients with SMI (n = 185, mainly schizophrenia spectrum disorders, 48%, and mood disorders, 33%) significantly differed from primary care attenders (n = 173) for: lower participation to occult stool blood screening test, Pap smear test and mammography; higher prevalence of current and past smoking habits; lower awareness towards their own physical symptoms and their perception of risks for cancer; lower physical exercise practicing; lower knowledge about risk factors for cancer (e.g. familiarity for cancer, smoke-habits, breast and uterine cancer). CONCLUSIONS: Patients suffering from SMI had higher at-risk behavior for cancer and showed fewer concerns and less knowledge about risk for cancer than primary care attendees. These findings can guide to implement screening for cancer (e.g., Pap test, blood) and to design evidence-based interventions to reduce cancer risk (e.g., educational and behavioral change for smoking cessation, dietary habits) among patients with SMI.

Grassi, L., Nanni, M. G., Caruso, R., et al. (2022). "A comparison of Dignity Therapy narratives among people with severe mental illness and people with cancer." Psychooncology **31**(4): 676-679. https://onlinelibrary.wiley.com/doi/pdfdirect/10.1002/pon.5913?download=true

OBJECTIVE: To examine Dignity Therapy (DT) narratives in patients with severe mental illness (SMI) and a control group of cancer patients. METHODS: 12 patients with SMI (schizophrenia, bipolar disorders, sever personality disorders) and 12 patients with non-advanced cancer individually participated to DT interviews. DT was tape-recorded, transcribed verbatim and shaped into a narrative through a preliminary editing process. A session was dedicated to the final editing process along with the participant, with a final written legacy (generativity document) provided to the participant. Interpretative Phenomenological Analysis was used to qualitatively analyze the generativity documents. RESULTS: Patients with SMI and patients with cancer presented similar main narrative categories relative to dignity, such as "Meaning making", "Resources", "Legacy", "Dignity"; in addition, inpatients with SMI "Stigma" and inpatients with cancer "Injustice" emerged as separate categories. Patients in both groups strongly appreciated DT as an opportunity to reflect on their life story and legacy. CONCLUSIONS: The study showed that DT is a valuable intervention for people with SMI, grounded in a practical, person-centered approach. All patients found DT as an opportunity to describe their past and present, highlighting changes in the way they relate to themselves and others.

These results can guide implementation of DT in mental health settings for people with SMI, as it is for people with cancer.

Grassi, L. et Riba, M. (2020). "Cancer and severe mental illness: Bi-directional problems and potential solutions." Psychooncology **29**(10): 1445-1451.
https://deepblue.lib.umich.edu/bitstream/handle/2027.42/163408/pon5534.pdf?sequence=2

OBJECTIVE: Given the reported increased rates of physical morbidity and higher mortality rates among people with severe mental illness (SMI) (schizophrenia and severe mood disorders), with a life expectancy shorter of 15-20 years with respect to the general population, the aim of this paper was to call attention to the problem of cancer in SMI. METHODS: We conducted a narrative review of the most significant papers published in the areas of cancer screening, incidence, mortality and palliative care in SMI. RESULTS: Data from the literature confirm disparities in screening (eg, mammography; pap-smear test; colorectal cancer screening) and prevention (eg, clinical breast examination; smoking cessation). The incidence of cancer was found to be variable with a portion of the studies reporting a higher prevalence while others a similar or a lower prevalence of cancer compared to the general population. A lower percentage of patients with SMI received proper cancer treatment resulting in survival after cancer diagnosis significantly worse than people without SMI. Likewise, end-of-life care has been shown to be lacking with poorer levels of physical, psychological and spiritual care. CONCLUSIONS: The problems of stigma and discrimination, poorer dignity, poorer health behavior, lack of integration in health-care services for people with SMI needs to be addressed and solved in cancer care. Psycho-oncology has a very specific and mandatory role in integrating the recommendation of the World Health Organization to improve the links between oncology and mental health settings for more specific psycho-oncology programs addressed for this vulnerable segment of the population.

Grassi, L. et Riba, M. B. (2021). "Disparities and inequalities in cancer care and outcomes in patients with severe mental illness: Call to action." Psychooncology **30**(12): 1997-2001.
https://onlinelibrary.wiley.com/doi/pdfdirect/10.1002/pon.5853?download=true

OBJECTIVES: People with severe mental illness (SMI) are at extreme risk of being stigmatized and to receive poor quality physical care. It has been demonstrated that they have higher morbidity and poorer prognosis of several medical diseases than the general population, with an at least 10-20-year reduction in life expectancy. METHODS: A special issue of Psycho-Oncology focusing on cancer care among patients affected by SMI was called by the Editorial Board of the journal, with the aim to explore cancer health disparities and inequalities among people with SMI, mortality from cancer, problems of communication between multidisciplinary oncology and psychiatric teams and need for more structured intervention (i.e., screening, prevention, treatment). RESULTS: Authors from eight countries contributed. The problem of stigma and barriers to cancer care provision for patients with SMI were studied (e.g., the complex nature of SMI and healthcare providers' misunderstanding of SMI). Key barriers were related to both patients, clinicians and institutional problems, such as fragmentation of care. A higher mortality from cancer and poor knowledge about cancer risk-factors was shown in patients with SMI. Models of intervention were also proposed. CONCLUSIONS: Several conclusions have been recommended by the authors, such as the need for guidelines and clinical procedures specific for cancer care in mental health settings; large-scale studies to address the disparities of care in people with SMI; a larger vision of psychosocial oncology as the facilitator of the liaison between oncology and psychiatry.

Grassi, L., Stivanello, E., Belvederi Murri, M., et al. (2021). "Mortality from cancer in people with severe mental disorders in Emilia Romagna Region, Italy." Psychooncology **30**(12): 2039-2051.
https://onlinelibrary.wiley.com/doi/pdfdirect/10.1002/pon.5805?download=true

OBJECTIVE: To examine cancer-related mortality in patients with severe mental disorders (SMI) in the Emilia Romagna (ER) Region, Northern Italy, during the period 2008-2017 and compare it with the regional population. METHODS: We used the ER Regional Mental Health Registry identifying all patients aged ≥18 years who had received an ICD-9CM system diagnosis of SMI (i.e., schizophrenia or other functional psychosis, mania, or bipolar affective disorders) during a 10-year period (2008-2017).

Information on deaths (date and causes of death) were retrieved through the Regional Cause of Death Registry. Comparisons were made with the deaths and cause of deaths of the regional population over the same period. RESULTS: Amongst 12,385 patients suffering from SMI (64.1% schizophrenia spectrum and 36.9% bipolar spectrum disorders), 24% (range 21%-29%) died of cancer. In comparison with the general regional population, the mortality for cancer was about 50% higher among patients with SMI, irrespective if affected by schizophrenia or bipolar disorders. As for the site-specific cancers, significant excesses were reported for stomach, central nervous system, respiratory, and pancreas cancer with a variability according to psychiatric diagnosis and gender. CONCLUSIONS: Patients suffering from SMI had higher mortality risk than the regional population with some differences according to cancer type, gender, and psychiatric diagnosis. Proper cancer preventive and treatment interventions, including more effective risk modification strategies (e.g., smoking cessation, dietary habits) and screening for cancer, should be part of the agenda of all mental health departments in conjunction with other health care organizations, including psycho-oncology.

Guan, A., Ma, V., Bakshi, A. C., et al. (2021). "The Importance of Patient-Centered Care in Colon Cancer Patients With Severe Mental Illness." Cureus **13**(7): e16386.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8362867/pdf/cureus-0013-00000016386.pdf

There is an abundance of literature that highlights the importance of patient-centered communication with cancer patients requiring surgical intervention. While the need for communication for patients requiring surgery is well understood, less attention is brought to patients with severe mental illnesses. More literature is needed to highlight the importance and application of patient-centered care for patients suffering from both severe mental illness and cancer requiring surgical intervention. It is unclear if poor communication between patients and cancer-care specialists is part of the reason for the underlying discrepancy. Efforts to reduce this discrepancy may be worth considering as a priority for health care systems. We present a case of a 63-year-old man with schizophrenia who received a late cancer diagnosis after a missed screening, resulting in an extensive surgical resection for colon cancer. We explore the possibility of careful communication between the treating physician, patient, and patient's caretakers potentially preventing the delay in his cancer diagnosis. Effective communication is especially important with mental health patients because of its effect on long-term physical and mental outcomes. We hope to further the discussion on how to better cater to this specific population of patients undergoing cancer surgery.

Guan, N. C., Termorshuizen, F., Laan, W., et al. (2013). "Cancer mortality in patients with psychiatric diagnoses: a higher hazard of cancer death does not lead to a higher cumulative risk of dying from cancer." Soc Psychiatry Psychiatr Epidemiol **48**(8): 1289-1295.
https://link.springer.com/article/10.1007/s00127-012-0612-8

PURPOSE: Both increased as well as decreased cancer mortality among psychiatric patients has been reported, but competing death causes were not included in the analyses. This study aims to investigate whether observed cancer mortality in patients with psychiatric disorders might be biased by competing death causes. METHOD: In this retrospective cohort study on data from the Psychiatric Case Register Middle Netherlands linked to the death register of Statistics Netherlands, the risk of cancer death among patients with schizophrenia (N = 4,590), bipolar disorder (N = 2,077), depression (N = 15,130) and their matched controls (N = 87,405) was analyzed using a competing risk model. RESULTS: Compared to controls, higher hazards of cancer death were found in patients with schizophrenia (HR = 1.61, 95 % CI 1.26-2.06), bipolar disorder (HR = 1.20, 95 % CI 0.81-1.79) and depression (HR = 1.26, 95 % CI 1.10-1.44). However, the HRs of death due to suicide and other death causes were more elevated. Consequently, among those who died, the 12-year cumulative risk of cancer death was significantly lower. CONCLUSIONS: Our analysis shows that, compared to the general population, psychiatric patients are at higher risk of dying from cancer, provided that they survive the much more elevated risks of suicide and other death causes.

Günther, M. P. et Schulze, J. B. (2021). "Mental disorders, length of hospitalization, and psychopharmacy-New approaches to identify barriers to psychological support for patients with cancer." **30**(10): 1773-1781.
https://onlinelibrary.wiley.com/doi/10.1002/pon.5743

BACKGROUND: Despite abundant evidence that emotional distress is frequent in cancer patients and associated with adverse health outcomes, distress screening rates and adequate referrals to psychological support programs among those in need are insufficient in many cancer centers. We therefore aimed to analyze patient- and treatment-related barriers to distress screening and referrals to psychological support as a mandatory component of best-practice cancer care. METHOD: In the present explorative study, latent class analysis was used to identify homogeneous subgroups among 4837 patients diagnosed with cancer between 2011 and 2019. RESULTS: Four subgroups were identified. Patients with a mental disorder and psychopharmacology were least probable to be screened for distress. Together with patients aged 65 or older and male patients, they were also less likely to receive psychological support. Patients hospitalized for 28 days or longer were most likely to be both screened and to receive psychological support. CONCLUSIONS: Clinicians and researchers are recommended not neglect patients with mental disorders and psychopharmacological treatment as well as male and elderly patients when screening for distress and providing access to psychological support.

Günther, M. P., Schulze, J. B., Kirchebner, J., et al. (2022). "Severe mental illness in cancer is associated with disparities in psycho-oncological support." Curr Probl Cancer **46**(3): 100849.
https://www.sciencedirect.com/science/article/pii/S0147027222000095?via%3Dihub

Patients with both cancer and a severe mental illness (SMI) have a higher risk of advanced stage cancer at diagnosis and poorer survival in comparison to individuals with cancer alone. The present study explores if similar disparities exist in terms of psycho-oncological support. Latent class analysis (LCA) was used to group 10,945 patients with any type of cancer, of which 72 (0.7%) had been diagnosed with a SMI (ICD10-codes F20-F22, F24, F25, F28-F31, F32.3, F33.3), and 1056 (9.6%) with another mental disorder. Subgrouping was based on presence of SMI, other mental illnesses, stage of cancer at its first detection, screening for distress and receipt of information on psycho-oncology, consultation with a psychotherapist and/or psychiatrist, prescription of different psychotropic medication, and use of a patient care attendant. Five subgroups were identified. Patients with SMI were most likely to suffer from further mental comorbidities, to be prescribed antipsychotics, antidepressants, or mood stabilizers, and be in need of a patient care attendant. In comparison to patients without SMI, the larger one of 2 subgroups of patients with SMI had a low probability to be screened for distress and informed about psycho-oncological support services. A smaller subgroup of patients with SMI was probable to be diagnosed with an advanced stage of cancer. In subgroups without patients with mental disorders, screening for distress and offering psycho-oncological support seemed to be economized unless benzodiazepines or opioids were prescribed. Contrary to published evidence, distress screening and offering psycho-oncological support is neglected in patients with SMI unless an advanced stage of cancer is being diagnosed.

Haskins, C. B., McDowell, B. D., Carnahan, R. M., et al. (2021). "Breast cancer endocrine therapy adherence in health professional shortage areas: Unique effects on patients with mental illness." Journal of Psychosomatic Research **140**: 110294.
https://www.sciencedirect.com/science/article/pii/S0022399920308564

Objective Evaluate whether breast cancer endocrine therapy adherence is affected by access to primary and mental health care, particularly among at-risk patients with mental illness. Methods The study included 21,892 SEER-Medicare women aged 68 or older with stage I-IV ER+ breast cancer, 2007 to 2013. Patient home counties during breast cancer diagnosis, if evaluated for HPSA care shortage status, were categorized as least, moderate, or highest shortage; unevaluated counties (no known shortage) were a fourth category. Endocrine therapy initiation and discontinuation were analyzed with Cox regression, and daily adherence with longitudinal linear regression. Results After multivariate adjustment, patients in high primary care shortage counties were less likely to initiate endocrine therapy, reference least shortage [HR 0.92 (95% CI 0.86–0.97)]. Unevaluated counties had more oncologists per capita, fewer residents below the federal poverty level, and higher incomes. Mental health shortages were not associated with outcomes, however subgroups living in unevaluated counties were less likely to discontinue: patients with bipolar and psychotic disorders [discontinuation HR 0.35 (95% CI 0.17–0.73)], substance use [HR 0.48 (95% CI 0.24–0.95)], anxiety disorders [HR 0.56 (95% CI 0.35–0.90)]. Conclusions Poor primary care access was associated with a lower likelihood of

initiating endocrine therapy but living in counties without established mental health shortages may reduce the harmful association between mental illness and incomplete treatment receipt. Patients with mental illness may be more equipped to complete cancer treatment if given better mental health care access, suggesting a need for care coordination between primary and mental health care.

Hendrie, H. C., Lindgren, D., Hay, D. P., et al. (2013). "Comorbidity profile and healthcare utilization in elderly patients with serious mental illnesses." Am J Geriatr Psychiatry **21**(12): 1267-1276.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3572246/pdf/nihms405315.pdf

OBJECTIVES: Patients with serious mental illness are living longer. Yet, there remain few studies that focus on healthcare utilization and its relationship with comorbidities in these elderly mentally ill patients. DESIGN: Comparative study. Information on demographics, comorbidities, and healthcare utilization was taken from an electronic medical record system. SETTING: Wishard Health Services senior care and community mental health clinics. PARTICIPANTS: Patients age 65 years and older-255 patients with serious mental illness (schizophrenia, major recurrent depression, and bipolar illness) attending a mental health clinic and a representative sample of 533 nondemented patients without serious mental illness attending primary care clinics. RESULTS: Patients having serious mental illness had significantly higher rates of medical emergency department visits ($p = 0.0027$) and significantly longer lengths of medical hospitalizations ($p < 0.0001$) than did the primary care control group. The frequency of medical comorbidities such as diabetes, coronary artery disease, congestive heart failure, chronic obstructive pulmonary disease, thyroid disease, and cancer was not significantly different between the groups. Hypertension was lower in the mentally ill group ($p < 0.0001$). Reported falls ($p < 0.0001$), diagnoses of substance abuse ($p = 0.02$), and alcoholism ($p = 0.0016$) were higher in the seriously mentally ill. The differences in healthcare utilization between the groups remained significant after adjusting for comorbidity levels, lifestyle factors, and attending primary care. CONCLUSIONS: Our findings of higher rates of emergency care, longer hospitalizations, and increased frequency of falls, substance abuse, and alcoholism suggest that seriously mentally ill older adults remain a vulnerable population requiring an integrated model of healthcare.

Henry, A. (2006). "[Joint decision making--a challenge. A psychiatric patient with end-stage cancer refuses antitumor treatment]." Wien Med Wochenschr **156**(9-10): 270-274.
https://link.springer.com/article/10.1007/s10354-006-0288-3

Decision making concerning patients with end stage cancer is a challenging process. Since quality of life is a very important issue for patients with short-term life expectancy, benefits of antitumor therapy and possible negative side effects have to be considered carefully. The patient's desires play a pivotal role in the final decision. Informed consent becomes even more difficult when the competence of a patient in choosing treatment is questionable. In this case report, a 60 year old female patient with exulcerating breast cancer, brain metastases and long-term untreated schizophrenia refuses antitumor treatment. How can the palliative care team make the best possible decision on her behalf? Medical, ethical and legal aspects are discussed.

Hippisley-Cox, J. et Coupland, C. (2021). "Predicting the risk of prostate cancer in asymptomatic men: a cohort study to develop and validate a novel algorithm." Br J Gen Pract **71**(706): e364-e371.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8087311/pdf/bjgpmay-2021-71-706-oa-e364.pdf

BACKGROUND: Diagnosis of prostate cancer at an early stage can potentially identify tumours when intervention may improve treatment options and survival. AIM: To develop and validate an equation to predict absolute risk of prostate cancer in asymptomatic men with prostate specific antigen (PSA) tests in primary care. DESIGN AND SETTING: Cohort study using data from English general practices, held in the QResearch database. METHOD: Routine data were collected from 1098 QResearch English general practices linked to mortality, hospital, and cancer records for model development. Two separate sets of practices were used for validation. In total, there were 844 455 men aged 25-84 years with PSA tests recorded who were free of prostate cancer at baseline in the derivation cohort; the validation cohorts comprised 292 084 and 316 583 men. The primary outcome was incident prostate cancer. Cox proportional hazards models were used to derive 10-year risk equations. Measures of performance were determined in both validation cohorts. RESULTS: There were 40 821 incident cases

of prostate cancer in the derivation cohort. The risk equation included PSA level, age, deprivation, ethnicity, smoking status, serious mental illness, diabetes, BMI, and family history of prostate cancer. The risk equation explained 70.4% (95% CI = 69.2 to 71.6) of the variation in time to diagnosis of prostate cancer (R (2)) (D statistic 3.15, 95% CI = 3.06 to 3.25; Harrell's C-index 0.917, 95% CI = 0.915 to 0.919). Two-step approach had higher sensitivity than a fixed PSA threshold at identifying prostate cancer cases (identifying 68.2% versus 43.9% of cases), high-grade cancers (49.2% versus 40.3%), and deaths (67.0% versus 31.5%). CONCLUSION: The risk equation provided valid measures of absolute risk and had higher sensitivity for incident prostate cancer, high-grade cancers, and prostate cancer mortality than a simple approach based on age and PSA threshold.

Ho, V. P., Steinhagen, E., Angell, K., et al. (2018). "Psychiatric disease in surgically treated colorectal cancer patients." J Surg Res **223**: 8-15.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5986280/pdf/nihms919384.pdf

BACKGROUND: Underlying psychiatric conditions may affect outcomes of surgical treatment for colorectal cancer (CRC) because of complex clinical presentation and treatment considerations. We hypothesized that patients with psychiatric illness (PSYCH) would have evidence of advanced disease at presentation, as manifested by higher rates of colorectal surgery performed in the presence of obstruction, perforation, and/or peritonitis (OPP-surgery). MATERIALS AND METHODS: Using data from the 2007-2011 National Inpatient Sample, we identified patients with a diagnosis of CRC undergoing colorectal surgery. In addition to somatic comorbid conditions flagged in the National Inpatient Sample, we used the Clinical Classification Software to identify patients with PSYCH, including schizophrenia, delirium/dementia, developmental disorders, alcohol/substance abuse, and other psychiatric conditions. Our study outcome was OPP-surgery. In addition to descriptive analysis, we conducted multivariable logistic regression analysis to analyze the independent association between each of the PSYCH conditions and OPP-surgery, after adjusting for patient demographics and somatic comorbidities. RESULTS: Our study population included 591,561 patients with CRC and undergoing colorectal cancer surgery, of whom 60.6% were aged 65 years or older, 49.4% were women, and 6.3% had five or more comorbid conditions. Then, 17.9% presented with PSYCH. The percent of patients undergoing OPP-surgery was 13.9% in the study population but was significantly higher for patients with schizophrenia (19.3%), delirium and dementia (18.5%), developmental disorders (19.7%), and alcohol/substance abuse (19.5%). In multivariable analysis, schizophrenia, delirium/dementia, and alcohol/substance abuse were each independently associated with increased rates of OPP-surgery. CONCLUSIONS: Patients with PSYCH may have obstacles in receiving optimal care for CRC. Those with PSYCH diagnoses had significantly higher rates of OPP-surgery. Additional evaluation is required to further characterize the clinical implications of advanced disease presentation for patients with PSYCH diagnoses and colorectal cancer.

Howard, L. M., Barley, E. A., Davies, E., et al. (2010). "Cancer diagnosis in people with severe mental illness: practical and ethical issues." Lancet Oncol **11**(8): 797-804.
https://www.thelancet.com/journals/lanonc/article/PIIS1470-2045(10)70085-1/fulltext

There has been increasing recognition of the high physical morbidity in patients with severe mental illness, but little has been written about cancer in these patients. Therefore, we review the published work on risk of cancer in patients with severe mental illness, treatment challenges, and ethical issues. Severe mental illness is associated with behaviours that predispose an individual to an increased risk of some cancers, including lung and breast cancer, although lower rates of other cancers are reported in this population. Severe mental illness is also associated with disparities in screening for cancer and with higher case-fatality rates. This higher rate is partly due to the specific challenges of treating these patients, including medical comorbidity, drug interactions, lack of capacity, and difficulties in coping with the treatment regimen as a result of psychiatric symptoms. To ensure that patients with severe mental illness receive effective treatment, inequalities in care need to be addressed by all health-care professionals involved, including those from mental health services and the surgical and oncology teams.

Hristov, S. (2013). "Cervical screening for women with severe mental illness." Aust Nurs Midwifery J **21**(3): 46.

Hwong, A. R. et Mangurian, C. (2017). "Improving Breast Cancer Screening and Care for Women With Severe Mental Illness." J Clin Oncol **35**(36): 3996-3998.

Hyer, J. M., Kelly, E. P., Paredes, A. Z., et al. (2021). "Mental illness is associated with increased risk of suicidal ideation among cancer surgical patients." Am J Surg **222**(1): 126-132.
https://www.americanjournalofsurgery.com/article/S0002-9610(20)30668-1/fulltext

BACKGROUND: Mental illness and depression can be associated with increased risk of suicidal ideation (SI). We sought to determine the association between mental illness and SI among cancer surgical patients. METHODS: Medicare beneficiaries who underwent resection of lung, esophageal, pancreatic, colon, or rectal cancer were analyzed. Patients were categorized as no mental illness, anxiety and/or depression disorders or bipolar/schizophrenic disorders. RESULTS: Among 211,092 Medicare beneficiaries who underwent surgery for cancer, the rate of suicidal ideation was 270/100,000 patients. Antecedent mental health diagnosis resulted in a marked increased SI. On multivariable analysis, patients with anxiety alone (OR 1.49, 95%CI 1.04-2.14), depression alone (OR 2.60, 95%CI 1.92-3.38), anxiety + depression (OR 4.50, 95%CI 3.48-5.86), and bipolar/schizophrenia (OR 7.30, 95%CI 5.27-10.30) had increased odds of SI. CONCLUSIONS: Roughly 1 in 370 Medicare beneficiaries with cancer who underwent a wide range of surgical procedures had SI. An antecedent mental health diagnosis was a strong risk factor for SI.

Irwin, K. E., Ko, N., Walsh, E. P., et al. (2022). "Developing a Virtual Equity Hub: Adapting the Tumor Board Model for Equity in Cancer Care." Oncologist.

We define cancer equity as all people having as the same opportunity for cancer prevention, treatment, and survivorship care. However, marginalized populations continue to experience avoidable and unjust disparities in cancer care, access to clinical trials, and cancer survival. Racial and ethnic minorities, and individuals with low socioeconomic status, Medicaid insurance, limited health literacy, disabilities, and mental health disorders are more likely to experience delays to cancer diagnosis and less likely to receive guideline-concordant cancer care. These disparities are impacted by the social determinants of health including structural discrimination, racism, poverty, and inequities in access to healthcare and clinical trials. There is an urgent need to develop and adapt evidence-based interventions in collaboration with community partners that have potential to address the social determinants of health and build capacity for cancer care for underserved populations. We established the Virtual Equity Hub by developing a collaborative network connecting a comprehensive cancer center, academic safety net hospital, and community health centers and affiliates. The Virtual Equity Hub utilizes a virtual tumor board, an evidence-based approach that increases access to multi-specialty cancer care and oncology subspecialty expertise. We adapted the tumor board model by engaging person-centered teams of multi-disciplinary specialists across health systems, addressing the social determinants of health, and applying community-based research principles with a focus on populations with poor cancer survival. The virtual tumor board included monthly videoconferences, case discussion, sharing of expertise, and a focus on addressing barriers to care and trial participation. Specifically, we piloted virtual tumor boards for breast oncology, neuro-oncology, and individuals with cancer and serious mental illness. The Virtual Equity Hub demonstrated promise at building capacity for clinicians to care for patients with complex needs and addressing barriers to care. Research is needed to measure the impact, reach, and sustainability of virtual equity models for patients with cancer.

Irwin, K. E., Park, E. R., Fields, L. E., et al. (2019). "Bridge: Person-Centered Collaborative Care for Patients with Serious Mental Illness and Cancer." Oncologist **24**(7): 901-910.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6656464/pdf/onco12828.pdf

BACKGROUND: Individuals with serious mental illness (SMI) experience increased cancer mortality due to inequities in cancer treatment. Psychiatric care at cancer diagnosis may improve care delivery, yet models for integrating psychiatry and cancer care are lacking. We assessed the feasibility and acceptability of a person-centered collaborative care trial for SMI and cancer. SUBJECTS, MATERIALS, AND METHODS: We developed the Bridge intervention for patients with SMI (schizophrenia, bipolar disorder, and severe major depression) and cancer. Bridge includes proactive identification of SMI,

person-centered care from a psychiatrist and case manager, and collaboration with oncology. We conducted a 12-week, single-group trial in patients with SMI and a new breast, gastrointestinal, lung, or head/neck cancer. We assessed the feasibility of patient identification, enrollment and study completion; evaluated acceptability and perceived benefit with exit interviews with patients, caregivers, and oncology clinicians; and examined change in psychiatric symptoms with the Brief Psychiatric Rating Scale (BPRS). RESULTS: From November 2015 to April 2016, 30/33 eligible patients (90.9%) enrolled, and 25/29 (86.2%) completed assessments at all timepoints, meeting feasibility criteria. Of 24 patients, 23 (95.8%) found meeting with the psychiatrist helpful; 16/19 caregivers (84.2%) shared that Bridge addressed key caregiving challenges. Oncology clinicians evaluated Bridge as "very" or "most" useful for 94.3% of patients. Exit interviews with all participant groups suggested that Bridge fostered patient-clinician trust, increased access to psychiatric treatment, and enabled patients to initiate and complete cancer treatment. Psychiatric symptoms on the BPRS improved from baseline to 12 weeks. CONCLUSION: Bridge is a feasible and acceptable care delivery model for patients with SMI, their caregivers, and oncology clinicians. Randomized trials are warranted to assess the efficacy of improving cancer outcomes in this underserved population. IMPLICATIONS FOR PRACTICE: Serious mental illness affects 13 million U.S. adults who experience increased cancer mortality. To improve outcomes, new models of integrated oncology and mental health care are urgently needed. This study found that it was feasible to identify, enroll, and retain patients with serious mental illness and a new cancer in a trial of integrated mental health and cancer care (Bridge). Patients, caregivers, and oncologists reported that Bridge facilitated the initiation and completion of cancer care. Randomized trials are warranted to investigate the impact on cancer outcomes. Trial procedures may inform consent, engagement, and trial retention for patients with mental illness.

James, M., Thomas, M., Frolov, L., et al. (2017). "Rates of Cervical Cancer Screening Among Women With Severe Mental Illness in the Public Health System." Psychiatr Serv **68**(8): 839-842.

OBJECTIVE: This study aimed to determine cervical cancer screening rates among women with severe mental illness. METHODS: California Medicaid administrative records (2010-2011) for 31,308 women with severe mental illness were examined. Participants received specialty mental health services and were not dually eligible for Medicare. Poisson models assessed association between selected predictors and cervical cancer screening. RESULTS: Overall, 20.2% of women with severe mental illness received cervical cancer screening during the one-year period. Compared with white women, Asian women (adjusted risk ratio [ARR]=1.23), black women (ARR=1.10), and Hispanic women (ARR=1.11) (p<.001) were more likely to have been screened. Women ages 28-37 were more likely than those ages 18-27 to have been screened (ARR=1.31, p<.001). Evidence of other health care use was the strongest predictor of screening (ARR=3.07, p<.001). CONCLUSIONS: Most women in the sample were not regularly screened for cervical cancer. Cervical cancer screening for this high-risk population should be prioritized.

Jayatilleke, N., Hayes, R. D., Dutta, R., et al. (2017). "Contributions of specific causes of death to lost life expectancy in severe mental illness." Eur Psychiatry **43**: 109-115.
https://www.cambridge.org/core/journals/european-psychiatry/article/abs/contributions-of-specific-causes-of-death-to-lost-life-expectancy-in-severe-mental-illness/6F34D51FBDD63ADA3BC32E512B941ABE

The life expectancy gap between people with severe mental illness (SMI) and the general population persists and may even be widening. This study aimed to estimate contributions of specific causes of death to the gap. Age of death and primary cause of death were used to estimate life expectancy at birth for people with SMI from a large mental healthcare case register during 2007-2012. Using data for England and Wales in 2010, death rates in the SMI cohort for each primary cause of death category were replaced with gender- and age-specific norms for that cause. Life expectancy in SMI was then re-calculated and, thus, the contribution of that specific cause of death estimated. Natural causes accounted for 79.2% of lost life-years in women with SMI and 78.6% in men. Deaths from circulatory disorders accounted for more life-years lost in women than men (22.0% versus 17.4%, respectively), as did deaths from cancer (8.1% versus 0%), but the contribution from respiratory disorders was lower in women than men (13.7% versus 16.5%). For women, cancer contributed more in those with non-affective than affective disorders, while suicide, respiratory and digestive disorders contributed more in those with affective disorders. In men, respiratory disorders contributed more in non-affective

disorders. Other contributions were similar between gender and affective/non-affective groups. Loss of life expectancy in people with SMI is accounted for by a broad range of causes of death, varying by gender and diagnosis. Interventions focused on multiple rather than individual causes of death should be prioritised accordingly.

Ji, X., Cummings, J. R., Gilleland Marchak, J., et al. (2020). "Mental health among nonelderly adult cancer survivors: A national estimate." Cancer **126**(16): 3768-3776.
https://acsjournals.onlinelibrary.wiley.com/doi/pdfdirect/10.1002/cncr.32988?download=true

BACKGROUND: This study assessed mental health (MH) outcomes across age groups in a nationally representative US sample of adult cancer survivors. METHODS: The 2015 to 2017 National Survey on Drug Use and Health was used to identify respondents aged 18 to 64 years. The authors compared MH outcomes between respondents with a cancer history and respondents without a cancer history in adjusted analyses controlling for demographics and socioeconomic status. Outcomes included past-year major depressive episodes, serious psychological distress, suicidal thoughts, suicidal plans, suicidal attempts, any mental illness, and serious mental illness. All analyses were stratified by age group (18-34, 35-49, or 50-64 years). RESULTS: In a comparison of 2656 survivors and 112,952 individuals without cancer, within each age group, survivors had an elevated prevalence of MH problems in 5 of the 7 outcome measures. Among young adults (aged 18-34 years), survivors were more likely than noncancer counterparts to experience major depressive episodes (18.1% vs 9.6%), serious psychological distress (34.2% vs 17.9%), suicidal thoughts (10.5% vs 7.0%), any mental illness (41.1% vs 23.3%), and serious mental illness (13.2% vs 5.9%) in the past year (P values <.05). These differences persisted in adjusted analyses (P values <.01). Similar survivor-comparison differences were observed among older groups but with a smaller magnitude. Among survivors, young adult survivors had the highest likelihood of experiencing MH problems across all outcomes (P values <.05). CONCLUSIONS: This population-based study shows an elevated prevalence of MH problems among adult cancer survivors in comparison with the general population. This finding highlights the importance of developing strategies to ensure the early detection of mental illness and to improve access to MH treatment for cancer survivors.

Kashyap, M., Harris, J. P., Chang, D. T., et al. (2021). "Impact of mental illness on end-of-life emergency department use in elderly patients with gastrointestinal malignancies." Cancer Med **10**(6): 2035-2044.
https://escholarship.org/content/qt09z35745/qt09z35745.pdf?t=r29h73

BACKGROUND: Elderly patients with gastrointestinal cancer and mental illness have significant comorbidities that can impact the quality of their care. We investigated the relationship between mental illness and frequent emergency department (ED) use in the last month of life, an indicator for poor end-of-life care quality, among elderly patients with gastrointestinal cancers. METHODS: We used SEER-Medicare data to identify decedents with gastrointestinal cancers who were diagnosed between 2004 and 2013 and were at least 66 years old at time of diagnosis (median age: 80 years, range: 66-117 years). We evaluated the association between having a diagnosis of depression, bipolar disorders, psychotic disorders, anxiety, dementia, and/or substance use disorders and ED use in the last 30 days of life using logistic regression models. RESULTS: Of 160,367 patients included, 54,661 (34.1%) had a mental illness diagnosis between one year prior to cancer diagnosis and death. Patients with mental illness were more likely to have > 1 ED visit in the last 30 days of life (15.6% vs. 13.3%, $p < 0.01$). ED use was highest among patients with substance use (17.7%), bipolar (16.5%), and anxiety disorders (16.4%). Patients with mental illness who were male, younger, non-white, residing in lower income areas, and with higher comorbidity were more likely to have multiple end-of-life ED visits. Patients who received outpatient treatment from a mental health professional were less likely to have multiple end-of-life ED visits (adjusted odds ratio 0.82, 95% confidence interval 0.78-0.87). CONCLUSIONS: In elderly patients with gastrointestinal cancers, mental illness is associated with having multiple end-of-life ED visits. Increasing access to mental health services may improve quality of end-of-life care in this vulnerable population.

Kesebir, S., Koc, M. I. et Yosmaoglu, A. (2020). "Bipolar Spectrum Disorder May Be Associated With Family History of Diseases." J Clin Med Res **12**(4): 251-254.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7188371/pdf/jocmr-12-251.pdf

BACKGROUND: This study aims at investigating into the presence of family history of diabetes, ischemic heart disease, thyroid disease, cancer, cerebrovascular disease, and epilepsy in bipolar patients. METHODS: Totally 1,148 patients admitted to our outpatient unit between January 2018 and January 2020, who were diagnosed with bipolar disorder according to Diagnostic and Statistical Manual of Mental Disorders, fifth edition (DSM-V), from whom informed consent was obtained, were cross-sectionally and consecutively evaluated. Each patient was questioned regarding a family history of diabetes, ischemic heart disease, thyroid disease, cancer (gastrointestinal, breast and prostate cancer, leukemia, and lymphoma), cerebrovascular disease and epilepsy in first- and second-degree relatives. RESULTS: Diabetes, ischemic heart disease, cancer, cerebrovascular disease and epilepsy were more common in the family histories than in bipolar patients. A strong correlation was found between family history positive for epilepsy and bipolar disorder with psychotic symptoms. Also, a correlation was found between family history for diabetes and seasonal course and family history positive for thyroid disease and comorbid anxiety disorder. CONCLUSIONS: This study is the first to investigate into the frequency of physical diseases in the family histories of bipolar patients. Current therapies target the association between common leading pathways and symptoms whereas it is the association between stress and neural circuits that underlie the pathophysiology that should be targeted.

Kisely, S. et Siskind, D. (2021). "Excess mortality from cancer in people with mental illness-Out of sight and out of mind." Acta Psychiatr Scand **144**(4): 315-317.
https://onlinelibrary.wiley.com/doi/pdfdirect/10.1111/acps.13363?download=true

Lamontagne-Godwin, F., Burgess, C., Clement, S., et al. (2018). "Interventions to increase access to or uptake of physical health screening in people with severe mental illness: a realist review." BMJ Open **8**(2): e019412.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5829934/pdf/bmjopen-2017-019412.pdf

OBJECTIVES: To identify and evaluate interventions aimed at increasing uptake of, or access to, physical health screening by adults with severe mental illness; to examine why interventions might work. DESIGN: Realist review. SETTING: Primary, secondary and tertiary care. RESULTS: A systematic search identified 1448 studies, of which 22 met the inclusion criteria. Studies were from Australia (n=3), Canada (n=1), Hong Kong (n=1), UK (n=11) and USA (n=6). The studies focused on breast cancer screening, infection preventive services and metabolic syndrome (MS) screening by targeting MS-related risk factors. The interventions could be divided into those focusing on (1) health service delivery changes (12 studies), using quality improvement, randomised controlled trial, cluster randomised feasibility trial, retrospective audit, cross-sectional study and satisfaction survey designs and (2) tests of tools designed to facilitate screening (10 studies) using consecutive case series, quality improvement, retrospective evaluation and pre-post audit study designs. All studies reported improved uptake of screening, or that patients had received screening they would not have had without the intervention. No estimation of overall effect size was possible due to heterogeneity in study design and quality. The following factors may contribute to intervention success: staff and stakeholder involvement in screening, staff flexibility when taking physical measurements (eg, using adapted equipment), strong links with primary care and having a pharmacist on the ward. CONCLUSIONS: A range of interventions may be effective, but better quality research is needed to determine any effect size. Researchers should consider how interventions may work when designing and testing them in order to target better the specific needs of this population in the most appropriate setting. Behaviour-change interventions to reduce identified barriers of patient and health professional resistance to screening this population are required. Resource constraints, clarity over professional roles and better coordination with primary care need to be addressed.

Lawrence, W. R., Kuliszewski, M. G., Hosler, A. S., et al. (2021). "Association between preexisting mental illnesses and mortality among medicaid-insured women diagnosed with breast cancer." Soc Sci Med **270**: 113643.

BACKGROUND: We investigated the impact of preexisting mental illnesses on all-cause and cause-specific mortality among Medicaid-insured women diagnosed with breast cancer. METHODS: Data from the New York State Cancer Registry for 10,444 women diagnosed with breast cancer from 2004

to 2016 and aged <65 years at diagnosis were linked with Medicaid claims. Women were categorized as having depression or a severe mental illness (SMI) if they had at least three relevant diagnosis claims with at least one claim within three years prior to breast cancer diagnosis. SMI included schizophrenia, bipolar disorder, and other psychotic disorders. Estimated menopausal status was determined by age (premenopausal age <50; postmenopausal age ≥50). Hazard ratios (HR) and 95% confidence intervals (95%CI) were calculated with Cox proportional hazards regression, adjusting for potential confounders. RESULTS: Preexisting SMI was associated with greater all-cause (HR = 1.36; 95%CI 1.18, 1.57) and cancer-specific (HR = 1.21; 95%CI 1.03, 1.44) mortality compared to those with no mental illnesses. No association was observed between preexisting depression and mortality. Among racial/ethnic subgroups, the association between SMI and all-cause mortality was observed among non-Hispanic white (HR = 1.47; 95%CI 1.19, 1.83) and non-Hispanic Asian/Pacific Islander (HR = 2.59; 95% 1.15, 5.87) women. Additionally, mortality hazards were greatest among women with preexisting SMI that were postmenopausal (HR = 1.49; 95%CI 1.25, 1.78), obese (HR = 1.58; 95%CI 1.26, 1.98), and had documented tobacco use (HR = 1.42; 95%CI 1.13, 1.78). CONCLUSION: Women with preexisting SMI prior to breast cancer diagnosis have an elevated mortality hazard and should be monitored and treated by a coordinated cross-functional clinical team.

Leahy, D., Donnelly, A., Irwin, K., et al. (2021). "Barriers and facilitators to accessing cancer care for people with significant mental health difficulties: A qualitative review and narrative synthesis." Psychooncology **30**(12): 2012-2022.
https://onlinelibrary.wiley.com/doi/abs/10.1002/pon.5848

Abstract Objectives Inequities in cancer care contribute to higher rates of cancer mortality for individuals with significant mental health difficulties (SMHD) compared to the general population. The aim of the current systematic review was to identify, appraise and synthesise qualitative evidence of patient and clinician/system barriers and facilitators to cancer screening and treatment for individuals with SMHD. Methods We conducted a systematic search across three electronic databases in May 2020 and we carried out a second search across five electronic databases in January 2021. A narrative synthesis was conducted across eligible studies. Results We identified the same six studies from both searches, with 133 individuals with SMHD and experiences of cancer care and 102 healthcare professionals. Key barriers to cancer care were related to patients' uncontrolled psychiatric symptoms and the adverse impact of their symptoms on engaging with cancer care; clinician barrier-attitudes included stigmatising attitudes from clinicians and other staff towards individuals with SMHD and systems barrier-fragmentation included the fragmentation of mental health and cancer care delivery. Key patient facilitators to accessing cancer care and completing cancer treatment included being connected with mental health services and controlled psychiatric symptoms. Stronger collaboration among healthcare professionals working across different sectors in addition to the development of a patient navigator role were identified as key facilitators to enhance patient care. Conclusions Innovative approaches are needed to decrease mental health stigma, foster collaboration across disciplines, and facilitate the integration of timely mental health and cancer care for individuals with SMHD to address the mortality gap.

Li, Z., Li, Y., Guo, L., et al. (2021). "Effectiveness of acceptance and commitment therapy for mental illness in cancer patients: A systematic review and meta-analysis of randomised controlled trials." International Journal of Clinical Practice **75**(6): e13982.
https://onlinelibrary.wiley.com/doi/abs/10.1111/ijcp.13982

Abstract Background Disease awareness is an important aspect of psychological adjustment in cancer patients; however, there is limited evidence that acceptance and commitment therapy (ACT) is recommended for the treatment of mental illness in cancer patients. Purpose To assess the effectiveness of ACT for cancer patients with mental illness. Methods Ten databases were searched for publications up to July 25, 2020, using combinations of search terms related to mental health, cancer, and randomised controlled trials (RCTs). Two researchers independently screened the literature, extracted data, and assessed the quality of the study. Results Seventeen RCTs (877 cancer patients) were mainly of low quality, compared with control group, ACT was associated with improved outcomes after treatment completion and at 1-3 months and at 3-6 months of follow-up for depression (Standardised mean difference [SMD] = −0.93, 95% CI, −1.36 to −0.51, P < .001), anxiety

(SMD = −1.22, 95% CI, −2.16 to −0.29, P = .01), quality of life (SMD = 0.85, 95% CI, 0.17 to 1.11, P = .01), psychological distress (SMD = −0.80, 95% CI, −1.24 to 0.35, P < .001), and stress (SMD = −0.54, 95% CI, −1.02 to −0.07, P = .03). After 6 months of follow-up, depression, anxiety, quality of life, and stress were still significant. ACT was associated with psychological flexibility and was not associated with a reduction in fear at treatment completion. However, psychological flexibility (1-3 months) decreased and fear (1-6 months) decreased, and the longer-term effect was still significant. Conclusion ACT can be an important component of future cancer care, as it may alleviate depression, anxiety, stress, and fear, and improve quality of life. However, further research is required to determine long-term treatment effects. High-quality RCTs are needed to more reliably estimate treatment effects.

Mahar, A. L., Kurdyak, P., Hanna, T. P., et al. (2020). "The effect of a severe psychiatric illness on colorectal cancer treatment and survival: A population-based retrospective cohort study." PLoS One **15**(7): e0235409. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7390537/pdf/pone.0235409.pdf

OBJECTIVES: To identify inequalities in cancer survival rates for patients with a history of severe psychiatric illness (SPI) compared to those with no history of mental illness and explore differences in the provision of recommended cancer treatment as a potential explanation. DESIGN: Population-based retrospective cohort study using linked cancer registry and administrative data at ICES. SETTING: The universal healthcare system in Ontario, Canada. PARTICIPANTS: Colorectal cancer (CRC) patients diagnosed between April 1st, 2007 and December 31st, 2012. SPI history (schizophrenia, schizoaffective disorders, other psychotic disorders, bipolar disorders or major depressive disorders) was determined using hospitalization, emergency department, and psychiatrist visit data and categorized as 'no history of mental illness, 'outpatient SPI history', and 'inpatient SPI history'. MAIN OUTCOME MEASURES: Cancer-specific survival, non-receipt of surgical resection, and non-receipt of adjuvant chemotherapy or radiation. RESULTS: 24,507 CRC patients were included; 482 (2.0%) had an outpatient SPI history and 258 (1.0%) had an inpatient SPI history. Individuals with an SPI history had significantly lower survival rates and were significantly less likely to receive guideline recommended treatment than CRC patients with no history of mental illness. The adjusted HR for cancer-specific death was 1.69 times higher for individuals with an inpatient SPI (95% CI 1.36-2.09) and 1.24 times higher for individuals with an outpatient SPI history (95% CI 1.04-1.48). Stage II and III CRC patients with an inpatient SPI history were 2.15 times less likely (95% CI 1.07-4.33) to receive potentially curative surgical resection and 2.07 times less likely (95% CI 1.72-2.50) to receive adjuvant radiation or chemotherapy. These findings were consistent across multiple sensitivity analyses. CONCLUSIONS: Individuals with an SPI history experience inequalities in colorectal cancer care and survival within a universal healthcare system. Increasing advocacy and the availability of resources to support individuals with an SPI within the cancer system are warranted to reduce the potential for unnecessary harm.

Mallet, J., Huillard, O., Goldwasser, F., et al. (2018). "Mental disorders associated with recent cancer diagnosis: Results from a nationally representative survey." Eur J Cancer **105**: 10-18. https://www.ejcancer.com/article/S0959-8049(18)31408-4/fulltext

BACKGROUND: Receiving a diagnosis of cancer may be associated with increased risk of mental disorders. Yet, in this context, no factor predicts the onset of a mental disorder besides the diagnosis of cancer itself. If patients with a history of mental disorder are at particular risk is unknown. METHODS: Data were derived from a large national sample of the US population. Face-to-face surveys were conducted on 36309 adults during 2012-2013 period. Data were used to examine the associations among the past-year prevalence of mental disorders (according to the Diagnostic and Statistical Manual of Mental Disorders-5), the treatment-seeking rates and a recent cancer diagnosis. Data were analysed according to the antecedents of mental disorder in participants and according the presence of a recent cancer diagnosis. RESULTS: Participants recently diagnosed with cancer (n = 1300) were significantly at higher risk to present suicide attempt (adjusted odds ratio [AOR] = 3.52; 95% confidence interval [CI] = 1.23-10.04), post-traumatic stress disorder (AOR = 2.25; 95% CI = 1.71-2.96), bipolar disorder (AOR = 2.22; 95% CI = 1.46-3.38) and drug use disorder (AOR = 1.64; 95% CI = 1.13-3.39). The prevalence of most of the mental disorders considered was significantly higher for participants with a history of mental disorder compared with participants without such a history. Conversely, a recent diagnosis of cancer was not associated with significant differences in the

incidence of mental disorders in participants with no history of mental disorder. CONCLUSIONS: Patients with a history of mental disorder receiving a cancer diagnosis are at high risk of relapse and should be closely monitored.

Manderbacka, K., Arffman, M., Lumme, S., et al. (2018). "The effect of history of severe mental illness on mortality in colorectal cancer cases: a register-based cohort study." Acta Oncol **57**(6): 759-764. https://www.tandfonline.com/doi/full/10.1080/0284186X.2018.1429649

BACKGROUND: While the link between mental illness and cancer survival is well established, few studies have focused on colorectal cancer. We examined outcomes of colorectal cancer among persons with a history of severe mental illness (SMI). MATERIAL AND METHODS: We identified patients with their first colorectal cancer diagnosis in 1990-2013 (n = 41,708) from the Finnish Cancer Registry, hospital admissions due to SMI preceding cancer diagnosis (n = 2382) from the Hospital Discharge Register and deaths from the Causes of Death statistics. Cox regression models were used to study the impact on SMI to mortality differences. RESULTS: We found excess colorectal cancer mortality among persons with a history of psychosis and with substance use disorder. When controlling for age, comorbidity, stage at presentation and treatment, excess mortality risk among men with a history of psychosis was 1.72 (1.46-2.04) and women 1.37 (1.20-1.57). Among men with substance use disorder, the excess risk was 1.22 (1.09-1.37). CONCLUSION: Understanding factors contributing to excess mortality among persons with a history of psychosis or substance use requires more detailed clinical studies and studies of care processes among these vulnerable patient groups. Collaboration between patients, mental health care and oncological teams is needed to improve outcomes of care.

Martin, J. L., McLean, G., Park, J., et al. (2014). "Impact of socioeconomic deprivation on rate and cause of death in severe mental illness." BMC Psychiatry **14**: 261. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4173101/pdf/12888_2014_Article_261.pdf

BACKGROUND: Socioeconomic status has important associations with disease-specific mortality in the general population. Although individuals with Severe Mental Illnesses (SMI) experience significant premature mortality, the relationship between socioeconomic status and mortality in this group remains under investigated. We aimed to assess the impact of socioeconomic status on rate and cause of death in individuals with SMI (schizophrenia and bipolar disorder) relative to the local (Glasgow) and wider (Scottish) populations. METHODS: Cause and age of death during 2006-2010 inclusive for individuals with schizophrenia or bipolar disorder registered on the Glasgow Psychosis Clinical Information System (PsyCIS) were obtained by linkage to the Scottish General Register Office (GRO). Rate and cause of death by socioeconomic status, measured by Scottish Index of Multiple Deprivation (SIMD), were compared to the Glasgow and Scottish populations. RESULTS: Death rates were higher in people with SMI across all socioeconomic quintiles compared to the Glasgow and Scottish populations, and persisted when suicide was excluded. Differences were largest in the most deprived quintile (794.6 per 10,000 population vs. 274.7 and 252.4 for Glasgow and Scotland respectively). Cause of death varied by socioeconomic status. For those living in the most deprived quintile, higher drug-related deaths occurred in those with SMI compared to local Glasgow and wider Scottish population rates (12.3% vs. 5.9%, p = <0.001 and 5.1% p = 0.002 respectively). A lower proportion of deaths due to cancer in those with SMI living in the most deprived quintile were also observed, relative to the local Glasgow and wider Scottish populations (12.3% vs. 25.1% p = 0.013 and 26.3% p = <0.001). The proportion of suicides was significantly higher in those with SMI living in the more affluent quintiles relative to Glasgow and Scotland (54.6% vs. 5.8%, p = <0.001 and 5.5%, p = <0.001). CONCLUSIONS: Excess mortality in those with SMI occurred across all socioeconomic quintiles compared to the Glasgow and Scottish populations but was most marked in the most deprived quintiles when suicide was excluded as a cause of death. Further work assessing the impact of socioeconomic status on specific causes of premature mortality in SMI is needed.

McFarland, D. C., Voigt, L. et Alici, Y. (2021). "Decisional capacity determination and serious mental illness in oncology: Implications for equitable and beneficent care." Psychooncology **30**(12): 2052-2059. https://onlinelibrary.wiley.com/doi/10.1002/pon.5812

BACKGROUND: Patients with Serious Mental Illness (SMI) have worse survival compared to cancer patients without SMI after controlling for delayed diagnosis. Decision-making capacity (DMC) may be impaired in both populations (cancer or SMI). DMC may be further impaired based on coupled vulnerability factors that challenge Shared Decision Making (SDM) for patients with cancer and SMI. METHODS: Psychiatric consultations for DMC in hospitalized patients with cancer (n = 97) were consecutively evaluated across a single institution cancer center. SMI data, demographic, and cancer-related variables were obtained from the medical record. Descriptive data were contrasted in patients with and without DMC and used for logistic regression modeling. RESULTS: Overall, 42% had DMC with no significant differences based on SMI ($\chi(2) = 2.60$, $p = 0.11$). Patients with SMI were younger, receiving anticancer treatment, and were less likely facing end of life issues. Age (OR 1.03, $p = 0.05$) and no recent anticancer treatments (OR 0.34, $p = 0.02$) were associated with decisional incapacity. At 3 months post discharge, almost two-thirds were dead with no difference based on SMI ($\chi(2) = 0.01$, $p = 0.91$). But End of Life (EOL) concerns were documented in 63% of non-SMI patients and only 36% of SMI patients ($\chi(2) = 5.63$, $p = 0.02$). Healthcare proxy (16%), four determinates of DMC (22%), and repeated psychiatric DCM assessments (35%) were documented with no differences based on SMI. CONCLUSION: SDM is not equitable for cancer patients with SMI. Advanced directives and a robust effort to provide value-congruent care for patient with SMI who develop cancer may lessen this health inequity for cancer patients with SMI.

McGinty, E. E., Zhang, Y., Guallar, E., et al. (2012). "Cancer incidence in a sample of Maryland residents with serious mental illness." Psychiatr Serv **63**(7): 714-717.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3878874/pdf/nihms-518777.pdf

OBJECTIVE: Persons with serious mental illness have an increased mortality rate and a higher burden of many medical conditions compared with persons without serious mental illness. Cancer risk in the population with serious mental illness is uncertain, and its incidence was examined by race, sex, and cancer site in a community-based cohort of adults with schizophrenia or bipolar disorder. METHODS: The authors calculated standardized incidence ratios of total and site-specific cancers in a cohort of 3,317 Maryland Medicaid adult beneficiaries with schizophrenia or bipolar disorder followed from 1994 through 2004 for comparison with the U.S. population. RESULTS: Total cancer incidence for adults with schizophrenia or bipolar disorder was 2.6 times higher in the cohort. Elevated risk was greatest for cancer of the lung. No differences in risk were found for African-American versus white Medicaid beneficiaries with serious mental illness. CONCLUSIONS: These findings suggest that there is a heightened risk of cancer among adults with schizophrenia or bipolar disorder. Clinicians should promote appropriate cancer screening and work to reduce modifiable risk factors, such as smoking, among persons with serious mental illness.

Mo, P. K., Mak, W. W., Chong, E. S., et al. (2014). "The prevalence and factors for cancer screening behavior among people with severe mental illness in Hong Kong." PLoS One **9**(9): e107237.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4182090/pdf/pone.0107237.pdf

OBJECTIVES: Screening is useful in reducing cancer incidence and mortality. People with severe mental illness (PSMI) are vulnerable to cancer as they are exposed to higher levels of cancer risks. Little is known about PSMI's cancer screening behavior and associated factors. The present study examined the utilization of breast, cervical, prostate, and colorectal cancer screening among PSMI in Hong Kong and to identify factors associated with their screening behaviors. METHOD: 591 PSMI from community mental health services completed a cross-sectional survey. RESULTS: The percentage of cancer screening behavior among those who met the criteria for particular screening recommendation was as follows: 20.8% for mammography; 36.5% for clinical breast examination (CBE); 40.5% for pap-smear test; 12.8% for prostate examination; and 21.6% for colorectal cancer screening. Results from logistic regression analyses showed that marital status was a significant factor for mammography, CBE, and pap-smear test; belief that cancer can be healed if found early was a significant factor for pap-smear test and colorectal screening; belief that one can have cancer without having symptoms was a significant factor for CBE and pap-smear test; belief that one will have a higher risk if a family member has had cancer was a significant factor for CBE; and self-efficacy was a significant factor for CBE and pap-smear test behavior. CONCLUSIONS: Cancer screening utilization among PSMI in Hong Kong is low. Beliefs about cancer and self-efficacy are associated with cancer screening behavior. Health care

professionals should improve the knowledge and remove the misconceptions about cancer among PSMI; self-efficacy should also be promoted.

Momen, N. C., Plana-Ripoll, O., Agerbo, E., et al. (2020). "Association between Mental Disorders and Subsequent Medical Conditions." N Engl J Med **382**(18): 1721-1731.
https://www.nejm.org/doi/pdf/10.1056/NEJMoa1915784?articleTools=true

BACKGROUND: Persons with mental disorders are at a higher risk than the general population for the subsequent development of certain medical conditions. METHODS: We used a population-based cohort from Danish national registries that included data on more than 5.9 million persons born in Denmark from 1900 through 2015 and followed them from 2000 through 2016, for a total of 83.9 million person-years. We assessed 10 broad types of mental disorders and 9 broad categories of medical conditions (which encompassed 31 specific conditions). We used Cox regression models to calculate overall hazard ratios and time-dependent hazard ratios for pairs of mental disorders and medical conditions, after adjustment for age, sex, calendar time, and previous mental disorders. Absolute risks were estimated with the use of competing-risks survival analyses. RESULTS: A total of 698,874 of 5,940,299 persons (11.8%) were identified as having a mental disorder. The median age of the total population was 32.1 years at entry into the cohort and 48.7 years at the time of the last follow-up. Persons with a mental disorder had a higher risk than those without such disorders with respect to 76 of 90 pairs of mental disorders and medical conditions. The median hazard ratio for an association between a mental disorder and a medical condition was 1.37. The lowest hazard ratio was 0.82 for organic mental disorders and the broad category of cancer (95% confidence interval [CI], 0.80 to 0.84), and the highest was 3.62 for eating disorders and urogenital conditions (95% CI, 3.11 to 4.22). Several specific pairs showed a reduced risk (e.g., schizophrenia and musculoskeletal conditions). Risks varied according to the time since the diagnosis of a mental disorder. The absolute risk of a medical condition within 15 years after a mental disorder was diagnosed varied from 0.6% for a urogenital condition among persons with a developmental disorder to 54.1% for a circulatory disorder among those with an organic mental disorder. CONCLUSIONS: Most mental disorders were associated with an increased risk of a subsequent medical condition; hazard ratios ranged from 0.82 to 3.62 and varied according to the time since the diagnosis of the mental disorder. (Funded by the Danish National Research Foundation and others; COMO-GMC ClinicalTrials.gov number, NCT03847753.).

Murphy, K., Corveleyn, A., Park, E. R., et al. (2022). "Rewards, Challenges and Lessons Learned From Familial and Community Caregivers of Individuals With Serious Mental Illness and Cancer." Psychooncology **31**: 33-34.
<Go to ISI>://WOS:000765384800074

Murphy, K. A., Daumit, G. L., Bandara, S. N., et al. (2020). "Association Between the Maryland Medicaid Behavioral Health Home Program and Cancer Screening in People With Serious Mental Illness." Psychiatr Serv **71**(6): 608-611.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7266726/pdf/nihms-1558966.pdf

OBJECTIVE: This study evaluated the association of the Maryland Medicaid behavioral health home (BHH) integrated care program with cancer screening. METHODS: Using administrative claims data from October 2012 to September 2016, the authors measured cancer screening among 12,176 adults in Maryland's psychiatric rehabilitation program who were eligible for cervical (N=6,811), breast (N=1,658), and colorectal (N=3,430) cancer screening. Marginal structural modeling was used to examine the association between receipt of annual cancer screening and whether participants had ever enrolled in a BHH (enrolled: N=3,298, 27%; not enrolled: N=8,878, 73%). RESULTS: Relative to nonenrollment, BHH enrollment was associated with increased screening for cervical and breast cancer but not for colorectal cancer. Predicted annual rates remained low, even in BHHs. CONCLUSIONS: Despite estimates of improvements in cervical and breast cancer screening after BHH implementation, cancer screening rates remained suboptimal. Broader cancer screening interventions are needed to improve cancer screening for people with mental illness.

Murphy, K. A., Daumit, G. L., McGinty, E. E., et al. (2021). "Predictors of cancer screening among Black and White Maryland Medicaid enrollees with serious mental illness." Psychooncology **30**(12): 2092-2098.
https://onlinelibrary.wiley.com/doi/10.1002/pon.5815

BACKGROUND: Cancer is the second leading cause of death for people with serious mental illness (SMI), such as schizophrenia and bipolar disorder. People with SMI receive cancer screenings at lower rates than the general population. AIMS: We sought to identify factors associated with cancer screening in a publicly insured population with SMI and stratified by race, a factor itself linked with differential rates of cancer screening. MATERIALS AND METHODS: We used Maryland Medicaid administrative claims data (2010-2018) to examine screening rates for cervical cancer (N = 40,622), breast cancer (N = 9818), colorectal cancer (N = 19,306), and prostate cancer (N = 4887) among eligible Black and white enrollees with SMI. We examined individual-level socio-demographic and clinical factors, including co-occurring substance use disorder, medical comorbidities, psychiatric diagnosis, obstetric-gynecologic and primary care utilization, as well as county-level characteristics, including metropolitan status, mean household income, and primary care workforce capacity. Generalized estimating equations with a logit link were used to examine the characteristics associated with cancer screening. RESULTS: Compared with white enrollees, Black enrollees were more likely to receive screening for cervical cancer (AOR: 1.18; 95% CI: 1.15-1.22), breast cancer (AOR: 1.27; 95% CI: 1.19-1.36), and colorectal cancer (AOR: 1.07; 95% CI: 1.02-1.13), while similar rates were observed for prostate cancer screening (AOR: 1.06; 95% CI: 0.96-1.18). Primary care utilization and longer Medicaid enrollment were positively associated with cancer screening while co-occurring substance use disorder was negatively associated with cancer screening. CONCLUSION: Improving cancer screening rates among populations with SMI should focus on facilitating continuous insurance coverage and access to primary care.

Murphy, K. A., Stone, E. M., Presskreischer, R., et al. (2021). "Cancer Screening Among Adults With and Without Serious Mental Illness: A Mixed Methods Study." Med Care **59**(4): 327-333.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7952680/pdf/nihms-1655258.pdf

Background: Persons with serious mental illness (SMI) die 10–20 years earlier than the general population; cancer is the second leading cause of death. Differences in cancer screening between SMI and the general population are not well understood. Objectives: To describe receipt of cancer screening among individuals with versus without SMI and to explore clinicians' perceptions around cancer screening for people with SMI. Methods: Mixed-methods study using 2010–2017 MarketScan commercial insurance administrative claims data and semi-structured clinician interviews. In the quantitative analyses, we used multivariate logistic regression analyses to calculate the likelihood of receiving cervical, breast, colorectal, or prostate cancer screening among people with versus without SMI, defined as schizophrenia or bipolar disorder. We conducted semi-structured interviews with 17 primary care physicians and 15 psychiatrists. Interview transcripts were coded using a hybrid deductive/inductive approach. Results: Relative to those without SMI, individuals with SMI were less likely to receive screening for cervical cancer [adjusted odds ratio (aOR): 0.80; 95% confidence interval (CI): 0.80–0.81], breast cancer (aOR: 0.79; 95% CI: 0.78–0.80), colorectal cancer (aOR: 0.90; 95% CI: 0.89–0.91), and prostate cancer (aOR: 0.85; 95% CI: 0.84–0.87). Clinicians identified 5 themes that may help explain the lower rates of cancer screening in persons with SMI: access to care, available support, prioritization of other issues, communication, and patient concerns. Conclusions: People with SMI were less likely to receive 4 common types of cancer screening. Improving cancer screening rates in the SMI population will likely require a multidisciplinary approach to overcome barriers to screening.

Olive, J. K., Zhou, N., Mitchell, K. G., et al. (2022). "Impact of Psychiatric Comorbidities on Surgical Outcomes for Non-Small Cell Lung Cancer." The Annals of Thoracic Surgery **113**(3): 1008-1014.
https://www.sciencedirect.com/science/article/pii/S0003497521005579

Background Psychiatric comorbidities (PCs) have been associated with poor surgical outcomes in several malignancies. However, the impact of PCs on surgical outcomes for non-small cell lung cancer (NSCLC) remains largely unknown. Methods NSCLC patients who underwent pulmonary resection at a single institution between 2006 and 2017 were included. Presence of preoperative PCs was identified by documented diagnostic codes. Demographic, histopathologic, perioperative, and survival data were analyzed. Categorical variables were compared using the χ2 or Fisher exact test. Overall and disease-free survival was analyzed using Kaplan-Meier method. Univariable and multivariable logistic regression analyses were performed for 30-day readmission. Results Among 2907 patients, PCs were

present preoperatively in 180 (6%), including anxiety, 130 (72%); depression, 52 (29%); adjustment disorder, 28 (16%); alcohol abuse, 16 (9%); sleep disorder, 8 (4%); and schizophrenia, 3 (2%). Patients with PCs were younger, with fewer cardiovascular complications. There were no differences in length of stay. However, PCs led to increased 30-day readmission (12% vs 6%, P = .004). Reasons for readmission did not differ between groups (P = .679). Multivariable analysis showed PCs independently predicted 30-day readmission (odds ratio, 2.00; P = .005). Importantly, there were no differences in 30- or 90-day mortality (P = .495 and P = .748, respectively), overall survival (P = .439), or disease-free survival (P = .924). Conclusions NSCLC patients with and without PCs experienced similar perioperative and long-term outcomes, suggesting that individuals should not be denied surgical care on the basis of such comorbidities. However, further research should seek to identify reasons for increased risk of readmission for patients with PCs and validate these findings in other settings.

Olson, R., McLay, M., Hamm, J., et al. (2021). "Identification of Tobacco-Related Cancer Diagnoses among Individuals with Psychiatric Disorders: A Population-Based Matched Cohort Study Using a Competing Risks Approach from British Columbia." Current Oncology **28**(6): 4953-4960.
https://mdpi-res.com/d_attachment/curroncol/curroncol-28-00415/article_deploy/curroncol-28-00415-v2.pdf?version=1637815121

Background: Individuals with psychiatric disorders (PD) have a high prevalence of tobacco use. Therefore, we assessed the hazard of receiving a tobacco-related (TR) cancer diagnosis among individuals with PD. Methods: Several population-based provincial databases were used to identify individuals in BC diagnosed with depression, schizophrenia, bipolar disorder, anxiety disorders, or multiple PD between 1990 and 2013. A primary population proxy comparison group (appendicitis) was also identified and matched to the psychiatric cohort based on age at cohort entry, gender, year of cohort entry, and postal code. We linked individuals in the cohort and comparison groups with the BC Cancer Registry. Using a competing risks approach, we estimated the effect of having a PD on the risk of receiving a TR cancer diagnosis, in light of the competing risk of mortality. Results: In total, 165,289 patients were included. Individuals with depression (HR = 0.81; p < 0.01; 95% CI: 0.73-0.91), anxiety disorders (HR = 0.84; p = 0.02; 95% CI: 0.73-0.97), or multiple PD (HR = 0.74; p < 0.01; 95% CI: 0.66-0.83) had a statistically significant lower risk of a TR cancer diagnosis compared to the comparison group. Individuals with schizophrenia (HR = 0.86; p = 0.40; 95% CI: 0.62-1.21) or bipolar disorder (HR = 0.58; p = 0.12; 95% CI: 0.29-1.14), however, showed no evidence of a statistically significant difference from the comparison group. Interpretation: We found that individuals with depression, anxiety disorders, or multiple PD diagnoses had a significantly reduced risk of receiving a tobacco-related cancer diagnosis. These results were unexpected and could be explained by individuals with a PD having barriers to a cancer diagnosis rather than a true decreased incidence.

Osborn, D. P., Levy, G., Nazareth, I., et al. (2007). "Relative risk of cardiovascular and cancer mortality in people with severe mental illness from the United Kingdom's General Practice Rsearch Database." Arch Gen Psychiatry **64**(2): 242-249.
https://jamanetwork.com/journals/jamapsychiatry/articlepdf/482163/yoa60048_242_249.pdf

CONTEXT: People with severe mental illness (SMI) appear to have an elevated risk of death from cardiovascular disease, but results regarding cancer mortality are conflicting. OBJECTIVE: To estimate this excess mortality and the contribution of antipsychotic medication, smoking, and social deprivation. DESIGN: Retrospective cohort study. SETTING: United Kingdom's General Practice Research Database. Patients Two cohorts were compared: people with SMI diagnoses and people without such diagnoses. Main Outcome Measure Mortality rates for coronary heart disease (CHD), stroke, and the 7 most common cancers in the United Kingdom. RESULTS: A total of 46 136 people with SMI and 300 426 without SMI were selected for the study. Hazard ratios (HRs) for CHD mortality in people with SMI compared with controls were 3.22 (95% confidence interval [CI], 1.99-5.21) for people 18 through 49 years old, 1.86 (95% CI, 1.63-2.12) for those 50 through 75 years old, and 1.05 (95% CI, 0.92-1.19) for those older than 75 years. For stroke deaths, the HRs were 2.53 (95% CI, 0.99-6.47) for those younger than 50 years, 1.89 (95% CI, 1.50-2.38) for those 50 through 75 years old, and 1.34 (95% CI, 1.17-1.54) for those older than 75 years. The only significant result for cancer deaths was an unadjusted HR for respiratory tumors of 1.32 (95% CI, 1.04-1.68) for those 50 to 75 years old, which

lost statistical significance after controlling for smoking and social deprivation. Increased HRs for CHD mortality occurred irrespective of sex, SMI diagnosis, or prescription of antipsychotic medication during follow-up. However, a higher prescribed dose of antipsychotics predicted greater risk of mortality from CHD and stroke. CONCLUSIONS: This large community sample demonstrates that people with SMI have an increased risk of death from CHD and stroke that is not wholly explained by antipsychotic medication, smoking, or social deprivation scores. Rates of nonrespiratory cancer mortality were not raised. Further research is required concerning prevention of this mortality, including cardiovascular risk assessment, monitoring of antipsychotic medication, and attention to diet and exercise.

Osborn, D. P., Limburg, H., Walters, K., et al. (2013). "Relative incidence of common cancers in people with severe mental illness. Cohort study in the United Kingdom THIN primary care database." Schizophr Res **143**(1): 44-49.

BACKGROUND: A recent United Kingdom (UK) report found that breast and colorectal cancers were more common in people with severe mental illness (SMI) and recommended targeted screening. Epidemiological evidence is however inconsistent. OBJECTIVES: To estimate relative incidence rates for colorectal, breast and lung cancer, and the overall incidence of the commonest other UK cancers, in people with SMI compared with people without SMI. METHOD: Cohort study in the UK using The Health Improvement Network (THIN) primary care database between 1990 and June 2008. Poisson regression was used to obtain adjusted incidence rate ratios (IRRs) for cancer, comparing two cohorts of people over 18; with and without a diagnosis of SMI. RESULTS: We identified 20,632 people with SMI and 116,152 people without, with median follow up of over 6years. No significant associations were observed between SMI and cancers of the breast (adjusted IRR 1.17; 95% confidence interval 0.95-1.45), colon (0.70; 0.46-1.05), rectum (1.05; 0.65-1.69) or lung (0.84; 0.65-1.10). The adjusted IRR for an aggregate cancer outcome in SMI was 0.95; 0.85-1.06. Results were similar for schizophrenia and bipolar disorder. CONCLUSIONS: In a cohort analysis within a large UK primary care database, the incidence of colo-rectal, breast and lung cancer, and of all common cancers, did not differ significantly in people with SMI, including schizophrenia, compared with people without SMI. Our results do not support enhanced screening procedures for cancer in people with SMI.

Paredes, A. Z., Hyer, J. M., Tsilimigras, D. I., et al. (2021). "Association of pre-existing mental illness with all-cause and cancer-specific mortality among Medicare beneficiaries with pancreatic cancer." HPB **23**(3): 451-458. https://www.sciencedirect.com/science/article/pii/S1365182X2031114X

Background Among patients with pancreatic cancer, the association of pre-existing mental illness with long-term outcomes remains unknown. Methods Individuals diagnosed with pancreatic adenocarcinoma were identified in the SEER-Medicare database. Patients were classified as having mental illness if an ICD9/10CM code for anxiety, depression, bipolar disorder, schizophrenia or other psychotic disorder was recorded. Results Among the 54,234 Medicare beneficiaries with pancreatic cancer, roughly 1 in 12 (n = 4793, 8.83%) individuals had a diagnosis of a mental illness. The majority (n = 4029, 84.1%) had anxiety or depression, while 16% (n = 764) had bipolar/schizophrenic disorders. On multivariable analysis, among patients with early stage cancer, individuals with pre-existing anxiety/depression and bipolar/schizophrenic disorders had 22% (OR 0.78, 95% CI 0.69–0.86) and 46% (OR 0.54, 95% CI 0.42–0.70) reduced odds, respectively, to undergo cancer-directed surgery. Furthermore, patients with a pre-existing history of bipolar/schizophrenic disorders had a 20% (HR 1.20, 95% CI 1.21–1.40) higher risk of all-cause mortality and 27% (HR 1.27, 95% CI 1.17–1.37) higher risk of pancreatic cancer-specific mortality compared to individuals without a history of mental illness. Conclusion One in twelve patients with pancreatic cancer had a pre-existing mental illness. Individuals with mental illness were more likely to have worse overall and cancer-specific long-term outcomes.

Park, S. J., Wai, A., Pavithran, K., et al. (2021). "Cancer and severe mental illness in low- and middle-income countries: The challenges and outlook for the future." Psychooncology **30**(12): 2002-2011. https://onlinelibrary.wiley.com/doi/pdfdirect/10.1002/pon.5796?download=true

OBJECTIVE: Patients with severe mental illness (SMI) face health inequalities that lead to under treatment of diseases such as cancer and result in increased mortality. There is literature addressing

this issue for SMI patients in high-income countries but few for those in low- and middle-income countries. This review aims to draw attention to the health inequalities and the compounding factors faced by SMI patients in low- and middle-income countries. The relevance of integration of psycho-oncology in the care of SMI patients with cancer is integral to reduce disparities and address varied contributory factors. METHODS: The literature review was conducted by searching through two databases which includes PubMed and Google Scholar. We searched for articles using keyword search terms: severe mental illness, SMI, schizophrenia, bipolar disorder, cancer, low- middle-income countries, low- and middle-income countries, psycho-oncology, HPV vaccine, cancer incidence, cancer mortality, cancer control, cancer screening, cancer treatment and palliative care. RESULTS: A total of 80 research articles were included in our literature review. We found that there was an increased requirement for adapting to the changing disease landscape in low- and middle-income countries. An improvement on aspects such as vaccination, screening and prevention is necessary, and also efforts to change social stance towards SMI is crucial. CONCLUSION: There is an increase incidence of cancer in low- and middle-income countries, and the number of patients with SMI in low- and middle-income countries is also rising. This is due to social, psychological, economical and healthcare factors. Low- and middle-income countries must consider improving these aspects in order to adapt to the changing landscape.

Protani, M. M., Jordan, S. J., Kendall, B. J., et al. (2021). "Colorectal cancer Outcomes in people with Severe Mental Illness Cohort (COSMIC): a protocol for an Australian retrospective cohort using linked administrative data." BMJ Open **11**(6): e044737.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8190058/pdf/bmjopen-2020-044737.pdf

INTRODUCTION: Colorectal cancer (CRC) mortality is significantly higher in those with severe mental illness (SMI) compared with the general population, despite similar incidence rates, suggesting that barriers to optimal screening and cancer care may contribute to disparities in CRC mortality in those with SMI. This study aims to compare participation in Australia's National Bowel Cancer Screening Programme (NBCSP) in those with SMI and those in the general population. We will also investigate treatment pathways after diagnosis to determine whether treatment variations could explain differences in CRC mortality. METHODS AND ANALYSIS: We will undertake a retrospective cohort study of Australians using linked administrative data to assess differences in screening and cancer care between those with and without SMI, aged 50-74 years on or after 1 January 2006. People with SMI will be defined using antipsychotic medication prescription data. The comparison group will be people enrolled in Medicare (Australia's universal healthcare system) who have not been prescribed antipsychotic medication. Data on outcomes (NBCSP participation, follow-up colonoscopy, CRC incidence and CRC-cause and all-cause mortality) and confounders will be obtained from national-based and state-based administrative health datasets. All people in New South Wales, aged 50-74 with a new diagnosis of CRC on or after 1 January 2006, will be ascertained to examine stage at diagnosis and cancer treatment in those with and without SMI. Poisson regression will be used to calculate incidence rates and rate ratios for each outcome. ETHICS AND DISSEMINATION: Ethics approval has been obtained from the University of Queensland Human Research Ethics Committee, the Australian Institute of Health and Welfare Ethics Committee and data custodians from every Australian State/Territory. Findings will be disseminated via publications in peer-reviewed journals and presented at appropriate conferences. TRIAL REGISTRATION NUMBER: ACTRN12620000781943.

Reilly, S., Olier, I., Planner, C., et al. (2015). "Inequalities in physical comorbidity: a longitudinal comparative cohort study of people with severe mental illness in the UK." BMJ Open **5**(12): e009010.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4679912/pdf/bmjopen-2015-009010.pdf

OBJECTIVES: Little is known about the prevalence of comorbidity rates in people with severe mental illness (SMI) in UK primary care. We calculated the prevalence of SMI by UK country, English region and deprivation quintile, antipsychotic and antidepressant medication prescription rates for people with SMI, and prevalence rates of common comorbidities in people with SMI compared with people without SMI. DESIGN: Retrospective cohort study from 2000 to 2012. SETTING: 627 general practices contributing to the Clinical Practice Research Datalink, a UK primary care database. PARTICIPANTS: Each identified case (346,551) was matched for age, sex and general practice with 5 randomly selected control cases (1,732,755) with no diagnosis of SMI in each yearly time point. OUTCOME MEASURES:

Prevalence rates were calculated for 16 conditions. RESULTS: SMI rates were highest in Scotland and in more deprived areas. Rates increased in England, Wales and Northern Ireland over time, with the largest increase in Northern Ireland (0.48% in 2000/2001 to 0.69% in 2011/2012). Annual prevalence rates of all conditions were higher in people with SMI compared with those without SMI. The discrepancy between the prevalence of those with and without SMI increased over time for most conditions. A greater increase in the mean number of additional conditions was observed in the SMI population over the study period (0.6 in 2000/2001 to 1.0 in 2011/2012) compared with those without SMI (0.5 in 2000/2001 to 0.6 in 2011/2012). For both groups, most conditions were more prevalent in more deprived areas, whereas for the SMI group conditions such as hypothyroidism, chronic kidney disease and cancer were more prevalent in more affluent areas. CONCLUSIONS: Our findings highlight the health inequalities faced by people with SMI. The provision of appropriate timely health prevention, promotion and monitoring activities to reduce these health inequalities are needed, especially in deprived areas.

Ribe, A. R., Laurberg, T., Laursen, T. M., et al. (2016). "Ten-Year Mortality after a Breast Cancer Diagnosis in Women with Severe Mental Illness: A Danish Population-Based Cohort Study." PLoS One **11**(7): e0158013. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4963132/pdf/pone.0158013.pdf

BACKGROUND: Breast cancer is the leading cause of cancer death in women worldwide. Nevertheless, it is unknown whether higher mortality after breast cancer contributes to the life-expectancy gap of 15 years in women with severe mental illness (SMI). METHODS: We estimated all-cause mortality rate ratios (MRRs) of women with SMI, women with breast cancer and women with both disorders compared to women with neither disorder using data from nationwide registers in Denmark for 1980-2012. RESULTS: The cohort included 2.7 million women, hereof 31,421 women with SMI (12,852 deaths), 104,342 with breast cancer (52,732 deaths), and 1,106 with SMI and breast cancer (656 deaths). Compared to women with neither disorder, the mortality was 118% higher for women with SMI (MRR: 2.18, 95% confidence interval (CI): 2.14-2.22), 144% higher for women with breast cancer (MRR: 2.44, 95% CI: 2.42-2.47) and 327% higher for women with SMI and breast cancer (MRR: 4.27, 95% CI: 3.98-4.57). Among women with both disorders, 15% of deaths could be attributed to interaction. In a sub-cohort of women with breast cancer, the ten-year all-cause-mortality was 59% higher after taking tumor stage into account (MRR: 1.59, 95% CI: 1.47-1.72) for women with versus without SMI. CONCLUSIONS: The mortality among women with SMI and breast cancer was markedly increased. More information is needed to determine which factors might explain this excess mortality, such as differences between women with and without SMI in access to diagnostics, provision of care for breast cancer or physical comorbidity, health-seeking-behavior, and adherence to treatment.

Rockson, L., Swarbrick, M. et Pratt, C. (2020). "Cancer Screening in Behavioral Health Care Programs." J Am Psychiatr Nurses Assoc **26**(2): 212-215. https://journals.sagepub.com/doi/10.1177/1078390319877227

OBJECTIVE: Adults with serious mental illnesses have a lower life expectancy attributable to many factors including metabolic disorders and cancer. Access to cancer screening has been shown to decrease morbidity and increase chances of survival. This study examined access to cancer screening services among individuals with serious mental illnesses served by a community behavioral health care agency partial hospitalization program at four locations. METHOD: A self-administered paper-and-pencil survey was provided to adults attending partial hospitalization programs. The survey consisted of open- and closed-ended questions about utilization, access to, and barriers to cervical, breast, and colorectal cancer screenings. RESULTS: Surveys were completed by 136 individuals. Participant screening rates were above national rates for cervical and breast cancer but lower for colorectal cancer. The main cited barrier to receiving the screening tests was lack of physician recommendations. CONCLUSIONS: Psychiatric nurses are ideally suited to communicate with this population and other behavioral health care professions about the importance of these screenings. Communication should also advocate for improved education and increased support for cancer screenings to address this health care disparity.

Ross, E., Maguire, A., Mairs, A., et al. (2021). "Disparities in Breast Cancer Screening Uptake for Women With Mental Illness in the United Kingdom." Am J Prev Med **60**(3): e123-e130.

https://www.sciencedirect.com/science/article/pii/S074937972030444X

Introduction Although there is evidence of disparities in breast cancer screening for women with mental illness in the U.S., there is a dearth of studies examining this association in the United Kingdom, where health care is provided free at the point of access. This population-based study examines the influence of mental illness, as assessed by the uptake of psychotropic medications, on breast screening uptake in the United Kingdom. Methods A cohort of 57,328 women identified from 2011 Census records within the Northern Ireland Longitudinal Study was followed through a single 3-year screening cycle (2011–2014) of the National Health Service Breast Screening Programme. Mental illness was identified by a receipt of psychotropic medication in the 3 months preceding screening invite. Individual- and household-level attributes were derived from Census records. Data were analyzed in 2019. Results More than a third of women received ≥1 prescription for psychotropic medication in the 3 months preceding screening invite. The odds of attendance in these individuals were reduced by 15% (OR=0.85, 95% CI=0.81, 0.88). Attendance was particularly low for women prescribed antipsychotics (OR=0.63, 95% CI=0.56, 0.70), anxiolytics (OR=0.61, 95% CI=0.57, 0.66), and hypnotics (OR=0.68, 95% CI=0.63, 0.72). Conclusions These findings confirm the existence of significant disparities in breast screening uptake for women with mental illness. Targeted interventions are warranted to prevent avoidable breast cancer deaths in these individuals, especially given the increasing prevalence of mental illness.

Sabia, A. et Anger, W. H., Jr. (2016). "Interventions to Encourage Uptake of Cancer Screening for People With Severe Mental Illness." Issues Ment Health Nurs **37**(7): 533.
https://www.tandfonline.com/doi/full/10.1080/01612840.2016.1188583

Safaie, N., Zeinali, H., Ghahramanfard, N., et al. (2021). "Psychiatric Disorders in New Cancer Patients in Semnan." Pakistan Journal of Medical & Health Sciences **15**(6): 1986-1989.

Introduction & Objective: Definitive diagnosis of cancer in patients, the duration of treatment, and grueling treatment methods can provide a basis for psychiatric disorders such as depression and anxiety in patients; accordingly, this study was conducted to evaluate the factors affecting these disorders in patients who were newly diagnosed with cancer. Materials and Methods: This descriptive-analytical study was performed on 122 cancer patients in 1397 in Semnan, Iran. Data were collected using the HADS questionnaire. In order to compare the subgroups in terms of frequencies, Chi-square test and, if necessary, more accurate Fisher test were used. Numerical variables were compared using T-test or Mann Whitney U test. Results: In the present study, the mean of total anxiety was about 28.6% and the mean of total depression among patients was 26.2%. 80% of women and 74.3% of people without income had anxiety and there was a significant relationship between gender and income with anxiety in cancer patients (p <0/05). The variables of age, sex, income level, education level were not significantly associated with depression (P> 0.05). Conclusion: Considering the levels of psychiatric disorders, especially anxiety and depression in cancer patients, to control this issue, providing psychiatric interventions in the treatment program of these patients can be effective.

Saleh, S., Mohammed, A., Davila, J., et al. (2022). "Disparities in Hepatocellular Cancer Screening in Cirrhotic Patients With Psychiatric Disorders." Cureus Journal of Medical Science **14**(3): 7.
<Go to ISI>://WOS:000778468900006

Background Patients with psychiatric disorders are at an increased risk of developing liver diseases, including hepatocellular carcinoma (HCC). HCC is a leading cause of cancer-related deaths in the United States. The aim of this study was to re-examine the association of psychiatric illness with HCC and assess its impact on screening practices and the outcomes of HCC. Materials and methods We performed a retrospective manual chart review of all patients diagnosed with HCC at a major safety-net hospital in Cleveland, Ohio, from January 2010 to December 2019. Patients were divided into two groups, those with and those without psychiatric illness. The patient characteristics recorded included psychiatric illnesses, etiology of liver disease, radiographic screening intervals, and tumor hoard recommendations upon initial diagnosis. We analyzed data using Statistical Product and Service Solutions version 26.0 (IBM Corp., Armonk, NY). We analyzed the qualitative and quantitative differences between the groups using the chi-square or Fisher's exact tests for categorical variables

and t-test for continuous variables. Results There were a total of 393 patients with a diagnosis of HCC. Among them, 128 (32.5%) were diagnosed with at least one psychiatric illness. Fewer patients with psychiatric illness (33.6%) underwent screening within six months before being diagnosed with HCC: compared to those without psychiatric illness (49.8%) (p= 0.(X)2). Patients with psychiatric illness (71.1%) were more likely to have been seen by a gastroenterologist or hepatologist before their diagnosis of HCC compared to those without psychiatric illness (55.1%) (p -0.002). Patients with psychiatric illness were more likely to be offered systemic chemotherapy or hospice (39.1%) compared to those without psychiatric illness (29.1%) (p=0.039). Discussion A significant number of HCC patients in our study group have an underlying psychiatric illness. Patients with psychiatric disorders are prone to high-risk behaviors, likely predisposing them to chronic liver disease and HCC. Patients with psychiatric disorders are less compliant with screening practices. Our findings suggest that psychiatric illnesses tend to he diagnosed with more extensive HCC, which is less amenable to curative treatment. Significant efforts need to be made to identify barriers to HCC screening in cirrhotic patients with psychiatric disorders.

Shen, Q., Ma, Y. J., Joud, A., et al. (2021). "Psychiatric Disorders and Cardiovascular Diseases During the Diagnostic Workup of Suspected Prostate Cancer." Jnci Cancer Spectrum **5**(1): 7.

Background: It is unknown whether the rate of psychiatric disorders and cardiovascular disease increases during the diagnostic workup of suspected prostate cancer. Methods: We designed a population-based cohort study including 579 992 men living during 2005-2014 in Skane, Sweden, according to the Swedish Total Population Register and the Skane Healthcare Register (SHR). We used the Swedish Cancer Register and the SHR to identify all men with a new diagnosis of prostate cancer (N = 10 996), and all men underwent a prostate biopsy without receiving a cancer diagnosis (biopsy group, N = 20 482) as exposed to a diagnostic workup. Using Poisson regression, we compared the rates of psychiatric disorders and cardiovascular disease during the period before diagnosis or biopsy of exposed men with the corresponding rates of unexposed men. Results: We found an increased rate of psychiatric disorders during the period before diagnosis or biopsy among men with prostate cancer (incidence rate ratio [IRR] = 1.87, 95% confidence interval [CI] = 1.67 to 2.10) and men in the biopsy group (IRR = 2.22, 95% CI = 2.08 to 2.37). The rate of cardiovascular disease increased during the period before diagnosis or biopsy among men with prostate cancer (IRR = 2.22, 95% CI = 2.12 to 2.32) and men in the biopsy group (IRR = 2.56, 95% CI = 2.49 to 2.63). Greater rate increases were noted for a diagnostic workup due to symptoms than due to other reasons. Conclusions: There was an increased risk of psychiatric disorders and cardiovascular disease during the diagnostic workup of suspected prostate cancer regardless of the final cancer diagnosis.

Shinden, Y., Kijima, Y., Hirata, M., et al. (2017). "Clinical characteristics of breast cancer patients with mental disorders." Breast **36**: 39-43.
https://www.thebreastonline.com/article/S0960-9776(17)30571-4/fulltext

BACKGROUND: Severe mental disorders are thought to affect the diagnosis and treatment of breast cancer because of their lower awareness and understanding of the disease and their reduced ability to cooperate with medical staff. We analyzed the clinical features of patients with breast cancer and pre-existing mental disorders such as schizophrenia, dementia, and intellectual disability. PATIENTS AND METHODS: We reviewed the records of 46 patients who were diagnosed with schizophrenia, dementia, or intellectual disability, before being diagnosed with breast cancer. Three patients had more than 2 mental disorders. All patients underwent curative surgical treatment between September 1992 and January 2015. Patients' clinicopathological information was compared with a control group of 727 breast-cancer patients without mental disorders seen during the same period. RESULTS: Patients with mental disorders were less likely to be aware of their own breast cancer; the lesions were often found by other people such as family, care staff, and medical staff. Breast cancer patients with mental disorders had significantly more advanced T factors and overall stage at the time of surgery than their counterparts without mental illness, more patients underwent total mastectomy, and fewer patients underwent postoperative adjuvant chemotherapy and radiation. Biological markers such as estrogen receptor, progesterone receptor, and human epidermal growth factor receptor 2 (HER2) expression were not significantly different between groups. Disease-free survival and overall survival were not significantly different between groups. CONCLUSION: Patients with

mental disorders receive less postoperative adjuvant chemotherapy; however, their outcomes were not worse than those of patients without mental disorders.

Tabares-Seisdedos, R., Dumont, N., Baudot, A., et al. (2011). "No paradox, no progress: inverse cancer comorbidity in people with other complex diseases." Lancet Oncol **12**(6): 604-608. https://www.thelancet.com/journals/lanonc/article/PIIS1470-2045(11)70041-9/fulltext

In the past 5 years, several leading groups have attempted to explain why individuals with Down's syndrome have a reduced risk of many solid tumours and an increased risk of leukaemia and testicular cancer. Niels Bohr, the Danish physicist, noted that a paradox could initiate progress. We think that the paradox of a medical disorder protecting against cancer could be formalised in a new model of inverse cancer morbidity in people with other serious diseases. In this Personal View, we review evidence from epidemiological and clinical studies that supports a consistently lower than expected occurrence of cancer in patients with Down's syndrome, Parkinson's disease, schizophrenia, diabetes, Alzheimer's disease, multiple sclerosis, and anorexia nervosa. Intriguingly, most comorbidities are neuropsychiatric or CNS disorders. We provide a brief overview of evidence indicating genetic and molecular connections between cancer and these complex diseases. Inverse comorbidity could be a valuable model to investigate common or related pathways or processes and test new therapies, but, most importantly, to understand why certain people are protected from the malignancy.

Takehara, T., Tani, T., Takiue, H., et al. (2020). "Outcome of patients with lung cancer and severe psychiatric disorder admitted to a medical psychiatric unit." Mol Clin Oncol **12**(3): 273-277. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7016514/pdf/mco-12-03-0273.pdf

The purpose of the present study was to evaluate the clinical profiles and treatment outcomes of patients with lung cancer admitted to the Medical Psychiatric Unit (MPU), which is built for patients with physical and severe psychiatric disorders. All medical records of patients with lung cancer admitted to the MPU of Tachikawa hospital were reviewed. The clinical outcomes of these patients were retrospectively evaluated between January 2010 and December 2016. A total of 24 patients in the MPU were histologically or cytologically diagnosed with primary lung cancer. Of these, 20 patients had schizophrenia, and 4 patients had a mood disorder. There were 15 patients who were diagnosed using bronchoscopy. The histology indicated adenocarcinoma, squamous cell carcinoma and non-small-cell lung cancer-not otherwise specified were in 11, 8, and 1 patient, respectively, while small-cell lung cancer was indicated in 4 patients. Surgery, chemoradiotherapy, radiotherapy, chemotherapy was performed in 13, 4, 2, 1 and 4 patients, respectively. The median survival time was 76.7 months for patients who underwent surgery, while it was 14.4 months for those who underwent chemoradiotherapy. In the MPU, patients with lung cancer and severe psychiatric disorders could be safely diagnosed, and patients with early-stage lung cancer exhibited long-term survival.

Tan, X. W., Lee, E. S., Toh, M., et al. (2021). "Comparison of mental-physical comorbidity, risk of death and mortality among patients with mental disorders - A retrospective cohort study." J Psychiatr Res **142**: 48-53.

AIM: To compare the risk of death, the prevalence of comorbid chronic physical illness and mortality among an Asian population of patients with mental disorders. METHODS: This was a retrospective data analysing of medical records of patients with schizophrenia, depression, anxiety, bipolar disorder, alcohol use disorder (AUD) or substance use disorder and the comorbid chronic physical illnesses. The hazard risk of death was calculated with Cox regression and compared between patients with and without comorbid chronic physical illness(es). Odds ratios of specific comorbid chronic physical illness were calculated with logistic regression and mean crude death rate was calculated for patients with different mental disorders. RESULTS: A total of 56,447 patients with mental disorders were included in the analysis. Compared to patients without comorbid physical illness, patients with mental-physical comorbidity were associated with a higher risk of death [2.36 (2.22-2.52); hazard ratio (95% CI)] and less estimated survival days [2157 (2142-2172) vs 2508 (2504-2513)]. Compared to other mental disorders, those with AUD had the highest prevalence of two or more comorbid chronic physical illnesses and associated with the highest odds of comorbid hypertension, diabetes mellitus, stroke, nephritis, chronic kidney disease, and cancer. The highest one-year crude death rate was similarly observed in patients with AUD. CONCLUSIONS: Mental-physical comorbidity was associated with a

higher risk of death compared to patients with mental disorders only. The highest prevalence of mental-physical comorbidity and mortality were observed in patients with AUD. More attention and resources may be needed to tackle the burden of AUD.

Toender, A., Munk-Olsen, T., Vestergaard, M., et al. (2018). "Impact of severe mental illness on cancer stage at diagnosis and subsequent mortality: A population-based register study." Schizophr Res.

BACKGROUND: Excess mortality in individuals with severe mental illness (SMI) is often explained by physical comorbidity and suboptimal healthcare. Cancer is a prevalent cause of death, and tumour stage at diagnosis is a strong predictor of mortality. We aimed to study cancer incidence, disease stage at diagnosis and subsequent mortality in individuals with SMI compared to individuals without SMI. METHODS: The entire Danish population was followed in 1978-2013 using nationwide registries. Cancer incidence and subsequent mortality stratified by disease stage were compared in individuals with and without SMI. Cox regression was used to estimate incidence rate ratios (IRR) and mortality rate ratios (MRR). Cancer was examined overall and grouped by major aetiological factors. RESULTS: The overall cancer incidence rate was lower in males with SMI than in males without SMI; IRR=0.89 (95% CI: 0.85-0.94), but rates were similar in females with SMI and without SMI; IRR=1.03 (95% CI: 0.99-1.07). The overall mortality rate was higher in individuals with SMI than those without; MRR=1.56 (95% CI: 1.48-1.64) for males and MRR=1.49 (95% CI: 1.43-1.56) for females. Incidence rates and mortality rates showed similar estimates when stratified by tumour stage and aetiology. CONCLUSIONS: We found lower cancer incidence in males with SMI compared to males without SMI and similar incidence in the two groups of women. Higher subsequent mortality was found in both sexes with SMI. The excess mortality was not explained by more advanced stages of cancer; future studies should evaluate the effect of cancer treatment and rehabilitation.

Tuesley, K. M., Jordan, S. J., Siskind, D. J., et al. (2018). "Colorectal, cervical and prostate cancer screening in Australians with severe mental illness: Retrospective nation-wide cohort study." Australian & New Zealand Journal of Psychiatry **53**(6): 550-558.
https://journals.sagepub.com/doi/10.1177/0004867418814945

Tuesley, K. M., Jordan, S. J., Siskind, D. J., et al. (2019). "Colorectal, cervical and prostate cancer screening in Australians with severe mental illness: Retrospective nation-wide cohort study." Aust N Z J Psychiatry **53**(6): 550-558.
https://journals.sagepub.com/doi/10.1177/0004867418814945

OBJECTIVE: People with severe mental illness have similar cancer incidence, but higher mortality than the general population. Participation in cancer screening may be a contributing factor but existing studies are conflicting. The aim of this study was to investigate the frequency of colorectal, prostate and cervical cancer screening among people with and without severe mental illness in Australia, who have access to universal health care. METHODS: We followed three cohorts using de-identified data from a random 10% sample of people registered for Australia's universal health care system: those aged 50-69 years (n = 760,058) for colorectal cancer screening; women aged 18-69 years (n = 918,140) for cervical cancer screening and men aged 50-69 years (n = 380,238) for prostate cancer screening. We used Poisson regression to estimate incidence rate ratios and 95% confidence intervals for the association between severe mental illness and rates of faecal occult blood testing, pap smears and prostate-specific antigen testing. RESULTS: Having severe mental illness was associated with a 17% reduction in rates of pap smear (incidence rate ratio = 0.83, 95% confidence interval: 0.82-0.84) and prostate-specific antigen testing (incidence rate ratio = 0.83, 95% confidence interval: 0.81-0.85), compared to the general population. By contrast, incidence rates of faecal occult blood testing were only lower in people with severe mental illness among the participants who visited their general practitioner less than an average of five times per year (incidence rate ratio = 0.83, 95% confidence interval = [0.73, 0.94]). CONCLUSION: Our results suggest that differences in screening frequency may explain some of the mismatch between cancer incidence and mortality in people with severe mental illness and indicate that action is required to improve preventive screening in this very disadvantaged group.

Virgilsen, L. F., Vedsted, P., Falborg, A. Z., et al. (2022). "Routes to cancer diagnosis for patients with pre-existing psychiatric disorders: a nationwide register-based cohort study." BMC Cancer **22**(1): 12. https://bmccancer.biomedcentral.com/track/pdf/10.1186/s12885-022-09598-x.pdf

Background Poor cancer prognosis has been observed in patients with pre-existing psychiatric disorders. Therefore, we need better knowledge about the diagnosis of cancer in this patient group. The aim of the study was to describe the routes to cancer diagnosis in patients with pre-existing psychiatric disorders and to analyse how cancer type modified the routes. Methods A register-based cohort study was conducted by including patients diagnosed with incident cancer in 2014-2018 (n = 155,851). Information on pre-existing psychiatric disorders was obtained from register data on hospital contacts and prescription medication. Multinomial regression models with marginal means expressed as probabilities were used to assess the association between pre-existing psychiatric disorders and routes to diagnosis. Results Compared to patients with no psychiatric disorders, the population with a psychiatric disorder had an 8.0% lower probability of being diagnosed through cancer patient pathways initiated in primary care and a 7.6% higher probability of being diagnosed through unplanned admissions. Patients with pre-existing psychiatric disorders diagnosed with rectal, colon, pancreatic, liver or lung cancer and patients with schizophrenia and organic disorders were less often diagnosed through cancer patient pathways initiated in primary care. Conclusion Patients with pre-existing psychiatric disorders were less likely to be diagnosed through Cancer Patient Pathways from primary care. To some extent, this was more pronounced among patients with cancer types that often present with vague or unspecific symptoms and among patients with severe psychiatric disorders. Targeting the routes by which patients with psychiatric disorders are diagnosed, may be one way to improve the prognosis among this group of patients.

Wang, G. X., Hwong, A. R., Mercaldo, S. F., et al. (2022). "Impact of a Same-Day Breast Biopsy Program on Disparities in Time to Biopsy for Patients With Serious Mental Illness." J Am Coll Radiol **19**(1 Pt B): 146-154. https://www.jacr.org/article/S1546-1440(21)00744-4/pdf

PURPOSE: The aim of this study was to investigate disparities in time between breast biopsy recommendation and completion and the impact of a same-day biopsy (SDB) program for patients with serious mental illness (SMI), with a focus on more vulnerable individuals with public payer insurance. METHODS: In August 2017, the authors' academic breast imaging center started routinely offering needle biopsies on the day of recommendation. Primary outcomes were the proportion of biopsies performed as SDBs and days from biopsy recommendation to completion over a 2.5-year pre- versus postintervention period, comparing all patients with SMI versus those without, and public payer-insured patients <65 years of age with SMI (SMI-PP) versus without SMI (non-SMI-PP). Multivariable proportional odds and logistic regression models were fit to assess association of SMI status, age, race/ethnicity, language, and insurance with days to biopsy and SDB within each period. RESULTS: There were 2,026 biopsies preintervention and 2,361 biopsies postintervention. Preintervention, 8.43% of patients with SMI (7 of 83) underwent SDB compared with 15.59% of those without SMI (303 of 1,943) (P = .076), and 2.7% of the SMI-PP subgroup (1 of 37) underwent SDB compared with 15.88% of the non-SMI-PP subgroup (47 of 296) (P = .031). Adjusted for age, race/ethnicity, and language, disparities persisted in odds for undergoing SDB (adjusted odds ratio, 0.13; 95% confidence interval, 0.02-0.92; P = .04) and having longer days to biopsy (adjusted odds ratio, 2.35; 95% confidence interval, 1.26-4.37; P = .01) for the SMI-PP subgroup compared with the non-SMI-PP subgroup in the preintervention period. There was no evidence of these disparities postintervention for the SMI-PP subgroup. SDB proportion increased from 15.3% (310 of 2,026) to 36.09% (852 of 2,361) (P < .001) across all patients. CONCLUSIONS: A same-day breast biopsy program mitigates disparities in time to biopsy for patients with SMI and helps improve breast cancer care equity for this vulnerable population.

Whitley, E., Batty, G. D., Mulheran, P. A., et al. (2012). "Psychiatric disorder as a risk factor for cancer: different analytic strategies produce different findings." Epidemiology **23**(4): 543-550. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4176762/pdf/emss-60282.pdf

BACKGROUND: Reported associations between psychiatric disorders and cancer incidence are inconsistent, with cancer rates in psychiatric patients that are variously higher than, similar to, or

lower than the general population. Understanding these associations is complicated by difficulties in establishing the timing of onset of psychiatric disorders and cancer, and by the possibility of reverse causality. Some studies have dealt with this problem by excluding patients with cancers predating their psychiatric illness; others have not considered the issue. METHODS: We examined associations between psychiatric hospitalization and cancer incidence in a cohort of 1,165,039 Swedish men, and we explored the impact of different analytic strategies on these associations using real and simulated data. RESULTS: Relative to men without psychiatric hospitalization, we observed consistent increases in smoking-related cancers in those with psychiatric hospitalizations, regardless of analytic approach (eg, hazard ratio = 1.73 [95% confidence interval = 1.52-1.96]). However, associations with cancers unrelated to smoking were highly dependent on analytic strategy. In analyses based on the full cohort, we observed no association or a modest increase in cancer incidence in those with psychiatric hospitalizations (1.14 [1.07-1.22]). In contrast, when men whose cancer predated their psychiatric hospitalizations were excluded, future cancer incidence was lower in psychiatric patients (0.72 [0.67-0.78]). Results from simulated data suggest that even modest exclusions of this type can lead to strong artifactual associations. CONCLUSIONS: Psychiatric disorder-cancer incidence associations are complex and influenced by analytic strategy. A better understanding of the temporal relationship between psychiatric disorder and cancer incidence is required.

Wu, C. Y., Chan, T. F., Shi, H. Y., et al. (2021). "Psychiatric problems of anxiety and depression disorder are associated with medical service utilization and survival among patients with cervical cancer." Taiwanese Journal of Obstetrics & Gynecology **60**(3): 474-479.
https://www.sciencedirect.com/science/article/pii/S1028455921000668?via%3Dihub

Objective: There are few nationwide studies regarding the long-term analysis of cervical cancer patients in Taiwan. Thus, this study aimed to evaluate medical service utilization, and survival among cervical cancer patients initially diagnosed with or without anxiety and/or depressive disorders. Materials and methods: This was a retrospective longitudinal study using data from the National Health Insurance Research Database from 1996 to 2010. The study subjects were cervical cancer patients identified by ICD-9-CM codes 180.X, while subjects with anxiety and/or depressive disorders were identified using the following codes: 300.0X-300.9X (minus 300.4X) for anxiety disorder, and 296.2X, 296.3X, 300.4, and 311.X for depressive disorder. The cervical patients with anxiety or/and depression disorder were classified as anxiety/depression (AD) group or the non-disorder (ND) group. Propensity score matching (PSM) was used to adjust for differences between the AD and ND groups. T-tests were used to evaluate differences in medical utilization and the Kaplan-Meier method was used to evaluate survival conditions between the two groups. Statistical analyses were performed using SPSS Statistics 20.0. Results: A total of 3664 patients were identified, with 862 (23.5%) having anxiety, 149 (4.1%) with depression, and 349 (9.5%) having both anxiety and depression. In total, 1360 cervical cancer patients had anxiety/ depression disorders. After PSM, the AD group had significantly more outpatient department (OPD) visits than the ND group ($p < 0.001$) but the survival status was better in the AD group than the ND group ($p < 0.001$). Conclusions: Cervical cancer patients with anxiety/depression disorders visited the OPD more frequently than those without anxiety/depression disorders but had better survival status. Gynecologists should also consider cancer patients' mental status during follow-up, referring patients to psychiatric professionals for appropriate psychiatric care if appropriate. (c) 2021 Taiwan Association of Obstetrics & Gynecology. Publishing services by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Zharinov, G. M., Khalchitsky, S. E., Loktionov, A., et al. (2021). "The presence of polymorphisms in genes controlling neurotransmitter metabolism and disease prognosis in patients with prostate cancer: a possible link with schizophrenia." Oncotarget **12**(7): 698-707.
https://www.oncotarget.com/article/27921/pdf/

Polymorphisms of neurotransmitter metabolism genes were studied in patients with prostate cancer (PC) characterized by either reduced or extended serum prostate-specific antigen doubling time (PSADT) corresponding to unfavorable and favorable disease prognosis respectively. The 'unfavorable prognosis' group (40 cases) was defined by PSADT ≤ 2 months, whereas patients in the 'favorable prognosis' group (67 cases) had PSADT ≥ 30 months. The following gene polymorphisms known to be

associated with neuropsychiatric disorders were investigated: a) the STin2 VNTR in the serotonin transporter SLC6A4 gene; b) the 30-bp VNTR in the monoamine oxidase A MAOA gene; c) the Val158Met polymorphism in the catechol-ortho-methyltransferase COMT gene; d) the promoter region C-521T polymorphism and the 48 VNTR in the third exon of the dopamine receptor DRD4 gene. The STin2 12R/10R variant of the SLC6A4 gene (OR = 2.278; 95% CI = 0.953-5.444) and the -521T/T homozygosity of the DRD4 gene (OR = 1.579; 95% CI = 0.663-3.761) tended to be overrepresented in PC patients with unfavorable disease prognosis. These gene variants are regarded as protective against schizophrenia, and the observed trend may be directly related to a reduced PC risk described for schizophrenia patients. These results warrant further investigation of the potential role of neurotransmitter metabolism gene polymorphisms in PC pathogenesis.

Cancers et schizophrénie

ÉTUDES FRANÇAISES

Fond, G., Salas, S., Pauly, V., et al. (2019). "End-of-life care among patients with schizophrenia and cancer: a population-based cohort study from the French national hospital database." The Lancet Public Health **4**(11): e583-e591.
https://www.thelancet.com/pdfs/journals/lanpub/PIIS2468-2667(19)30187-2.pdf

Fond, G., Pauly, V., Orleans, V., et al. (2021). "Increased in-hospital mortality from COVID-19 in patients with schizophrenia." L'Encéphale: Revue de psychiatrie clinique biologique et thérapeutique **47**(2): 89-95.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7392112/pdf/main.pdf

Il existe peu d'informations décrivant les caractéristiques et les résultats des patients atteints de schizophrénie (SCZ) nécessitant une hospitalisation pour maladie à coronavirus 2019 (COVID-19). Objectifs: Nous avons cherché à comparer les caractéristiques cliniques et les résultats des patients SCZ atteints de COVID-19 avec ceux des patients non SCZ. Méthode: Il s'agissait d'une étude cas-témoins de patients COVID-19 admis dans 4 hôpitaux de soins aigus AP–HM/AMU à Marseille, dans le sud de la France. L'infection par COVID-19 a été confirmée par un résultat positif au test d'amplification en chaîne par polymérase d'un échantillon nasopharyngé et/ou au scanner thoracique effectué chez les patients nécessitant une hospitalisation. Le principal critère de jugement a été la mortalité hospitalière. Le critère de jugement secondaire était l'admission en unité de soins intensifs (USI). Résultats: Un total de 1092 patients a été inclus. Le taux global de mortalité hospitalière était de 9,0 %. Les patients SCZ ont eu une mortalité accrue par rapport aux autres patients (26,7 % contre 8,7 %, p = 0,039), ce qui a été confirmé par l'analyse multivariée après ajustement pour l'âge, le sexe, le tabagisme, l'obésité et les comorbidités (odds ratio ajusté de 4,36 [IC95 % : 1,09–17,44] ; p = 0,038). En revanche, les patients SCZ n'ont pas été plus souvent admis à l'unité de soins intensifs que les patients non SCZ. Il est important de noter que les patients des SCZ étaient pour la plupart institutionnalisés (63,6 %, soit 100 % des décès) et qu'ils étaient plus susceptibles d'avoir des cancers et des comorbidités respiratoires. Conclusions: Cette étude suggère que les SCZ ne sont pas surreprésentées parmi les patients hospitalisés pour COVID-19, mais que la SCZ est associée à une surmortalité due à COVID-19, confirmant l'existence de disparités de santé décrites dans d'autres maladies somatiques. (PsycInfo Database Record (c) 2021 APA, all rights reserved)

ÉTUDES ETRANGERES

Abdullah, K. N., Janardhan, R., Hwang, M., et al. (2015). "Adjuvant radiation therapy for breast cancer in patients with schizophrenia." Am J Surg **209**(2): 378-384.
https://www.americanjournalofsurgery.com/article/S0002-9610(14)00491-7/fulltext

BACKGROUND: Schizophrenia affects approximately 1% of subjects in all populations studied thus far. We sought to evaluate how patients with schizophrenia who are later diagnosed with breast cancer fare when adjuvant radiation therapy (ART) is clinically indicated. METHODS: We searched patient treatment file, the national inpatient computer database of the Department of Veterans Affairs, to identify patients with schizophrenia who subsequently developed breast cancer. RESULTS: Forty patients had

schizophrenia, who later developed breast cancer and were candidates for ART, according to well-established guidelines. Of the 40 patients who were considered candidates for ART, we found data about the decision to offer ART in 35; only 22 (63%) were offered ART and 5 of those 22 (23%) refused it. CONCLUSIONS: Patients with schizophrenia and breast cancer often do not understand the nature of their illnesses well. They often do not comply with recommended standard therapies such as ART. Treatment strategies that rely on ART are likely to be met with noncompliance. Breast-preserving treatment plans may be impractical. Initial radical surgery without ART may be preferable.

Agay, N., Flaks-Manov, N., Nitzan, U., et al. (2017). "Cancer prevalence in Israeli men and women with schizophrenia." Psychiatry Res **258**: 262-267.

The aim of this cross-sectional study was to compare cancer prevalence rates among patients with schizophrenia to those of the non-schizophrenia population. The study population included members of Clalit Health Services aged 25 to 74 years and all data was taken from patients' electronic health records. Of the 2,060,314 members who were included in the study, 32,748 had a diagnosis of schizophrenia. Cancer prevalence rates in women with and without schizophrenia were 491 per 10,000 and 439 per 10,000, respectively; in men, cancer prevalence rates were 226 per 10,000 and 296 per 10,000, respectively. The age-adjusted prevalence rate of all-type cancer was significantly lower among men with schizophrenia, compared to men without schizophrenia; specifically, men with schizophrenia had a lower rate of prostate cancer, and of cancers in the "other" category, compared to men without schizophrenia. Reduced cancer rates in men with schizophrenia may reflect under-diagnosis of some cancer types, likely due to insufficient medical attention. An effort to improve screening regimes should be made.

Ajdacic-Gross, V., Tschopp, A., Bopp, M., et al. (2014). "Cancer comortality patterns in schizophrenia and psychotic disorders: a new methodological approach for unique databases." Int J Methods Psychiatr Res **23**(1): 19-24. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6878395/pdf/MPR-23-19.pdf

The aim of this study was to determine the pattern of cancer comortality in deaths registered with schizophrenia and psychotic disorders. It focused on the question of whether the proportions of different types of cancer diverge when they are co-registered with schizophrenia/psychotic disorders or with other causes of death in mortality statistics. We developed an analysis approach applicable to common mortality statistics data when no linkage with morbidity databases or other registers is possible. The analysis covered Swiss mortality data from a 39-year period (1969 - 2007) and was confined to the most frequent cancers. We applied a two-step case-control analysis with bootstrapping (1000 repetitions). The cases were defined by the cancer-schizophrenia registrations for each specific cancer, whereas the controls were matched from the remaining cases (matching criteria: sex, age, region, subperiod). Cancers with deviant standardized mortality ratios (SMRs) included stomach cancer (1.6; 2.2 after reweighting), lung cancer (0.8; 0.5 after reweighting) and breast cancer (1.6; 1.5 after reweighting). The comortality pattern of cancers in schizophrenia and psychotic disorders diverges from the pattern found in other co-registered causes of death. The relatively low frequency of lung cancers is particularly paradoxical in view of the smoking habits of schizophrenia patients.

Arai, H., Watanbe, T., Hayashi, F., et al. (2017). "Schizophrenic Patients with Cancer Hospitalized at Psychiatric Hospitals in Japan." J Palliat Med **20**(1): 5.
https://www.liebertpub.com/doi/10.1089/jpm.2016.0351?url_ver=Z39.88-2003&rfr_id=ori%3Arid%3Acrossref.org&rfr_dat=cr_pub%3Dpubmed

Asada, M., Ebihara, S., Numachi, Y., et al. (2008). "Reduced tumor growth in a mouse model of schizophrenia, lacking the dopamine transporter." Int J Cancer **123**(3): 511-518.
https://onlinelibrary.wiley.com/doi/pdfdirect/10.1002/ijc.23562?download=true

The incidence of cancer in patients with schizophrenia has been reported to be lower that in the general population. On the other hand, it is well established that patients with schizophrenia have a hyper-dopaminergic system and dopamine has the ability to inhibit tumor angiogenesis. Therefore, in order to investigate the molecular mechanisms responsible for the lower cancer risk in schizophrenic patients, we used a mouse model of schizophrenia, which shows hyper-dopaminergic transmission in the nerve terminals of dopaminergic neurons. Here, we hypothesized that tumor growth was reduced in a mouse model of schizophrenia, lacking the dopamine transporter (DAT), and investigated tumor growth and

angiogenesis in DAT knockout mice. The subcutaneous tumor in mice inoculated with cancer cells was smaller in DAT-/- mice than in the wild type ($p < 0.05$); however, the level of plasma dopamine in DAT-/- mice was lower than that of control littermates. Using human umbilical vascular endothelial cells (HUVEC), we examined dopamine signaling through dopamine D(1) receptor (D(1)R) and D(2)R. Dopamine stimulation slightly decreased the surface expression of vascular endothelial growth factor receptor-2 (VEGF-R2) but induced the phosphorylation of VEGF-R2 through Src in HUVEC. In addition, DAT-/- mice had less D(1)R. Both pharmacological and genetic interruption of D(1)R showed inhibited tumor growth. These results suggest that modulation of the dopaminergic system may contribute to cancer therapy.

Barak, Y., Achiron, A., Mandel, M., et al. (2005). "Reduced cancer incidence among patients with schizophrenia." Cancer **104**(12): 2817-2821.
https://acsjournals.onlinelibrary.wiley.com/doi/pdfdirect/10.1002/cncr.21574?download=true

BACKGROUND: The incidence of cancer in patients with schizophrenia has been conversely reported to be higher, lower, or similar to that in the general population. The effects of lifestyle factors such as excess smoking, exposure to neuroleptic medications, and genetic factors that may influence the incidence of cancer in this group are not clear. The current study was performed to evaluate the frequency of cancer in a large cohort of patients with schizophrenia and to determine the standardized incidence ratios (SIRs) of any malignancy in this group. METHODS: Data regarding the design, setting, and participants of the current study were analyzed from a cohort of 3226 patients with schizophrenia who were enrolled in the computerized health registry of the Abarbanel Mental Health Center between 1993-2003. The mean age of the patients at the time of the diagnosis of cancer was 49 +/- 14.7 years, with the majority of patients (61%) being male. All patients with schizophrenia records in the database were combined with the records of the Israeli National Cancer Registry to identify pathologically confirmed cancer comorbidity. The cancer incidence rates among patients with schizophrenia were compared with the expected incidence in an age-matched and gender-matched general population sample for the same time interval. RESULTS: Among 1247 female patients with schizophrenia, 22 (1.8%) developed breast cancer and 68 (5.5%) developed cancers of any type. Fifty-two of the 1979 male schizophrenic patients (2.6%) developed cancer. The SIRs were 0.58 (95% confidence interval [95% CI], 0.48-0.69) with a P value of < 0.05 for all cancers in the cohort, and 0.60 (95% CI, 0.37-0.90) for female breast cancer. CONCLUSIONS: The results of the current study demonstrate a reduced risk of cancer in patients with schizophrenia. The mechanisms responsible for the lower risk need be investigated further.

Bergamo, C., Sigel, K., Mhango, G., et al. (2014). "Inequalities in lung cancer care of elderly patients with schizophrenia: an observational cohort study." Psychosom Med **76**(3): 215-220.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4747031/pdf/nihms-562566.pdf

OBJECTIVE: Cancer mortality is higher in individuals with schizophrenia, a finding that may be due, in part, to inequalities in care. We evaluated gaps in lung cancer diagnosis, treatment, and survival among elderly individuals with schizophrenia. METHODS: The Surveillance, Epidemiology, and End Results database linked to Medicare records was used to identify patients 66 years or older with primary non-small cell lung cancer. Lung cancer stage, diagnostic evaluation, and rates of stage-appropriate treatment were compared among patients with and without schizophrenia using unadjusted and multiple regression analyses. Survival was compared among groups using Kaplan-Meier methods. RESULTS: Of the 96,702 patients with non-small cell lung cancer in the Surveillance, Epidemiology, and End Results database, 1303 (1.3%) had schizophrenia. In comparison with the general population, patients with schizophrenia were less likely to present with late-stage disease after controlling for age, sex, marital status, race/ethnicity, income, histology, and comorbidities (odds ratio = 0.82, 95% confidence interval = 0.73-0.93) and were less likely to undergo appropriate evaluation ($p < .050$ for all comparisons). Adjusting for similar factors, patients with schizophrenia were also less likely to receive stage-appropriate treatment (odds ratio = 0.50, 95% confidence interval = 0.43-0.58). Survival was decreased among patients with schizophrenia (mean survival = 22.3 versus 26.3 months, $p = .002$); however, no differences were observed after controlling for treatment received ($p = .40$). CONCLUSIONS: Elderly patients with schizophrenia present with earlier stages of lung cancer but are less likely to undergo diagnostic evaluation or to receive stage-appropriate treatment, resulting in poorer outcomes. Efforts to increase treatment rates for elderly patients with schizophrenia may lead to improved survival in this group.

Borovcanin, M. M. et Vesic, K. (2021). "Breast cancer in schizophrenia could be interleukin-33-mediated." World J Psychiatry **11**(11): 1065-1074.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8613763/pdf/WJP-11-1065.pdf

Recent epidemiological and genetic studies have revealed an interconnection between schizophrenia and breast cancer. The mutual underlying pathophysiological mechanisms may be immunologically driven. A new cluster of molecules called alarmins may be involved in sterile brain inflammation, and we have already reported the potential impact of interleukin-33 (IL-33) on positive symptoms onset and the role of its soluble trans-membranes full length receptor (sST2) on amelioration of negative symptoms in schizophrenia genesis. Furthermore, these molecules have already been shown to be involved in breast cancer etiopathogenesis. In this review article, we aim to describe the IL-33/suppressor of tumorigenicity 2 (ST2) axis as a crossroad in schizophrenia-breast cancer comorbidity. Considering that raloxifene could be tissue-specific and improve cognition and that tamoxifen resistance in breast carcinoma could be improved by strategies targeting IL-33, these selective estrogen receptor modulators could be useful in complementary treatment. These observations could guide further somatic, as well as psychiatric therapeutical protocols by incorporating what is known about immunity in schizophrenia.

Bradford, D. W., Goulet, J., Hunt, M., et al. (2016). "A Cohort Study of Mortality in Individuals With and Without Schizophrenia After Diagnosis of Lung Cancer." J Clin Psychiatry **77**(12): e1626-e1630.

OBJECTIVE: Individuals with serious mental illness have increased mortality relative to those without these illnesses. Although cancer is a leading cause of death, few studies have evaluated potential disparities relative to mortality for individuals with serious mental illness who are diagnosed with cancer. In this study, we evaluated mortality after diagnosis of a common malignancy (lung cancer) in a prototypical serious mental illness (schizophrenia). METHODS: Using administrative data in the Veterans Affairs system, we identified 34,664 individuals who were diagnosed with lung cancer between October 1, 2001, and September 30, 2005. We conducted a survival analysis comparing individuals with and without ICD-9-CM schizophrenia using data through September 30, 2010. Controlling variables were age, gender, smoking status, marital status, service connection, homelessness status, and presence of a substance use disorder. RESULTS: Our results demonstrated significantly poorer survival after lung cancer diagnosis for individuals with schizophrenia compared to those without schizophrenia. The hazard ratio for all-cause mortality associated with schizophrenia was 1.33 (95% CI, 1.22-1.44). CONCLUSIONS: Individuals with schizophrenia are at higher risk of death after diagnosis of lung cancer than those without schizophrenia. Future studies should further characterize cause of death, quality of cancer care received, and barriers to care.

Brown, J. S., Jr. (2016). "Cancer Immune Equilibrium and Schizophrenia Have Similar Interferon-gamma, Tumor Necrosis Factor-alpha, and Interleukin Expression: A Tumor Model of Schizophrenia." Schizophr Bull **42**(6): 1407-1417.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5049534/pdf/sbw064.pdf

For at least a century, a debate has continued as to whether cancer risk is reduced in schizophrenia. Genetic studies have also suggested the 2 conditions may share protein transcriptional pathways. The author predicted that if the pathophysiology of schizophrenia confers protection from cancer, then the immunology of schizophrenia should reflect a state of tumor suppression, ie, the opposite of tumor escape. To examine this possibility, the author performed a literature search for measurements of cytokines in drug-naive first episode subjects with schizophrenia for comparison with cytokine expression in tumor escape vs tumor suppression. The comparison showed that instead of either tumor suppression or escape, schizophrenia appears to be in a state of tumor equilibrium. Based on this finding, the author hypothesized that the clinical presentation of schizophrenia may involve cell transformation similar to an early stage of cancer initiation or an attenuated tumorigenesis. While this condition could reflect the presence of an actual tumor such as an ovarian teratoma causing anti-NMDA receptor encephalitis, it would only explain a small percentage of cases. To find a more likely tumor model, the author then compared the cytokine profile of schizophrenia to individual cancers and found the best match was melanoma. To demonstrate the viability of the theory, the author compared the hallmarks, emerging hallmarks, and enabling characteristics of melanoma to schizophrenia and found that many findings in schizophrenia are understood if schizophrenia is a condition of attenuated tumorigenesis.

Bushe, C. J., Bradley, A. J., Wildgust, H. J., et al. (2009). "Schizophrenia and breast cancer incidence: a systematic review of clinical studies." Schizophr Res **114**(1-3): 6-16.

OBJECTIVES: Studies examining the incidence of breast cancer in schizophrenia patients report increased, reduced or similar incidence compared to the general population. We undertook a systematic review of published data to investigate possible reasons for the variable findings. METHODS: The review was conducted according to the recommendations of the Meta-Analysis of Observational Studies in Epidemiology (MOOSE) group [Stroup, D.F., Berlin, J.A., Morton, S.C., Olkin, I., Williamson, G.D., Rennie, D., Moher, D., Becker, B.J., Sipe, T.A., Thacker, S.B. 2000. Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis of Observational Studies in Epidemiology (MOOSE) group. JAMA. 283(15) 2008-2012.]. Methodological issues (Quality Markers) that may explain the variability in the data were identified. Data relating to these issues and the standard incidence rates were extracted. Results were then interpreted in relation to these quality markers. RESULTS: Data are available from over 6000 female patients with schizophrenia from 13 studies and are reported in comparison to age matched general populations from the relevant country from 1986 to 2008. Although results are widely discrepant ranging from 52% increase in risk to 40% decrease, these data may be understood in terms of cohort age, size and length of follow up as the confounders. Six of 13 studies report an increased or marginally increased incidence of breast cancer. These tend to be studies with more than 100 incident cases of breast cancer, greater than 100,000 person years follow up and older populations. CONCLUSIONS: Breast cancer may be increased in female subjects with schizophrenia. Inconsistencies in study findings may be due to methodological issues such as low statistical power and the age range of cohorts studied. There is no proven risk factor to explain these data; however reduced parity and hyperprolactinaemia may represent putative aetiological factors. Consideration of screening of female patients with schizophrenia for breast cancer is important for clinicians and researchers.

Bushe, C. J. et Hodgson, R. (2010). "Schizophrenia and cancer: in 2010 do we understand the connection?" Can J Psychiatry **55**(12): 761-767.
https://journals.sagepub.com/doi/pdf/10.1177/070674371005501203

OBJECTIVE: in recent years, there has been a plethora of cancer mortality and incidence data reported in schizophrenia. Despite this, there has been little focus on cancer in schizophrenia guidelines. Additionally, there have been suggestions that schizophrenia may provide inherent protection against cancer. The goal of this review is to establish, using recent data, the incidence and mortality rates for cancer in schizophrenia. METHOD: we identified systematic reviews and meta-analyses and undertook a search using the Medical Subject Headings' entry terms schizophrenia and neoplasm. RESULTS: incidence and mortality rates for cancer in schizophrenia are increased, compared with relevant general populations. Data are not uniformly reported and cohort ages tend to be young for expected cancer incidence. Despite the young cohort ages, the incidence of the major cancers-lung and breast-are substantially increased. Confounders are often not measured in the epidemiologic databases. When lung cancer is adjusted for smoking rates, there appears to be a lower risk of lung cancer than expected providing some basis to support an inherently reduced risk of cancer. There may also be a dissonance between incidence and mortality rates that suggest a prejudice against either diagnosis or treatment of these vulnerable patients. CONCLUSION: a single definitive study of schizophrenia and cancer is unfeasible, and future research will lean heavily on systematic review and meta-analysis. Researchers should report cancer data to include age and follow-up data and cohort overlap. Cancer accounts for almost an equivalent mortality as cardiovascular disease.

Byrne, E. M., Ferreira, M. A. R., Xue, A., et al. (2019). "Is Schizophrenia a Risk Factor for Breast Cancer?-Evidence From Genetic Data." Schizophr Bull **45**(6): 1251-1256.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6811821/pdf/sby162.pdf

Observational epidemiological studies have found an association between schizophrenia and breast cancer, but it is not known if the relationship is a causal one. We used summary statistics from very large genome-wide association studies of schizophrenia (n = 40675 cases and 64643 controls) and breast cancer (n = 122977 cases and 105974 controls) to investigate whether there is evidence that the association is partly due to shared genetic risk factors and whether there is evidence of a causal relationship. Using LD-score regression, we found that there is a small but significant genetic correlation (rG) between the 2 disorders (rG = 0.14, SE = 0.03, P = 4.75 x 10-8), indicating shared genetic risk factors.

Using 142 genetic variants associated with schizophrenia as instrumental variables that are a proxy for having schizophrenia, we estimated a causal effect of schizophrenia on breast cancer on the observed scale as bxy = 0.032 (SE = 0.009, P = 2.3 x 10-4). A 1 SD increase in liability to schizophrenia increases risk of breast cancer 1.09-fold. In contrast, the estimated causal effect of breast cancer on schizophrenia from 191 instruments was not significantly different from zero (bxy = -0.005, SE = 0.012, P = .67). No evidence for pleiotropy was found and adjusting for the effects of smoking or parity did not alter the results. These results provide evidence that the previously observed association is due to schizophrenia causally increasing risk for breast cancer. Genetic variants may provide an avenue to elucidating the mechanism underpinning this relationship.

Capasso, R. M., Lineberry, T. W., Bostwick, J. M., et al. (2008). "Mortality in schizophrenia and schizoaffective disorder: an Olmsted County, Minnesota cohort: 1950-2005." Schizophr Res **98**(1-3): 287-294.

INTRODUCTION: Increased mortality in people with schizophrenia, compared to the general population, has been consistently reported worldwide. This mortality has been attributed predominantly to "unnatural" deaths-suicide, accidents, and homicide. Recent studies have shown an increase in natural causes of death. Our objective is to compare the mortality of schizophrenic and schizoaffective subjects to the general US population. METHODS: 319 Olmsted County residents meeting DSM-IV-TR criteria for schizophrenia or schizoaffective disorder seen at the Mayo Clinic between 1950 and 1980 were followed until February 2005 for a median of 23.5 years. RESULTS: At the end of follow-up, 44% of patients were deceased. Mortality was significantly (p<0.001) increased compared to the Caucasian population in the US for persons of like age, gender, and calendar year of birth. The median survival following diagnosis was 36.2 years. Death certificate cited cause of death was cardiac (29%), cancer--including lung (19%), and pulmonary disease (17%). Concerningly, there was no association with the year of diagnosis to survival. CONCLUSIONS: Tsuang and colleagues showed in 1975 that mortality in schizophrenics and later, those with schizoaffective disorder was significantly increased compared to the US general population. Thirty years later, with a demographically similar population, we have found the same pattern of increased mortality. In light of continued improvements in the general population's lifespan, the survival gap in schizophrenia/schizoaffective disorder appears to be increasing.

Catts, V. S., Catts, S. V., O'Toole, B. I., et al. (2008). "Cancer incidence in patients with schizophrenia and their first-degree relatives - a meta-analysis." Acta Psychiatr Scand **117**(5): 323-336.
https://onlinelibrary.wiley.com/doi/10.1111/j.1600-0447.2008.01163.x

OBJECTIVE: Controversy concerning cancer incidence in schizophrenia exists because of heterogeneous study findings. METHOD: A meta-analysis was performed on standardized incidence ratios (SIR) of cancer in patients with schizophrenia and first-degree relatives and compared with general population samples. RESULTS: The pooled overall cancer incidence in patients was not significantly increased (SIR = 1.05, CI 0.95-1.15). Lung cancer incidence was slightly increased (SIR = 1.31, CI 1.01-1.71), but was reduced after adjusting for smoking prevalence. The incidence of several cancers unrelated to smoking was reduced in patients. Breast cancer rates were significantly increased in female patients. The pooled overall cancer incidence in siblings (SIR = 0.89, CI 0.84-0.94) and parents (SIR = 0.90, CI 0.88-0.93) was significantly reduced. A meta-regression detected a significant relationship between cancer risk in the general population and relative risk in patients. CONCLUSION: The meta-analysis aided exploration of inconsistent study findings. There is a discrepancy between cancer risk exposure and cancer incidence in schizophrenia consistent with a protective effect.

Chang, C. C., Hsieh, M. H., Wang, J. Y., et al. (2018). "Association between Thioridazine Use and Cancer Risk in Adult Patients with Schizophrenia-A Population-Based Study." Psychiatry Investig **15**(11): 1064-1070.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6259001/pdf/pi-2018-10-10-1.pdf

OBJECTIVE: Several cell line studies have demonstrated thioridazine's anticancer, multidrug resistance-reversing and apoptosis-inducing properties in various tumors. We conducted this nationwide population-based study to investigate the association between thioridazine use and cancer risk among adult patients with schizophrenia. METHODS: Based on the Psychiatric Inpatient Medical Claim of the National Health Insurance Research Database of Taiwan, a total of 185,689 insured psychiatric patients during 2000 to 2005 were identified. After excluding patients with prior history of schizophrenia, only 42,273 newly diagnosed patients were included. Among them, 1,631 patients ever receiving thioridazine

for more than 30 days within 6 months were selected and paired with 6,256 randomly selected non-thioridazine controls. These patients were traced till 2012/12/31 to see if they have any malignancy. RESULTS: The incidence rates of hypertension and cerebrovascular disease were higher among cases than among matched controls. The incidence of hyperlipidemia, coronary artery disease and chronic pulmonary disease did not differ between the two groups. By using Cox proportional hazard model for cancer incidence, the crude hazard ratio was significantly higher in age, hypertension, hyperlipidemia, cerebrovascular disease, coronary artery disease and chronic pulmornary disease. However, after adjusting for other covariates, only age and hypertension remained significant. Thioridazine use in adult patients with schizophrenia had no significant association with cancer. CONCLUSION: Despite our finding that thioridazine use had no prevention in cancer in adult patients with schizophrenia. Based on the biological activity, thioridazine is a potential anticancer drug and further investigation in human with cancer is warranted.

Chen, L. Y., Hung, Y. N., Chen, Y. Y., et al. (2018). "Cancer incidence in young and middle-aged people with schizophrenia: nationwide cohort study in Taiwan, 2000-2010." Epidemiol Psychiatr Sci **27**(2): 146-156. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6998952/pdf/S2045796016000883a.pdf

AIMS: For nearly a century, the incidence of cancer in people with schizophrenia was lower than in the general population. In the recent decade, the relationship between cancer and schizophrenia has become obscured. Thus, we investigated the cancer risk among young and middle-aged patients with schizophrenia. METHODS: Records of newly admitted patients with schizophrenia (n = 32 731) from January 2000 through December 2008 were retrieved from the Psychiatric Inpatient Medical Claims database in Taiwan, and the first psychiatric admission of each patient during the same period was defined as the baseline. We obtained 514 incident cancer cases that were monitored until December 2010. Standardised incidence ratios (SIRs) were calculated to compare the risk of cancer between those with schizophrenia and the general population. Stratified analyses of cancer incidences were performed by gender, site of cancers and duration since baseline (first psychiatric admission). RESULTS: The incidence of cancer for all sites was slightly higher than that of the general population for the period (SIR = 1.15 [95% CI 1.06-1.26], p = 0.001). Men had a significantly higher incidence of colorectal cancer (SIR = 1.48 [95% CI 1.06-2.06], p = 0.019). Women had a higher incidence of breast cancer (SIR = 1.47 [95% CI 1.22-1.78], p < 0.001). Intriguingly, the risk for colorectal cancer was more pronounced 5 years after the first psychiatric admission rather than earlier (SIR = 1.94 [1.36-2.75], p < 0.001) and so was the risk for breast cancer (SIR = 1.85 [1.38-2.48], p < 0.001). The cancer incidence was higher in patients with schizophrenia contradicting the belief that schizophrenia was protective of cancers. CONCLUSIONS: Our analyses suggest that men and women with schizophrenia were more vulnerable to certain types of cancers, which indicates the need for gender-specific cancer screening programs. The fact that risk of colorectal cancer was more pronounced 5 years after the first psychiatric admission could imply the impact of unhealthy lifestyles or the possibility of delayed diagnoses.

Chen, S. F., Yang, Y. C., Hsu, C. Y., et al. (2021). "Risk of schizophrenia in patients with polycystic ovary syndrome: a nationwide population-based cohort study from Taiwan." J Psychosom Obstet Gynaecol **42**(4): 272-278. https://www.tandfonline.com/doi/full/10.1080/0167482X.2020.1735342

OBJECTIVES: To investigate whether patients with polycystic ovary syndrome (PCOS) are at increased risk for incident schizophrenia and whether PCOS treatment (clomiphene, cyproterone, or metformin) affects the incidence of schizophrenia. METHODS: An overall of 7146 PCOS patients and 28,580 non-PCOS controls matched by age, index year, and Charlson Comorbidity Index (CCI) score were included between 2000 and 2012 and followed up until 2013 using a validated nationally representative sample from Taiwan. Participants newly diagnosed as schizophrenia were defined as incidents. Cox regression analysis was used to calculate the hazard ratio (HR) with a 95% confidence interval (CI) of the schizophrenia incidence rate between the two studied groups. RESULTS: PCOS patients were at increased risk of incident schizophrenia compared to non-PCOS controls after adjusting for age, CCI score, comorbidities, and different treatment options (0.49 versus 0.09 per 1000 person-years, HR: 6.93, 95% CI: 3.25-14.7). After adjusting for above-mentioned covariates, metformin treatment had a protective effect against the incident schizophrenia compared to non-users (HR: 0.16, 95% CI: 0.06-0.41). Also, treatment with clomiphene and cyproterone had only a limited impact on the incident schizophrenia. CONCLUSION: This study shows PCOS patients are at increased risk of incident schizophrenia, and the metformin treatment has a protective effect against incident schizophrenia.

Chochinov, H. M., Martens, P. J., Prior, H. J., et al. (2009). "Does a diagnosis of schizophrenia reduce rates of mammography screening? A Manitoba population-based study." Schizophr Res **113**(1): 95-100.

Chou, F. H., Tsai, K. Y., Su, C. Y., et al. (2011). "The incidence and relative risk factors for developing cancer among patients with schizophrenia: a nine-year follow-up study." Schizophr Res **129**(2-3): 97-103.

OBJECTIVE: To estimate the incidence and relative risk of developing cancer as well as the mortality rate after cancer diagnosis for patients with schizophrenia compared with the general population. METHODS: Our population for this study was identified before the end of 1999. The study included 59,257 patients with schizophrenia and 178,156 age- and gender-matched individuals without schizophrenia as controls, who were selected from the 23,981,020 subjects in the National Health Insurance Research Database (NHIRD), which consists of 96% of the entire Taiwanese population. From the 2000 to 2008 NHIRD, we calculated the cancer incidence and survival time after cancer diagnosis in each of the two groups. Based on the International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM), the cancers were divided into nine groups. RESULTS: During the nine-year follow-up period, 1145 (1.93%) of the patients with schizophrenia and 5294 (2.97%) of the control group developed cancer. The patients with schizophrenia had a significantly lower cancer incidence than those in the control group in both the male (OR=0.50, 95% CI, 0.46-0.55) and female (OR=0.81, 95% CI, 0.74-0.88) populations. Patients with schizophrenia were less likely to develop cancer than individuals in the control group for every cancer type except breast and cervical/uterine cancer. After adjustment using the Cox regression model, patients with schizophrenia had an overall decreased cancer risk (adjusted hazard ratio 0.71, 95% CI, 0.66-0.76) compared to the control population. For all cancer patients, the mortality adjusted hazard ratio for patients with schizophrenia versus the control group was 1.36 (95% CI, 1.24-1.50) after adjusting for other variables. CONCLUSIONS: Although the likelihood of developing cancer among patients with schizophrenia (0.64) was less than that of the non-schizophrenia group, the mortality rate among patients with schizophrenia was higher than that of the control group.

Chou, F. H., Tsai, K. Y., Wu, H. C., et al. (2016). "Cancer in patients with schizophrenia: What is the next step?" Psychiatry Clin Neurosci **70**(11): 473-488.
https://onlinelibrary.wiley.com/doi/pdfdirect/10.1111/pcn.12420?download=true

People with schizophrenia, who constitute approximately 0.3-1% of the general population, have a nearly 20% shorter life expectancy than the general population. The incidence of varied types of cancers in patients with schizophrenia is controversial. The majority of previous research has demonstrated that patients who have schizophrenia and cancer have early mortality compared to the general population with cancer. The causes of early mortality in patients with schizophrenia and cancer might be attributed to a lower cancer screening rate and lack of effective treatment, including: (i) patient factors, such as poor lifestyle, passive attitude toward treatment, or comorbidity; (ii) physician factors, such as physician bias, which may decrease the delivery of care for individuals with mental disorders; and (iii) hospital administration factors, such as stigma and discrimination. Additional studies on patients with schizophrenia and cancer are warranted and should include the following: a comprehensive review of previous studies; a focus on differentiating the specific types of cancer; and methods for improvement. To decrease the early mortality of patients with schizophrenia, the following measures are proposed: (i) enhance early detection and early treatment, such as increasing the cancer screening rate for patients with schizophrenia; (ii) provide effective, timely treatment and rehabilitation; (iii) improve patients' psychiatric symptoms and cognitive impairment; (iv) promote healthy behavior in the general population and emphasize healthy lifestyles in vulnerable populations; and (v) remove the stigma of schizophrenia. To reduce disparities in physical health, public health strategies and welfare policies must continue to focus on this group of patients.

Coakley, D. V. (1979). "No lung cancer in schizophrenics?" Br J Psychiatry **134**: 649.
https://www.cambridge.org/core/services/aop-cambridge-core/content/view/B7A2FDF94AFBA35EC1D6D8C6365835D4/S0007125000059614a.pdf/div-class-title-no-lung-cancer-in-schizophrenics-div.pdf

Cohen, M., Dembling, B. et Schorling, J. (2002). "The association between schizophrenia and cancer: a population-based mortality study." Schizophr Res **57**(2-3): 139-146.

BACKGROUND: For most of this century there has been speculation that persons diagnosed with schizophrenia have a reduced incidence of cancer. OBJECTIVE: To determine if a history of cancer was more common in persons diagnosed with schizophrenia when compared with the general population, controlling for known risk and demographic factors. DESIGN: We used the 1986 National Mortality Followback Survey (NMFS) which sampled 1% of all deaths in the US from that year. Data were obtained from death certificates and records of hospitalizations in the last year of life. Additional health and demographic data were obtained through interviews with decedents' families and other informants. We compared persons diagnosed with schizophrenia (n=130) to individuals without schizophrenia (n=18,603) and used logistic regression to determine the odds ratio for the occurrence of cancer in persons diagnosed with schizophrenia. Adjustment for age at death was done to correct for the fact that persons diagnosed with schizophrenia die on average 10 years younger than the general population. MAIN OUTCOME MEASURE: A diagnosis of cancer on a hospital record or the death certificate. RESULTS: The unadjusted odds ratio for cancer among individuals with schizophrenia was 0.62 (95% confidence interval (CI) 0.40-0.96). After controlling for age, race, gender, marital status, education, net worth, smoking, and hospitalization in the year before death, we determined that the odds ratio for the diagnosis of cancer in persons with schizophrenia was 0.59 (95% CI 0.38-0.93). CONCLUSION: In this population-based study, we demonstrated a reduced risk of cancer among persons diagnosed with schizophrenia.

Cole, M. et Padmanabhan, A. (2012). "Breast cancer treatment of women with schizophrenia and bipolar disorder from Philadelphia, PA: lessons learned and suggestions for improvement." J Cancer Educ **27**(4): 774-779. https://link.springer.com/article/10.1007/s13187-012-0391-7

Treating cancer in patients with concurrent severe mental illness is complex and challenging for patients, families, and health care providers. Two such illnesses include schizophrenia and bipolar disorder. In this review, cases of women with breast cancer and severe mental illness from Philadelphia, PA illustrate the obstacles these women face in maintaining adequate cancer care. Barriers to receiving cancer treatment include understanding their disease, continuing medications and appointments, and experiencing complications of their psychiatric disorders. Learning from these cases is critical for health care providers and allows for innovation in treating and educating this difficult population. Increasing patient visit time, using social support services, and psychiatrist and psychiatrist-liaisons are necessary to improve care. In addition, family or caregivers should be included in discussions when possible. These techniques will assist in educating patients, improve insight into their disease and treatment, and allow them to benefit from cancer therapy.

Crump, C., Winkleby, M. A., Sundquist, K., et al. (2013). "Comorbidities and mortality in persons with schizophrenia: a Swedish national cohort study." Am J Psychiatry **170**(3): 324-333.

OBJECTIVE: Schizophrenia is associated with premature mortality, but the specific causes and pathways are unclear. The authors used outpatient and inpatient data for a national population to examine the association between schizophrenia and mortality and comorbidities. METHOD: This was a national cohort study of 6,097,834 Swedish adults, including 8,277 with schizophrenia, followed for 7 years (2003-2009) for mortality and comorbidities diagnosed in any outpatient or inpatient setting nationwide. RESULTS: On average, men with schizophrenia died 15 years earlier, and women 12 years earlier, than the rest of the population, and this was not accounted for by unnatural deaths. The leading causes were ischemic heart disease and cancer. Despite having twice as many health care system contacts, schizophrenia patients had no increased risk of nonfatal ischemic heart disease or cancer diagnoses, but they had an elevated mortality from ischemic heart disease (adjusted hazard ratio for women, 3.33 [95% CI=2.73-4.05]; for men, 2.20 [95% CI=1.83-2.65]) and cancer (adjusted hazard ratio for women, 1.71 [95% CI=1.38-2.10; for men, 1.44 [95% CI=1.15-1.80]). Among all people who died from ischemic heart disease or cancer, schizophrenia patients were less likely than others to have been diagnosed previously with these conditions (for ischemic heart disease, 26.3% compared with 43.7%; for cancer, 73.9% compared with 82.3%). The association between schizophrenia and mortality was stronger among women and the employed. Lack of antipsychotic treatment was also associated with elevated mortality. CONCLUSIONS: Schizophrenia patients had markedly premature mortality, and the leading causes were ischemic heart disease and cancer, which appeared to be underdiagnosed. Preventive interventions should prioritize

primary health care tailored to this population, including more effective risk modification and screening for cardiovascular disease and cancer.

Dalton, S. O., Laursen, T. M., Mellemkjaer, L., et al. (2004). "Risk for cancer in parents of patients with schizophrenia." Am J Psychiatry **161**(5): 903-908.

OBJECTIVE: This study attempted to determine whether a genetic protection against cancer might be manifest in parents of offspring with schizophrenia. METHOD: Using data from the Danish Central Population Registry, the authors identified 1,999,072 parents of offspring born after 1935. By linking this nationwide population-based parent cohort to the Danish Psychiatric Central Register, they identified 19,856 parents of offspring with schizophrenia. Follow-up for cancer in the Danish Cancer Registry began on the date of birth of the oldest child or April 1, 1969, and ended on the date of cancer diagnosis, death, or Dec. 31, 1997, yielding a total of 48,343,430 person-years at risk and 211,681 cases of cancer. The relative risk for cancer among parents with schizophrenic offspring compared to parents with no schizophrenic offspring was estimated by Poisson regression analysis and adjusted for age, period, and number of children. RESULTS: The risk for all cancer was 1.01 for fathers and 1.00 for mothers of schizophrenics. Mothers of schizophrenic patients had an increased risk of 1.20 for lung cancer and a nonsignificant risk of 1.14 for tobacco-related cancers combined. Apart from a reduced risk for leukemia in both mothers and fathers of schizophrenics, there was no difference in risk for any other cancer. DISCUSSION: This study does not confirm a previously reported reduced risk for cancer in parents of schizophrenic patients and provides no support for genetic protection against cancer in families with schizophrenia.

Dalton, S. O., Mellemkjaer, L., Thomassen, L., et al. (2005). "Risk for cancer in a cohort of patients hospitalized for schizophrenia in Denmark, 1969-1993." Schizophr Res **75**(2-3): 315-324.

We investigated the cancer risk of patients hospitalized for schizophrenia in a nationwide cohort study. All 22766 adults admitted for schizophrenia, ICD-8 295, in Denmark between 1969 and 1993 were followed up for cancer through 1995. The incidence of site-specific cancers was compared with national incidence rates, adjusted for sex, age and calendar time. The risk for cancer was increased for both men and women during the first year of follow-up. When the first year of follow-up was excluded, the risk for all tobacco-associated cancers and for prostate and rectal cancers was reduced for male patients with schizophrenia. The standardized incidence ratio (SIR) of lung cancer was marginally reduced (SIR, 0.86; 95% CI: 0.65, 1.02) for male patients with schizophrenia; this was due, however, to a reduction in risk for older patients. An increased risk for breast cancer found for female patients with schizophrenia (SIR, 1.20; 95% CI: 1.05, 1.38) should be interpreted with caution, given the high proportion of nulliparous women with schizophrenia in Denmark. The data might support reduced risks for prostate and rectal cancer among male patients with schizophrenia, whereas a changing smoking pattern might explain the reduced risk for tobacco-related cancers.

Dalton, S. O., Suppli, N. P., Ewertz, M., et al. (2018). "Impact of schizophrenia and related disorders on mortality from breast cancer: A population-based cohort study in Denmark, 1995-2011." Breast **40**: 170-176. https://www.thebreastonline.com/article/S0960-9776(18)30106-1/fulltext

OBJECTIVES: To investigate overall and breast cancer-specific mortality in early-stage breast cancer patients with and without schizophrenia or related disorders. METHODS: We used Danish national registers to identify all women with no prior history of cancer or organic mental disorders, who were diagnosed with early-stage breast cancer 1995-2011. Logistic regression models were used to calculate the odds ratios (ORs) for not being allocated to guideline treatment. Cox regression models were used to compute hazard ratios (HRs) for overall and breast cancer-specific deaths among women allocated or not allocated to guideline treatment. RESULTS: We identified 56,152 women with early-stage breast cancer diagnosed in 1995-2011, of whom 499 women also had been diagnosed with schizophrenia or related disorders. The likelihood of women with schizophrenia or related disorders for not being allocated to guideline treatment was increased (adjusted OR, 1.50; 95% confidence interval (CI), 1.15-1.94). The adjusted HR for all-cause mortality was 1.55; 95% CI, 1.32-1.82 and 1.12 (95% CI, 0.98-1.50) for breast cancer-specific mortality; women allocated to guideline treatment had an adjusted HR for breast cancer-specific death of 1.42 (95% CI, 1.11-1.82). The adjusted HR for death due to unnatural causes was 3.67 (95% CI, 1.80-7.35). CONCLUSION: The survival of women with schizophrenia or related disorders after

breast cancer is significantly worse than that of women without these disorders. These patients are less likely to be allocated to guideline treatment, and, among those who are, mortality from both breast cancer and other causes is increased.

Damjanovic, A., Ivkovic, M., Jasovic-Gasic, M., et al. (2006). "Comorbidity of schizophrenia and cancer: clinical recommendations for treatment." Psychiatr Danub **18**(1-2): 55-60.

The paper analyzes some issues on the comorbidity between schizophrenia and cancer. Epidemiological studies have reported contradictory results, but it is certain that patients with schizophrenia are more likely to suffer from risk factors for cancer development, such as increased alcohol abuse, obesity, nicotine dependence and decreased physical activity. The paper gives guidelines for the treatment of cancer in patients with schizophrenia, and discusses possible interactions between chemotherapy and psychotropic drugs. Particular attention is paid to the use of antipsychotics which increase the level of prolactin, in view of the possible risk of breast and endometrial cancer in patients with schizophrenia.

De Hert, M., Peuskens, J., Sabbe, T., et al. (2016). "Relationship between prolactin, breast cancer risk, and antipsychotics in patients with schizophrenia: a critical review." Acta Psychiatr Scand **133**(1): 5-22. https://onlinelibrary.wiley.com/doi/10.1111/acps.12459

OBJECTIVE: A recent meta-analysis showed that breast cancer probably is more common in female patients with schizophrenia than in the general population (effect size = 1.25, P < 0.05). Increasing experimental and epidemiological data have alerted researchers to the influence of prolactin (PRL) in mammary carcinogenesis. We therefore investigated the possible relationship between antipsychotic-induced hyperprolactinemia (HPRL) and breast cancer risk in female patients with schizophrenia. METHOD: A literature search (1950 until January 2015), using the MEDLINE database, was conducted for English-language published clinical trials to identify and synthesize data of the current state of knowledge concerning breast cancer risk (factors) in women with schizophrenia and its (their) relationship between HPRL and antipsychotic medication. RESULTS: Although an increasing body of evidence supports the involvement of PRL in breast carcinogenesis, results of human prospective studies are limited, equivocal, and correlative (with risk ratios ranging from 0.70 to 1.9 for premenopausal women and from 0.76 to 2.03 for postmenopausal women). Moreover, these studies equally do not take into account the local production of PRL in breast epithelium, although amplification or overexpression of the local autocrine/paracrine PRL loop may be a more important mechanism in tumorigenesis. Until now, there is also no conclusive evidence that antipsychotic medication can increase the risk of breast malignancy and mortality. CONCLUSION: Other breast risk factors than PRL, such as nulliparity, obesity, diabetes mellitus, and unhealthy lifestyle behaviours (alcohol dependence, smoking, low physical activity), probably are of greater relevance in individual breast cancer cases within the population of female patients with schizophrenia.

du Pan, R. M. et Muller, C. (1977). "[Cancer mortality in patients of psychiatric hospitals]." Schweiz Med Wochenschr **107**(17): 597-604.

Studies on cancer mortality in psychiatric patients, especially schizphrenics, are reviewed. The divergences between these studies may be partially explained by the different statistical methods employed. It is difficult to compare the populations observed, due to the influence of such elements as the method of sampling, the period of observation of psychotic patients, diagnostic methods and criteria etc. On the whole, it is concluded that no major difference could be demonstrated with certainty between a non-selected population of psychotic patients (excluding psychoorganic cases) and the general population. With regard to schizophrenics, the hypothesis of a lower mortality from cancer cannot be ruled out on the grounds of studies carried out at the Lausanne psychiatric clinic. However, reports on cancer incidence have not yet confirmed this hypothesis and further studies are needed to verify it. Various factors are discussed which may modify cancer risk in psychiatric patients in hospital such as tobacco, food, sexual activity, neuropleptics, and biochemical and immunological factors. Lastly, the psychosomatic hypothesis of carcinogenesis is discussed in the framework of this review.

Dynes, J. B. (1969). "Cause of death in schizophrenia." Behav Neuropsychiatry **1**(2): 12-14.

Farasatpour, M., Janardhan, R., Williams, C. D., et al. (2013). "Breast cancer in patients with schizophrenia." Am J Surg **206**(5): 798-804.
https://www.americanjournalofsurgery.com/article/S0002-9610(13)00225-0/fulltext

BACKGROUND: Schizophrenia has a powerful impact on the outcomes of treatment for physical disorders. This study sought to estimate how the presence of schizophrenia disrupts the course of diagnosis and initial treatment of breast cancer. METHODS: We searched the Patient Treatment File, a comprehensive computer-based system for inpatient data in the Department of Veterans Affairs (DVA) medical system, to identify patients with codes for schizophrenia or schizoaffective disorder who later developed breast cancer. These data were augmented with chart-based clinical data. RESULTS: There were 56 evaluable patients from 34 DVA facilities; 37 (66%) were female. Delay in diagnosis was common. The mean size of the primary tumor was 4 cm in those for whom these data were recorded. Delay in diagnosis was common and many never received the indicated surgery. Distant metastases were present on diagnosis in 12 (21%) and developed after diagnosis in 14 (25%) others, including 7 who inappropriately delayed or refused indicated surgery and 4 who inappropriately delayed or refused indicated neoadjuvant chemotherapy. Twelve verbally abused or physically attacked caregivers. CONCLUSIONS: Patients with schizophrenia who later develop breast cancer often deny they have cancer. They often have high-stage disease at diagnosis and often delay or refuse therapy. Breast-conserving multimodality therapy is often not feasible.

Foster, H. D. et Hoffer, A. (2004). "Schizophrenia and cancer: the adrenochrome balanced morphism." Med Hypotheses **62**(3): 415-419.

Cancer might be expected to be more common amongst schizophrenics than the general population. They frequently live in selenium deficient regions, have seriously compromised antioxidant defense systems and chain-smoke. The available literature on the cancer-schizoprenia relationship in patients from England, Wales, Ireland, Denmark, USA and Japan, however, strongly suggests that the reverse is true. One of the authors (Hoffer) has treated 4000 schizophrenics since 1952. Only four of these patients has developed cancer. Since low cancer incidence has been recorded amongst patients treated by both conventional physicians using pharmaceuticals and by orthomolecular doctors who emphasize vitamins and minerals, it follows that this depressed cancer incidence must be related to the biochemistry of the disorder itself. Taken as a whole, therefore, the evidence seems to suggest that schizophrenics, their siblings and parents are less susceptible to cancer than the general population. These relationships seem compatible with one or more genetic risk factors for schizophrenia that offer(s) a selective advantage against cancer. There is experimental evidence that appears to support this possibility. Matrix Pharmaceuticals Inc. has received a US patent covering the composition of IntraDose Injectable Gel. This gel contains cisplatin and epinephrine (adrenaline) and is designed to be injected directly into tumour masses. Cisplatin is a very powerful oxidant which will almost certainly rapidly convert the adrenaline to adrenochrome. While the manufacturers of IntraDose consider cisplatin to be the active cytotoxic agent in IntraDose, it seems more likely that adrenochrome and its derivatives may, in fact, be more effective. IntraDose gel has undergone or is undergoing a series of Phase III open-label clinical studies, being injected into patients' tumours that have been identified as the most troublesome by their physicians. The results have been impressive for breast cancer, malignant melanoma, esophageal cancer and cancer of the head, neck and liver. The evidence suggests that there are balanced morphisms in schizophrenia that result in above normal exposure to catecholamine derivatives. Since such catecholamines are both hallucinogenic and anticarcinogenic abnormally high exposure to them simultaneously increases susceptibility to schizophrenia and reduces the probability of developing cancer. These observations have significant implications for the treatment of both illnesses.

Fujiwara, M., Inagaki, M., Nakaya, N., et al. (2017). "Cancer screening participation in schizophrenic outpatients and the influence of their functional disability on the screening rate: A cross-sectional study in Japan." Psychiatry Clin Neurosci **71**(12): 813-825.
https://onlinelibrary.wiley.com/doi/pdfdirect/10.1111/pcn.12554?download=true

AIM: The influence of schizophrenic patients' functional disability on cancer screening participation worldwide is unclear. There are few findings on the disparities in schizophrenic patients' participation in cancer screening programs in Asia. The aim of this study was to investigate the screening rate and the

associations between screening and symptom severity/functional disability in patients with schizophrenia. METHODS: This cross-sectional study was conducted in a psychiatric hospital outpatient clinic in Japan. We recruited schizophrenic patients meeting the national program criteria for cancer screening for colorectal, gastric, lung, breast, and cervical cancer (n = 224, 223, 224, 110, and 175, respectively). Receipt of cancer screenings was assessed using a self-report questionnaire. Scores on the modified Global Assessment of Functioning (mGAF) were evaluated by participants' primary psychiatrists. RESULTS: Rates of cancer screenings were as follows: 24.1% for colorectal, 21.5% for gastric, 30.8% for lung, 25.5% for breast, and 19.4% for cervical cancer. A multivariable logistic analysis showed that a 1-point increase in severity/disability (100 minus mGAF score) was associated with significantly lower odds ratios (OR) for receipt of cancer screenings, except for breast cancer (OR, 0.95, 95% confidence interval [CI], 0.93-0.98 for colorectal; OR, 0.96, 95%CI, 0.93-0.98 for gastric; OR, 0.95, 95%CI, 0.93-0.97 for lung; OR, 0.97, 95%CI, 0.94-1.00 for breast; and OR, 0.95, 95%CI, 0.92-0.98 for cervical cancer). CONCLUSION: The findings demonstrated low rates of cancer screenings in schizophrenic patients in Japan. Our study suggests the need to encourage attendance at cancer screenings, especially in schizophrenic patients with severe symptoms/functional disability.

Fujiwara, M., Inagaki, M., Shimazu, T., et al. (2019). "A randomised controlled trial of a case management approach to encourage participation in colorectal cancer screening for people with schizophrenia in psychiatric outpatient clinics: study protocol for the J-SUPPORT 1901 (ACCESS) study." BMJ Open **9**(11): e032955. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6830660/pdf/bmjopen-2019-032955.pdf

INTRODUCTION: One of the reasons for the high mortality rate from cancer in people with schizophrenia is delay in diagnosis. Many studies have shown lower cancer screening rates in people with schizophrenia; however, there are no interventions for people with schizophrenia to increase cancer screening. Therefore, we developed a case management (CM) intervention to encourage participation in cancer screening. The purpose of this study was to examine the efficacy of CM to encourage participation in cancer screening for people with schizophrenia, with particular focus on colorectal cancer screening by faecal occult blood testing, compared with usual intervention (UI), namely, municipal public education. METHODS AND ANALYSIS: This is an individually randomised, parallel group trial with blinded outcome assessments. The participants will be randomly allocated to either the CM plus UI group or UI alone group in a 1:1 ratio using a web-based program at a data management centre. The primary end point of the study is participation in colorectal cancer screening in the year of intervention, which will be assessed based on municipal records. ETHICS AND DISSEMINATION: This study is performed in accordance with Ethical Guidelines for Medical and Health Research Involving Human Subjects published by Japan's Ministry of Education, Science, and Technology and the Ministry of Health, Labour, and Welfare and the modified Act on the Protection of Personal Information as well as the Declaration of Helsinki. This study was approved by the institutional ethics committee at the Okayama University Graduate School of Medicine, Dentistry, and Pharmaceutical Sciences and Okayama University Hospital on 23 April 2019 (approval number: RIN1904-003). The findings of this trial will be submitted to an international peer-reviewed journal. TRIAL REGISTRATION NUMBER: UMIN000036017.

Fujiwara, M., Yamada, Y., Shimazu, T., et al. (2021). "Encouraging participation in colorectal cancer screening for people with schizophrenia: A randomized controlled trial." Acta Psychiatr Scand **144**(4): 318-328. https://onlinelibrary.wiley.com/doi/10.1111/acps.13348

OBJECTIVE: We examined the efficacy of a case management approach to improve participation in colorectal cancer screening among people with schizophrenia. METHODS: This was a randomized, parallel group trial. We recruited outpatients with schizophrenia aged 40 years or over from two psychiatric hospitals in Japan. Participants were randomly assigned (1:1) to treatment as usual or case management intervention plus treatment as usual using a web-based system. Attending clinicians and participants were unmasked to the allocation. Case management included education and patient navigation for colorectal cancer screening using a fecal occult blood test. Treatment as usual included direct mail government recommendations. The primary endpoint was participation in colorectal cancer screening assessed using municipal records. We also assessed the secondary endpoint of participation in other cancer screenings (lung, gastric, breast, and cervical). RESULTS: Between 3 June and 9 September 2019, 172 eligible participants were randomly assigned to the case management plus treatment as usual group (n = 86) or treatment as usual group (n = 86). One participant was ineligible and another withdrew consent; both were excluded from analysis. A significantly higher proportion of participants received

colorectal cancer screening in the case management plus treatment as usual group than in the treatment as usual group (40 [47.1%] of 85 participants vs. 10 [11.8%] of 85 participants, p < 0.0001). The proportion of lung cancer screening also increased. No serious adverse events associated with the study intervention occurred. CONCLUSION: The case management intervention to encourage participation in colorectal cancer screening was effective for patients with schizophrenia.

Gal, G., Goral, A., Murad, H., et al. (2012). "Cancer in parents of persons with schizophrenia: is there a genetic protection?" Schizophr Res **139**(1-3): 189-193.

A reduced risk for cancer has been noted among persons with schizophrenia as well as their first degree relatives. One explanation for these findings suggests that genes associated with schizophrenia confer reduced cancer susceptibility. Given the well documented genetic factor in schizophrenia it could thus be expected that cancer incidence rates should be lower in persons with schizophrenia with a known family history of schizophrenia compared to persons with sporadic schizophrenia, as well as their first degree relatives. This study investigated the risk for cancer among the biological parents of persons with schizophrenia accounting for the familial aggregation. Linkage was conducted between national population, psychiatric and cancer databases. Standardized incidence rates for all cancer sites were calculated by comparing the parents' rates with those of the general population. In addition, the association between familial aggregation of schizophrenia and risk for cancer was calculated among the parents. A reduced cancer risk was found among the parents compared to the general population (SIR 0.8, 95% CI 0.8-0.9). However, no evidence of decreased risk was associated with familial schizophrenia. Thus, no association between familial aggregation and cancer incidents was found with regard to most cancer sites. Moreover, a small, but not statistically significant increased risk of colon cancer was associated with familial aggregation scores among the parents (OR 1.2, 95% CI 1.0-1.5). These findings undermine the support to the genetic explanation for the reduced risk for cancer in schizophrenia among patients and their biological parents.

Galzigna, L. (1980). "Hypothesis on illnesses depending on state transition in cooperative systems: relevance to cancer and schizophrenia." Med Hypotheses **6**(3): 269-276.

1. There are some remarkable analogies between neoplastic growth of tissue cells and other pathological events such as functional alterations of the central nervous system resulting in schizophrenic behaviour. 2. Body tissues in general and the central nervous system in particular are highly cooperative systems which can undergo state transitions at critical points. 3. Circadian rhythms may be regarded as giant fluctuations near a critical point. 4. Temperature shifts and changes of other environmental conditions can induce reversible state transitions whose occurrence is indeterminate but whose progress, once they have occurred, is inevitable. 5. Hypothermia may be a useful form of treatment of illnesses such as cancer, that can be reversed, since it is a mean of bringing a system back to its equilibrium. 6. If we assume that characters such as vitamin dependency are gentically transmitted we may envisage that homozygotes for that character have a phenotypic expression which may lead to high probabilities of developing schizophrenia and cancer at two different ages as a result of environment-dependent phase transitions.

Galzigna, L., Bossi, M. et Burlina, A. (1974). "Parrallel enzymatic changes detectable in cancer and schizophrenic patients as a possible result of environmental stimulation." Agressologie **15**(3): 197-202.

Ganzini, L., Socherman, R., Duckart, J., et al. (2010). "End-of-life care for veterans with schizophrenia and cancer." Psychiatr Serv **61**(7): 725-728.

OBJECTIVE: This study compared the quality of end-of-life care between veterans with and without schizophrenia who died of cancer in the northwestern United States. METHODS: In this cross-sectional study, medical records of 60 veterans with schizophrenia and 196 with no major mental illness who died of cancer were compared on hospice enrollment, palliative and life-sustaining interventions, advance directives, and site of death. RESULTS: Among veterans with schizophrenia, 58% had an advance directive, 73% received an opiate before hospice enrollment, 63% had a physician order to forgo cardiopulmonary resuscitation, 55% were hospice enrolled, and 27% died in the hospital. Schizophrenia patients had longer hospice stays (107+/-144 versus 63+/-96 days, p=.05) and more physician orders for life-sustaining treatment (15% versus 5%, p=.006) compared with veterans without mental illness.

CONCLUSIONS: On most measures, veterans with schizophrenia who died of cancer received comparable or better end-of-life care than veterans without mental illness.

Ge, F., Huo, Z., Liu, Y., et al. (2022). "Association between schizophrenia and prostate cancer risk: Results from a pool of cohort studies and Mendelian randomization analysis." Compr Psychiatry **115**: 152308. https://www.sciencedirect.com/science/article/pii/S0010440X22000141?via%3Dihub

BACKGROUND: Observational studies analyzing the risk of prostate cancer in schizophrenia patients have generated mixed results. We performed a meta-analysis and a Mendelian randomization (MR) analysis to evaluate the relationship and causality between schizophrenia and the risk of prostate cancer. METHODS: A comprehensive and systematic search of cohort studies was conducted, and a random-effects model meta-analysis was performed to calculate the standardized incidence ratios (SIRs) for prostate cancer incidence among schizophrenia patients versus the general population. To investigate the correlation between genetically-predicted schizophrenia and prostate cancer risk, we used summary statistics from the Prostate Cancer Association Group to Investigate Cancer Associated Alterations in the Genome (PRACTICAL) consortium (61,106 controls and 79,148 cases), and 75 schizophrenia-associated single nucleotide polymorphisms (SNP) from European descent as the instrumental variable. RESULTS: In the meta-analysis of 13 cohort studies with 218,076 men involved, a decreased risk of prostate cancer was observed among schizophrenia patients [SIR 0.610; 95% confidence interval (CI) 0.500-0.740; p < 0.001] with significant heterogeneity (I(2) = 83.3%; p < 0.001). However, MR analysis did not sustain the link between genetically-predicted schizophrenia and prostate cancer [odds ratio (OR) 1.033; 95% CI 0.998-1.069; p = 0.065]. The result was robust against extensive sensitivity analyses. CONCLUSIONS: Our study indicated a decreased risk of prostate cancer in schizophrenia patients through meta-analysis, while MR analysis did not support the connection between schizophrenia and prostate cancer. Due to the interaction of genetic variants between binary exposures, we need to be cautious in interpreting and presenting causal associations. Moreover, further research is needed to investigate underlying factors that might link schizophrenia to the risk of prostate cancer.

Goldacre, M. J., Kurina, L. M., Wotton, C. J., et al. (2005). "Schizophrenia and cancer: an epidemiological study." Br J Psychiatry **187**: 334-338. https://www.cambridge.org/core/services/aop-cambridge-core/content/view/9EC8C368AD6D3E931E9011B48F0B819B/S0007125000168035a.pdf/div-class-title-schizophrenia-and-cancer-an-epidemiological-study-div.pdf

BACKGROUND: For decades there has been interest in the possibility that people with schizophrenia might have some protection against cancer, and that, if this were so, it might hold clues about aetiological mechanisms in schizophrenia. AIMS: To study cancer incidence in schizophrenia. METHOD: Cohort analysis of linked hospital and death records was used to compare cancer rates in people with schizophrenia with a reference cohort. RESULTS: We did not find a reduced risk for cancer overall (rate ratio 0.99,95% CI 0.90-1.08) or for most individual cancers. There was, however, a significantly low rate ratio for skin cancer (0.56,95% CI 0.36-0.83). CONCLUSIONS: We found no evidence that schizophrenia confers protection against cancer in general. Low rates of cancer are consistent with the hypothesis that sun exposure may influence the development of schizophrenia, although other explanations are also possible.

González-Rodríguez, A., Labad, J. et Seeman, M. V. (2020). "Schizophrenia and cancer." Curr Opin Support Palliat Care **14**(3): 232-238.

PURPOSE OF REVIEW: The cancer mortality rate in persons with schizophrenia is higher than it is in the general population. The purpose of this review is to determine why, and to identify solutions. RECENT FINDINGS: The recent literature points to three groups of reasons why mortality is high: patient reasons such as nonadherence to treatment, provider reasons such as diagnostic overshadowing, and health system reasons such as a relative lack of collaboration between medicine and psychiatry. Strategies for cancer prevention, early detection, and effective treatment are available but difficult to put into practice because of significant barriers to change, namely poverty, cognitive and volitional deficits, heightened stress, stigma, and side effects of antipsychotic medication. The literature makes recommendations about surmounting these barriers and also offers suggestions with respect to support and palliative care in advanced stages of cancer. Importantly, it offers examples of effective collaboration between mental

health and cancer care specialists. SUMMARY: The high mortality rate from cancer in the schizophrenia population is a matter of urgent concern. Although reasons are identifiable, solutions remain difficult to implement. As we work toward solutions, quality palliative care at the end of life is required for patients with severe mental illness. VIDEO ABSTRACT.

Grinshpoon, A., Barchana, M., Ponizovsky, A., et al. (2005). "Cancer in schizophrenia: is the risk higher or lower?" Schizophr Res **73**(2-3): 333-341.

Studies exploring the relationship between schizophrenia and cancer have shown conflicting results. Our study explores this association in three Jewish-Israeli population groups defined by their continent/place of birth (Israel, Europe-America, and Africa-Asia). The identification of the patients was made through the linkage of the nationwide psychiatric and cancer registries. The incidence of cancer in patients diagnosed with schizophrenia was compared with the incidence in the general population. The results showed that the cancer standardized incidence ratios (SIRs) for all sites were significantly lower among men and women with schizophrenia, 0.86 [95% confidence interval (CI) 0.80-0.93] and 0.91 (95% CI 0.85-0.97), respectively. This reduced overall risk was clearest for those born in Europe-America, both men (SIR 0.85, 95% CI 0.74-0.97) and women (SIR 0.86, 95% CI 0.77-0.94). Among women diagnosed with schizophrenia, the SIR was statistically higher for cancer in the breast among those born in Asia-Africa (1.37, 95% CI 1.12-1.63) and in the corpus uteri among the Israel-born (2.75, 95% CI 1.69-3.81) than among their counterparts in the general population. Lung cancer was significantly higher in men born in Asia-Africa diagnosed with schizophrenia than in the respective comparison population group (1.58, 95% CI 1.13-2.2). Our findings, and those of the literature, justify conducting a multinational study that includes identification of cancer-related risk factors among patients with schizophrenia and their families, and information on the use of psychotropic medications. This effort may clarify an epidemiological puzzle that remains outstanding.

Gulbinat, W., Dupont, A., Jablensky, A., et al. (1992). "Cancer incidence of schizophrenic patients. Results of record linkage studies in three countries." Br J Psychiatry Suppl(18): 75-83.

Guo, J. J. (2008). "Schizophrenia associated with increased risk of colon cancer but reduced risk of respiratory cancer." Evid Based Ment Health **11**(3): 93.
https://ebmh.bmj.com/content/11/3/93.long

Hendrie, H. C., Tu, W., Tabbey, R., et al. (2014). "Health outcomes and cost of care among older adults with schizophrenia: a 10-year study using medical records across the continuum of care." Am J Geriatr Psychiatry **22**(5): 427-436.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3830672/pdf/nihms419365.pdf

OBJECTIVES: The population of older patients with schizophrenia is increasing. This study describes health outcomes, utilization, and costs over 10 years in a sample of older patients with schizophrenia compared with older patients without schizophrenia. METHODS: An observational cohort study of 31,588 older adults (mean age: 70.44 years) receiving care from an urban public health system, including a community mental health center, during 1999-2008. Of these, 1,635 (5.2%) were diagnosed with schizophrenia and 757 (2.4%) had this diagnosis confirmed in the community mental health center. Patients' electronic medical records were merged with Medicare claims, Medicaid claims, the Minimum Dataset, and the Outcome and Assessment Information Set. Information on medication use was not available. MEASUREMENTS: Rates of comorbid conditions, healthcare utilization, costs, and mortality. RESULTS: Patients with schizophrenia had significantly higher rates of congestive heart failure (45.05% versus 38.84%), chronic obstructive pulmonary disease (52.71% versus 41.41%), and hypothyroidism (36.72% versus 26.73%) than the patients without schizophrenia ($p < 0.001$). They had significantly lower rates of cancer (30.78% versus 43.18%) and significantly higher rates of dementia (64.46% versus 32.13%). The patients with schizophrenia had significantly higher mortality risk (hazard ratio: 1.25, 95% confidence interval: 1.07-1.47) than the patients without schizophrenia. They also had significantly higher rates of healthcare utilization. The mean costs for Medicare and Medicaid were significantly higher for the patients with schizophrenia than for the patients without schizophrenia. CONCLUSIONS: The management of older adult patients with schizophrenia is creating a serious burden for our healthcare system, requiring the development of integrated models of healthcare.

Higgins-Chen, A. T., Boks, M. P., Vinkers, C. H., et al. (2020). "Schizophrenia and Epigenetic Aging Biomarkers: Increased Mortality, Reduced Cancer Risk, and Unique Clozapine Effects." Biol Psychiatry **88**(3): 224-235. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7368835/pdf/nihms-1568907.pdf

BACKGROUND: Schizophrenia (SZ) is associated with increased all-cause mortality, smoking, and age-associated proteins, yet multiple previous studies found no association between SZ and biological age using Horvath's epigenetic clock, a well-established aging biomarker based on DNA methylation. However, numerous epigenetic clocks that may capture distinct aspects of aging have been developed. This study tested the hypothesis that altered aging in SZ manifests in these other clocks. METHODS: We performed a comprehensive analysis of 14 epigenetic clocks categorized according to what they were trained to predict: chronological age, mortality, mitotic divisions, or telomere length. To understand the etiology of biological age differences, we also examined DNA methylation predictors of smoking, alcohol, body mass index, serum proteins, and cell proportions. We independently analyzed 3 publicly available multiethnic DNA methylation data sets from whole blood, a total of 567 SZ cases and 594 nonpsychiatric controls. RESULTS: All data sets showed accelerations in SZ for the 3 mortality clocks up to 5 years, driven by smoking and elevated levels of 6 age-associated proteins. The 2 mitotic clocks were decelerated in SZ related to antitumor natural killer and CD8T cells, which may help explain conflicting reports about low cancer rates in epidemiological studies of SZ. One cohort with available medication data showed that clozapine is associated with male-specific decelerations up to 7 years in multiple chronological age clocks. CONCLUSIONS: Our study demonstrates the utility of studying the various epigenetic clocks in tandem and highlights potential mechanisms by which mental illness influences long-term outcomes, including cancer and early mortality.

Hippisley-Cox, J., Vinogradova, Y., Coupland, C., et al. (2007). "Risk of malignancy in patients with schizophrenia or bipolar disorder: nested case-control study." Arch Gen Psychiatry **64**(12): 1368-1376. https://jamanetwork.com/journals/jamapsychiatry/articlepdf/482503/yoa70040_1368_1376.pdf

CONTEXT: There is conflicting evidence on whether people with schizophrenia have a different risk of cancer from that of the general population. OBJECTIVE: To determine the risk of 6 common cancers in patients with schizophrenia or bipolar disorder. DESIGN: Population-based, nested, case-control study. SETTING: A total of 454 practices contributing to the QRESEARCH general practice database. PARTICIPANTS: We analyzed 40,441 incident cases of 6 cancers (breast, colon, rectal, gastroesophageal, prostate, and respiratory) and up to 5 controls per case matched by single year of age, sex, general practice, and calendar time. MAIN OUTCOME MEASURES: Odds ratios (ORs) for cancer risk associated with schizophrenia and bipolar disorder, adjusting for smoking, body mass index, socioeconomic status, comorbidities, and prescribed medications, including antipsychotics. RESULTS: For breast cancer, we identified 10,535/50,074 cases/controls; colon cancer, 5108/24,458; rectal cancer, 3248/15,552; gastroesophageal cancer, 3854/18,477; prostate cancer, 10,190/48,748; and respiratory cancer, 7506/35,981. After adjustment, patients with schizophrenia had a 190% increased colon cancer risk (adjusted OR, 2.90; 95% confidence interval [CI], 1.85-4.57), a marginal increased breast cancer risk (adjusted OR, 1.52; 95% CI, 1.10-2.11), and a 47% decreased respiratory cancer risk (adjusted OR, 0.53, 95% CI, 0.34-0.85). Patients with schizophrenia taking antipsychotics had a 308% increased colon cancer risk (adjusted OR, 4.08; 95% CI, 2.43-6.84). Patients with bipolar disorder had cancer risks similar to patients with neither condition after adjustment. CONCLUSIONS: Patients with schizophrenia have a significantly higher risk of colon cancer and a lower risk of respiratory cancer compared with patients without schizophrenia after adjustment for confounders. In contrast, the risks of cancer in patients with and without bipolar disorder are similar, suggesting that residual confounding is unlikely to explain the findings. The increased risk of colon cancer is particularly marked in patients with schizophrenia who take antipsychotic medications.

Hodgson, R., Wildgust, H. J. et Bushe, C. J. (2010). "Cancer and schizophrenia: is there a paradox?" J Psychopharmacol **24**(4 Suppl): 51-60. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2951592/pdf/10.1177_1359786810385489.pdf

People with schizophrenia are more likely to die prematurely than the general population from both suicide and physical ill health. Published studies examining the incidence of cancer in schizophrenia patients report increased, reduced or similar incidence compared with the general population. Older studies tended to report lower incidence rates which fuelled speculation as to the biological and other

mechanisms for this protective effect. Furthermore, mortality rates in patients with schizophrenia appear higher than expected. We undertook a non-systematic review of published data to give an overview for these variable findings and illustrate methodological confounders by highlighting a systematic review of breast cancer studies.

Huang, H. K., Wang, Y. W., Hsieh, J. G., et al. (2018). "Disparity of end-of-life care in cancer patients with and without schizophrenia: A nationwide population-based cohort study." Schizophr Res **195**: 434-440.

BACKGROUND: Cancer patients with schizophrenia may face disparities in end-of life care, and it is unclear whether schizophrenia affects their medical care and treatment. METHODS: We conducted a nationwide population-based cohort study based on the National Health Insurance Research Database of Taiwan. The study population included patients >20years old who were newly diagnosed as having one of six common cancers between 2000 and 2012 (schizophrenia cohort: 1911 patients with both cancer and schizophrenia; non-schizophrenia cohort: 7644 cancer patients without schizophrenia). We used a multiple logistic regression model to analyze the differences in medical treatment between the two cohorts in the final 1 and 3months of life. RESULTS: In the 1month before death, there was higher intensive care unit utilization in the schizophrenia group [odd ratio (OR)=1.21, 95% confidence interval (CI)=1.07-1.36] and no significant differences between the groups in-hospital stay length or hospice care. The schizophrenia patients received less chemotherapy (OR=0.60, 95% CI=0.55-0.66) but more invasive interventions, such as cardiopulmonary resuscitation (OR=1.34, 95% CI=1.15-1.57). Advanced diagnostic examinations, such as computed tomography/magnetic resonance imaging/sonography (OR=0.80, 95% CI=0.71-0.89), were used less often for the schizophrenia patients. The 1- and 3-month prior to death results were similar. CONCLUSION: End-of-life cancer patients with schizophrenia underwent more frequent invasive treatments but less chemotherapy and examinations. Treatment plans/advance directives should be discussed with patients/families early to enhance end-of-life care quality and reduce health care disparities caused by schizophrenia.

Huang, K. C., Yang, K. C., Lin, H., et al. (2013). "Analysis of schizophrenia and hepatocellular carcinoma genetic network with corresponding modularity and pathways: novel insights to the immune system." BMC Genomics **14 Suppl 5**: S10.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3852078/pdf/1471-2164-14-S5-S10.pdf

BACKGROUND: Schizophrenic patients show lower incidences of cancer, implicating schizophrenia may be a protective factor against cancer. To study the genetic correlation between the two diseases, a specific PPI network was constructed with candidate genes of both schizophrenia and hepatocellular carcinoma. The network, designated schizophrenia-hepatocellular carcinoma network (SHCN), was analysed and cliques were identified as potential functional modules or complexes. The findings were compared with information from pathway databases such as KEGG, Reactome, PID and ConsensusPathDB. RESULTS: The functions of mediator genes from SHCN show immune system and cell cycle regulation have important roles in the eitology mechanism of schizophrenia. For example, the over-expressing schizophrenia candidate genes, SIRPB1, SYK and LCK, are responsible for signal transduction in cytokine production; immune responses involving IL-2 and TREM-1/DAP12 pathways are relevant for the etiology mechanism of schizophrenia. Novel treatments were proposed by searching the target genes of FDA approved drugs with genes in potential protein complexes and pathways. It was found that Vitamin A, retinoid acid and a few other immune response agents modulated by RARA and LCK genes may be potential treatments for both schizophrenia and hepatocellular carcinoma. CONCLUSIONS: This is the first study showing specific mediator genes in the SHCN which may suppress tumors. We also show that the schizophrenic protein interactions and modulation with cancer implicates the importance of immune system for etiology of schizophrenia.

Hwang, M., Farasatpour, M., Williams, C. D., et al. (2012). "Adjuvant chemotherapy for breast cancer in patients with schizophrenia." Oncol Lett **3**(4): 845-850.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3362378/pdf/OL-03-0845.pdf

The outcomes of treatment of physical illnesses are strongly affected by the presence of schizophrenia. We aimed to quantify the clinical course of schizophrenic breast cancer patients who were eligible for adjuvant chemotherapy to determine whether patients with this mental illness receive appropriate treatment for this physical illness. We searched the national Department of Veterans Affairs (DVA)

computer database using computer codes for schizophrenia to identify patients who later developed breast cancer and were treated in DVA medical centers. Computer-based data were supplemented with chart-based clinical indicators. There were 55 subjects who appeared to be appropriate candidates for adjuvant systemic therapy. A number of these candidates were not offered postoperative endocrine or cytotoxic chemotherapy, while others refused treatment or were non-compliant. Behaviors typical of schizophrenic subjects, including hostility to caregivers, often disrupt their care. Schizophrenic patients often have advanced-stage cancer at diagnosis, often delay diagnosis and are frequently hostile towards healthcare workers. Many of these patients refuse therapy and/or are non-compliant.

Hwong, A., Wang, K., Bent, S., et al. (2020). "Breast Cancer Screening in Women With Schizophrenia: A Systematic Review and Meta-Analysis." Psychiatr Serv **71**(3): 263-268.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7323869/pdf/nihms-1541427.pdf

OBJECTIVE: Women with schizophrenia appear to receive breast cancer diagnoses at later stages of the disease compared with the general population. To study this disparity, this report reviewed and quantified the differences in rates of mammography screening for women with schizophrenia and other psychotic disorders compared with the general population. METHODS: A systematic literature search was conducted in PubMed, Embase, Web of Science, and PsycINFO databases. Each database was searched from inception to September 14, 2018. The search strategy included search terms for breast cancer, mammography, schizophrenia, and psychosis. Two reviewers independently screened and evaluated eligible studies. The main outcome measure was the rate of mammography screening among women with schizophrenia and psychotic disorders versus a comparable population of women without these diagnoses. Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines were used for abstracting data, and the Newcastle-Ottawa Scale was used for assessing data quality. A meta-analysis with a random-effects model was performed. RESULTS: From a total of 304 abstracts reviewed, 11 studies met the inclusion criteria, representing 25,447 women with diagnoses of schizophrenia or psychosis across four countries. The meta-analysis showed that women with schizophrenia were less likely than women without schizophrenia to receive mammography screening (pooled OR=0.50, 95% confidence interval=0.38-0.64, p<0.001). In subgroup analysis, this association was not significantly affected by quality of the study. CONCLUSIONS: Women with schizophrenia and other psychotic disorders were about half as likely as the general population to receive mammography screening. Further research is needed to determine causes of this disparity.

Inagaki, M., Fujiwara, M., Nakaya, N., et al. (2018). "Low Cancer Screening Rates among Japanese People with Schizophrenia: A Cross-Sectional Study." Tohoku J Exp Med **244**(3): 209-218.
https://www.jstage.jst.go.jp/article/tjem/244/3/244_209/_pdf

Health care disparities among people with schizophrenia is a global concern. Our previous study revealed cancer screening rates in Japanese people with schizophrenia lower than rates of approximately 40% of the general population. However, that study was based on self-reports, which can be inaccurate, and rates did not differentiate the types of cancer screening provider (i.e., municipal screening, collective opportunistic screening, and individual opportunistic screening). This study aimed to investigate records-based cancer screening rates, focusing on participation rates of people with schizophrenia who are subject to municipal cancer screening programs. We conducted a cross-sectional study at a psychiatric hospital outpatient clinic from September to November 2016. We randomly extracted 420 potential participants from among 680 eligible patients and asked them to participate. We then selected subgroups of participants living in Okayama city who were enrolled in the National Health Insurance or Public Assistance systems and were subject to colorectal, gastric, lung, breast, or cervical cancer screening provided by Okayama city (n = 97, 96, 97, 42, and 64, respectively). Participation in cancer screenings was assessed based on local government records. Municipal cancer screening rates were as follows: 13.4% (95% confidence interval: 6.6%-20.2%) for colorectal, 7.3% (2.1%-12.5%) for gastric, 16.5% (9.1%-23.9%) for lung, 21.4% (9.0%-33.8%) for breast, and 14.1% (5.6%-22.6%) for cervical cancers. The findings demonstrated extremely low cancer screening rates among people with schizophrenia subject to municipal cancer screenings in Japan. A strategy to promote municipal cancer screening for people with schizophrenia is needed.

Inagaki, T., Yasukawa, R., Okazaki, S., et al. (2006). "Factors disturbing treatment for cancer in patients with schizophrenia." Psychiatry Clin Neurosci **60**(3): 327-331.

https://onlinelibrary.wiley.com/doi/pdfdirect/10.1111/j.1440-1819.2006.01509.x?download=true

> Patients with schizophrenia who develop cancer often have a variety of complicated medical and psychiatric problems. Problems associated with receiving a diagnosis of cancer and with understanding or cooperating with medical treatment may develop. Research in managing and treating schizophrenia patients with cancer is scarce. Presented herein is the experience of the authors' consultation-liaison psychiatry service in treating patients with schizophrenia who have cancer, and discussion of the medical management of such cases. Fourteen patients were treated between April 1999 and March 2003 and included patients receiving consultation psychiatric services at Shimane University Hospital as well as patients referred from other psychiatric hospitals. These patients were divided into two groups based on whether they were amenable to cancer treatment or not. The treated group consisted of patients who accepted cancer treatment, and the untreated group consisted of patients who refused or interrupted the cancer treatment. The clinical course, clinical psychiatric symptoms, problems in understanding cancer, cancer treatment course and convalescence were retrospectively assessed. Psychiatric symptoms and state were measured using the Brief Psychiatric Rating Scale (BPRS) and the Positive and Negative Syndrome Scale (PANSS). The mean of the duration of schizophrenia in these two groups was not significantly different. The mean scores on measures of psychiatric symptoms in each group (treated and untreated) were as follows: BPRS, 45.3+/-15.4 and 64.9+/-9.2 (P<0.05); positive symptoms scores on PANSS, 14.4+/-8.8 and 20.6+/-6.0 (NS); negative symptoms scores on PANSS, 20.6+/-4.7 and 33.6+/-4.4 (P<0.01); and total scores on PANSS, 31.7+/-7.0 and 48.6+/-7.4 (P<0.01). Patients with severe negative symptoms had greater difficulty understanding and cooperating with the cancer treatment. Regarding cancer stage, when cancer was discovered, the disease had already advanced and was no longer amenable to first-line treatment. Regarding notification of the diagnosis, it was rarely possible to give sufficiently early notice to patients in the untreated group. The important role of consultation-liaison psychiatrist in treating cancer patients is suggested. Some steps are proposed for managing schizophrenia patients with cancer who are not able to give informed consent.

Irwin, K. E., Henderson, D. C., Knight, H. P., et al. (2014). "Cancer care for individuals with schizophrenia." Cancer **120**(3): 323-334.
https://acsjournals.onlinelibrary.wiley.com/doi/pdfdirect/10.1002/cncr.28431?download=true

> Individuals with schizophrenia are a vulnerable population that has been relatively neglected in health disparities research. Despite having an equivalent risk of developing most cancers, patients with schizophrenia are more likely to die of cancer than the general population. Cancer care disparities are likely the result of patient-, provider-, and systems-level factors and influenced by the pervasive stigma of mental illness. Individuals with schizophrenia have higher rates of health behaviors linked with cancer mortality including cigarette smoking. They also have significant medical comorbidity, are less likely to have up-to-date cancer screening, and may present at more advanced stages of illness. Patients with schizophrenia may be less likely to receive chemotherapy or radiotherapy, have more postoperative complications, and have less access to palliative care. However, opportunities exist for the interdisciplinary team, including medical, surgical, and radiation oncologists; psychiatrists; and primary care physicians, to intervene throughout the continuum of cancer care to promote survival and quality of life. This review summarizes data on overall and cancer-specific mortality for individuals with schizophrenia and reviews specific disparities across the cancer care continuum of screening, diagnosis, treatment, and end-of-life care. Using a case, the authors illustrate clinical challenges for this population including communication, informed consent, and risk of suicide, and provide suggestions for care. Finally, recommendations for research to address the disparities in cancer care for individuals with schizophrenia are discussed. Despite significant challenges, with collaboration between oncology and mental health teams, individuals with schizophrenia can receive high-quality cancer care.

Irwin, K. E., Park, E. R., Fields, L. E., et al. (2019). "Bridge: Person-Centered Collaborative Care for Patients with Serious Mental Illness and Cancer." Oncologist **24**(7): 901-910.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6656464/pdf/onco12828.pdf

> BACKGROUND: Individuals with serious mental illness (SMI) experience increased cancer mortality due to inequities in cancer treatment. Psychiatric care at cancer diagnosis may improve care delivery, yet models for integrating psychiatry and cancer care are lacking. We assessed the feasibility and acceptability of a person-centered collaborative care trial for SMI and cancer. SUBJECTS, MATERIALS, AND METHODS: We

developed the Bridge intervention for patients with SMI (schizophrenia, bipolar disorder, and severe major depression) and cancer. Bridge includes proactive identification of SMI, person-centered care from a psychiatrist and case manager, and collaboration with oncology. We conducted a 12-week, single-group trial in patients with SMI and a new breast, gastrointestinal, lung, or head/neck cancer. We assessed the feasibility of patient identification, enrollment and study completion; evaluated acceptability and perceived benefit with exit interviews with patients, caregivers, and oncology clinicians; and examined change in psychiatric symptoms with the Brief Psychiatric Rating Scale (BPRS). RESULTS: From November 2015 to April 2016, 30/33 eligible patients (90.9%) enrolled, and 25/29 (86.2%) completed assessments at all timepoints, meeting feasibility criteria. Of 24 patients, 23 (95.8%) found meeting with the psychiatrist helpful; 16/19 caregivers (84.2%) shared that Bridge addressed key caregiving challenges. Oncology clinicians evaluated Bridge as "very" or "most" useful for 94.3% of patients. Exit interviews with all participant groups suggested that Bridge fostered patient-clinician trust, increased access to psychiatric treatment, and enabled patients to initiate and complete cancer treatment. Psychiatric symptoms on the BPRS improved from baseline to 12 weeks. CONCLUSION: Bridge is a feasible and acceptable care delivery model for patients with SMI, their caregivers, and oncology clinicians. Randomized trials are warranted to assess the efficacy of improving cancer outcomes in this underserved population. IMPLICATIONS FOR PRACTICE: Serious mental illness affects 13 million U.S. adults who experience increased cancer mortality. To improve outcomes, new models of integrated oncology and mental health care are urgently needed. This study found that it was feasible to identify, enroll, and retain patients with serious mental illness and a new cancer in a trial of integrated mental health and cancer care (Bridge). Patients, caregivers, and oncologists reported that Bridge facilitated the initiation and completion of cancer care. Randomized trials are warranted to investigate the impact on cancer outcomes. Trial procedures may inform consent, engagement, and trial retention for patients with mental illness.

Irwin, K. E., Park, E. R., Shin, J. A., et al. (2017). "Predictors of Disruptions in Breast Cancer Care for Individuals with Schizophrenia." Oncologist **22**(11): 1374-1382.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5679818/pdf/onco12178.pdf

BACKGROUND: Patients with schizophrenia experience markedly increased breast cancer mortality, yet reasons for this disparity are poorly understood. We sought to characterize disruptions in breast cancer care for patients with schizophrenia and identify modifiable predictors of those disruptions. MATERIALS AND METHODS: We performed a medical record review of 95 patients with schizophrenia and breast cancer treated at an academic cancer center between 1993 and 2015. We defined cancer care disruptions as processes that interfere with guideline-concordant cancer care, including delays to diagnosis or treatment, deviations from stage-appropriate treatment, and interruptions in treatment. We hypothesized that lack of psychiatric treatment at cancer diagnosis would be associated with care disruptions. RESULTS: Half of patients with schizophrenia experienced at least one breast cancer care disruption. Deviations in stage-appropriate treatment were associated with breast cancer recurrence at 5 years ($p = .045$). Patients without a documented psychiatrist experienced more delays ($p = .016$), without documented antipsychotic medication experienced more deviations ($p = .007$), and with psychiatric hospitalizations after cancer diagnosis experienced more interruptions ($p < .0001$). Independent of stage, age, and documented primary care physician, lack of documented antipsychotic medication (odds ratio [OR] = 4.97, 95% confidence interval [CI] = 1.90, 12.98) and psychiatric care (OR = 4.56, 95% CI = 1.37, 15.15) predicted cancer care disruptions. CONCLUSION: Disruptions in breast cancer care are common for patients with schizophrenia and are associated with adverse outcomes, including cancer recurrence. Access to psychiatric treatment at cancer diagnosis may protect against critical disruptions in cancer care for this underserved population. IMPLICATIONS FOR PRACTICE: Disruptions in breast cancer care are common for patients with schizophrenia, yet access to mental health treatment is rarely integrated into cancer care. When oncologists documented a treating psychiatrist and antipsychotic medication, patients had fewer disruptions in breast cancer care after adjusting for age, cancer stage, and access to primary care. Addressing psychiatric comorbidity at breast cancer diagnosis may increase the likelihood that patients with schizophrenia receive timely, stage-appropriate cancer treatment. Comanagement of schizophrenia and breast cancer at cancer diagnosis may be one key strategy to decrease inequities in cancer treatment and improve cancer survival in this underserved population.

Irwin, K. E., Steffens, E. B., Yoon, Y., et al. (2019). "Lung Cancer Screening Eligibility, Risk Perceptions, and Clinician Delivery of Tobacco Cessation Among Patients With Schizophrenia." Psychiatr Serv **70**(10): 927-934.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8386131/pdf/nihms-1531855.pdf

OBJECTIVE: Individuals with schizophrenia experience increased lung cancer mortality and decreased access to cancer screening and tobacco cessation treatment. To promote screening among individuals with schizophrenia, it is necessary to investigate the proportion who meet screening criteria and examine smoking behaviors, cancer risk perception, and receipt of tobacco cessation interventions from psychiatry and primary care. METHODS: The authors performed a cross-sectional survey and medical record review with 112 adults with schizophrenia treated with clozapine in a community mental health clinic (CMHC). RESULTS: Among older participants (ages 55-77 years) with schizophrenia, 34% met the criteria for lung screening on the basis of smoking history (heavy current or former smokers), and more than half believed they had a low risk of developing lung cancer. Of all participants, 88% had visited their primary care provider (PCP) in the past year; PCPs represented 35 different practices. Only one in three current smokers reported that their PCP or psychiatrist assisted them in obtaining medications for tobacco cessation. CONCLUSIONS: Given smoking history, many older adults with schizophrenia have potential to benefit from lung screening, yet most older participants underestimated their lung cancer risk. Although participants regularly accessed care, PCP and psychiatric visits may be missed opportunities to engage patients with schizophrenia in tobacco cessation and decrease preventable premature mortality. Embedding interventions in a CMHC, a centralized access point of care delivery for patients with schizophrenia, may have unique potential to increase uptake of cancer screening and tobacco cessation interventions.

Ishikawa, H., Yasunaga, H., Matsui, H., et al. (2016). "Differences in cancer stage, treatment and in-hospital mortality between patients with and without schizophrenia: retrospective matched-pair cohort study." Br J Psychiatry **208**(3): 239-244.
https://www.cambridge.org/core/services/aop-cambridge-core/content/view/EA9A58FB9DA7585C003AB14D9BDB6381/S0007125000279397a.pdf/div-class-title-differences-in-cancer-stage-treatment-and-in-hospital-mortality-between-patients-with-and-without-schizophrenia-retrospective-matched-pair-cohort-study-div.pdf

BACKGROUND: Healthcare access and outcomes in cancer patients with schizophrenia remain unclear. AIMS: To investigate the likelihood of early diagnosis and treatment in patients with schizophrenia who have cancer and their prognosis. METHOD: A retrospective matched-pair cohort of gastrointestinal cancer patients was identified using a national in-patient database in Japan. Multivariable ordinal/binary logistic regressions was modelled to compare cancer stage at admission, invasive treatments and 30-day in-hospital mortality between patients with schizophrenia (n = 2495) and those without psychiatric disorders (n = 9980). RESULTS: The case group had a higher proportion of stage IV cancer (33.9% v. 18.1%), a lower proportion of invasive treatment (56.5% v. 70.2%, odds ratio (OR) = 0.77, 95% CI 0.69-0.85) and higher in-hospital mortality (4.2% v. 1.8%, OR = 1.35, 95% CI 1.04-1.75). CONCLUSIONS: Patients with schizophrenia who had gastrointestinal cancer had more advanced cancer, a lower likelihood of invasive treatment and higher in-hospital mortality than those without psychiatric disorders.

James, M., Thomas, M., Frolov, L., et al. (2017). "Rates of Cervical Cancer Screening Among Women With Severe Mental Illness in the Public Health System." Psychiatr Serv **68**(8): 839-842.

OBJECTIVE: This study aimed to determine cervical cancer screening rates among women with severe mental illness. METHODS: California Medicaid administrative records (2010-2011) for 31,308 women with severe mental illness were examined. Participants received specialty mental health services and were not dually eligible for Medicare. Poisson models assessed association between selected predictors and cervical cancer screening. RESULTS: Overall, 20.2% of women with severe mental illness received cervical cancer screening during the one-year period. Compared with white women, Asian women (adjusted risk ratio [ARR]=1.23), black women (ARR=1.10), and Hispanic women (ARR=1.11) ($p<.001$) were more likely to have been screened. Women ages 28-37 were more likely than those ages 18-27 to have been screened (ARR=1.31, $p<.001$). Evidence of other health care use was the strongest predictor of screening (ARR=3.07, $p<.001$). CONCLUSIONS: Most women in the sample were not regularly screened for cervical cancer. Cervical cancer screening for this high-risk population should be prioritized.

Jayatilleke, N., Hayes, R. D., Dutta, R., et al. (2017). "Contributions of specific causes of death to lost life expectancy in severe mental illness." Eur Psychiatry **43**: 109-115.

https://www.cambridge.org/core/journals/european-psychiatry/article/abs/contributions-of-specific-causes-of-death-to-lost-life-expectancy-in-severe-mental-illness/6F34D51FBDD63ADA3BC32E512B941ABE

> The life expectancy gap between people with severe mental illness (SMI) and the general population persists and may even be widening. This study aimed to estimate contributions of specific causes of death to the gap. Age of death and primary cause of death were used to estimate life expectancy at birth for people with SMI from a large mental healthcare case register during 2007-2012. Using data for England and Wales in 2010, death rates in the SMI cohort for each primary cause of death category were replaced with gender- and age-specific norms for that cause. Life expectancy in SMI was then re-calculated and, thus, the contribution of that specific cause of death estimated. Natural causes accounted for 79.2% of lost life-years in women with SMI and 78.6% in men. Deaths from circulatory disorders accounted for more life-years lost in women than men (22.0% versus 17.4%, respectively), as did deaths from cancer (8.1% versus 0%), but the contribution from respiratory disorders was lower in women than men (13.7% versus 16.5%). For women, cancer contributed more in those with non-affective than affective disorders, while suicide, respiratory and digestive disorders contributed more in those with affective disorders. In men, respiratory disorders contributed more in non-affective disorders. Other contributions were similar between gender and affective/non-affective groups. Loss of life expectancy in people with SMI is accounted for by a broad range of causes of death, varying by gender and diagnosis. Interventions focused on multiple rather than individual causes of death should be prioritised accordingly.

Ji, J., Sundquist, K., Ning, Y., et al. (2013). "Incidence of cancer in patients with schizophrenia and their first-degree relatives: a population-based study in Sweden." Schizophr Bull **39**(3): 527-536.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3627760/pdf/sbs065.pdf

> CONTEXT: Previous studies of the association between schizophrenia and cancer have produced conflicting results, probably because of the failure to control for confounding factors. OBJECTIVE: To test if the possible association between schizophrenia and cancer is genetic by investigating the incidence of cancer in patients with schizophrenia and their relatives. DESIGN: Retrospective cohort study with follow-up between 1965 and 2008. Estimated smoking rates were used to adjust the incidence rates of smoking-related cancers. PARTICIPANTS: The entire Swedish population. MAIN OUTCOME MEASURES: Risk of overall cancer and 34 site-/type-specific cancers. RESULTS: A total of 59,233 patients in Sweden with schizophrenia were identified, of whom 6137 developed cancer during the study period, giving a decreased standardized incidence ratio (SIR) of 0.79 (95% CI 0.77-0.81). The decrease was more pronounced (SIR 0.40, 95% CI 0.38-0.43) before the first diagnosis of schizophrenia. The overall risk was significantly reduced among their unaffected parents (SIR 0.96, 95% CI 0.94-0.98) and siblings (SIR 0.92, 95% CI 0.89-0.96). Sex-stratified analyses indicated different incidence rates between males and females, with female patients having higher cancer risks than the general population. CONCLUSIONS: The significantly decreased incidences of cancers in patients diagnosed with schizophrenia and their unaffected relatives suggest that familiar/genetic factors contributing to schizophrenia may protect against the development of cancer, especially for those cancer sites observed in both settings. The increased risk of breast, cervical, and endometrial cancers after the first diagnosis of schizophrenia could be attributed to nongenetic factors such as antipsychotics administration, which may justify preventive medical screening.

Kaneshiro, K., Kubo, M., Taniguchi, M., et al. (2021). "Current Status and Problems of Breast Cancer Treatment with Schizophrenia." Clin Breast Cancer.
https://www.clinical-breast-cancer.com/article/S1526-8209(21)00297-4/pdf

> BACKGROUND: Schizophrenia is a devastating mental disease that affects approximately 1% of the world's population. Breast cancer is the second most common type of cancer in the world that causes death in women. It is often unclear whether patients with schizophrenia receive recommended cancer treatment that met the guideline. This study characterized breast cancer treatment disruptions in schizophrenia patients and sought to identify and resolve correctable predictors of those disruptions. MATERIALS AND METHODS: A retrospective cohort study was conducted on 55 primary breast cancer patients diagnosed with schizophrenia and treated for breast cancer. We evaluated the characteristics of the breast cancer patients with schizophrenia compared to those of 610 breast cancer patients without schizophrenia. RESULTS: Compared to the control group, the schizophrenia group had significantly

advanced T and N factors and disease stage. Significantly fewer patients in the schizophrenia group than in the control group received chemotherapy (P < .0001) or recommended cancer treatment (P = .0004). Within the schizophrenia group, the patients in need of ADL support were significantly less likely to receive recommended cancer treatment. CONCLUSION: Patients with schizophrenia are often diagnosed with breast cancer in advanced stages. In addition, patients with schizophrenia with reduced ADL are less likely to receive chemotherapy or recommended cancer treatment. It is highly recommended that patients with schizophrenia undergo breast cancer screening so that they can be diagnosed early and treated adequately.

Kim, S. Y. et Kim, A. R. (2021). "Effectiveness of community-based interventions for patients with schizophrenia spectrum disorders: a study protocol for a systematic review." Syst Rev **10**(1): 106. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8042964/pdf/13643_2021_Article_1662.pdf

BACKGROUND: Schizophrenia requires a community-based intervention approach combined with standard treatment to prevent relapses. A literature review is required to understand the effectiveness of community-based interventions and to enhance quality in countries where they have not been fully established. This is a protocol for a systematic review of the effectiveness of community-based interventions for patients with schizophrenia spectrum disorders. METHODS: We will search (from inception to January 2021) PubMed/MEDLINE, EMBASE, PsycINFO, CENTRAL, CINAHL, and Research Information Sharing Service/Korean databases. Randomized controlled trials on community-based interventions for patients with schizophrenia spectrum disorders will be eligible. The comparison groups will include patients with schizophrenia spectrum disorders who are only receiving the usual care and those who also receive community-based interventions. The schizophrenia spectrum disorders referred to in this study are defined according to the DSM-5: delusional disorders, schizophrenic disorders, and schizoaffective disorder will be included. Relapse/re-hospitalization rates (primary outcome) and quality of life (secondary outcome) will be identified for each group. Two reviewers will independently screen study titles, abstract data, and full-text articles and perform the data extraction process. Potential conflicts will be resolved through discussion. The study risk of bias will be appraised using the Cochrane Risk of Bias 2.0 tool. Results will be descriptively synthesized and will be structured according to patients' characteristics, intervention type and exposure, and outcome type. If feasible and appropriate, outcome data will be used to perform random effects meta-analyses. Discrete variables will be calculated via odds ratio, and continuous variables will be calculated via standardized mean difference using RevMan 5.3 software. DISCUSSION: We will provide a summary of the available evidence on the effectiveness of community-based interventions and specific guidelines to improve their outcomes. SYSTEMATIC REVIEW REGISTRATION: PROSPERO (CRD42019145660).

Kolli, V., Denton, K., Borra, D., et al. (2013). "Treating chemotherapy induced agranulocytosis with granulocyte colony-stimulating factors in a patient on clozapine." Psychooncology **22**(7): 1674-1675. https://onlinelibrary.wiley.com/doi/10.1002/pon.3209

BACKGROUND: Clozapine is reserved for overcoming treatment resistance in schizophrenia. Malignancy is common in schizophrenia; however, there is limited evidence available on continuing clozapine with chemotherapy, with both having hematological adverse effects. OBJECTIVE: To report a case on the use of granulocyte colony-stimulating factor (G-CSF) in conjunction with clozapine and chemotherapy. METHODS: We searched PubMed for any available information on the use of granulocyte G-CSF with clozapine and chemotherapy. We report the case of a patient with schizophrenia who developed B-cell lymphoma and was treated with chemotherapy consisting of CHOP regimen, rituximab, and methotrexate. He was continued on clozapine and G-CSF. RESULTS: We did not find any reports on G-CSF use in conjunction with clozapine and chemotherapy. We found case reports and a case series on the use of G-CSF in clozapine rechallenge with clozapine-induced agranulocytosis with mixed results. In our patient on clozapine, the white blood cell counts reduced by chemotherapy, were successfully replenished with the use of filgrastim, a G-CSF. CONCLUSIONS: With risks of psychosis relapse and exacerbation with discontinuing clozapine, the addition of G-CSF could be a useful aid in replenishing white cell counts lost to chemotherapy whilst continuing clozapine. However, further study is needed on this combination.

Konishi, T., Fujiogi, M., Michihata, N., et al. (2021). "Breast cancer surgery in patients with schizophrenia: short-term outcomes from a nationwide cohort." Br J Surg **108**(2): 168-173.

BACKGROUND: Although patients with schizophrenia have a higher risk of developing breast cancer than the general population, studies that have investigated postoperative complications after breast cancer surgery in patients with schizophrenia are scarce. This study examined associations between schizophrenia and short-term outcomes following breast cancer surgery. METHODS: Patients who underwent surgery for stage 0-III breast cancer between July 2010 and March 2017 were identified from a Japanese nationwide inpatient database. Multivariable analyses were conducted to compare postoperative complications and hospitalization costs between patients with schizophrenia and those without any psychiatric disorder. Three sensitivity analyses were performed: a 1 : 4 matched-pair cohort analysis with matching for age, institution, and fiscal year at admission; analyses excluding patients with schizophrenia who were not taking antipsychotic medication; and analyses excluding patients with schizophrenia who were admitted to hospital involuntarily. RESULTS: The study included 3660 patients with schizophrenia and 350 860 without any psychiatric disorder. Patients with schizophrenia had a higher in-hospital morbidity (odds ratio (OR) 1.37, 95 per cent c.i. 1.21 to 1.55), with more postoperative bleeding (OR 1.34, 1.05 to 1.71) surgical-site infections (OR 1.22, 1.04 to 1.43), and sepsis (OR 1.20, 1.03 to 1.41). The total cost of hospitalization (coefficient €743, 95 per cent c.i. 680 to 806) was higher than that for patients without any psychiatric disorder. All sensitivity analyses showed similar results to the main analyses. CONCLUSION: Although causal inferences remain premature, multivariable regression analyses showed that schizophrenia was associated with greater in-hospital morbidity and higher total cost of hospitalization after breast cancer surgery than in the general population.

Kopylov, A. T., Petrovsky, D. V., Stepanov, A. A., et al. (2021). "Convolutional neural network in proteomics and metabolomics for determination of comorbidity between cancer and schizophrenia." J Biomed Inform **122**: 103890.
https://www.sciencedirect.com/science/article/pii/S1532046421002197?via%3Dihub

The association between cancer risk and schizophrenia is widely debated. Despite many epidemiological studies, there is still no strong evidence regarding the molecular basis for the comorbidity between these two pathological conditions. The vast majority of assays have been performed using clinical records of schizophrenic patients or those undergoing cancer treatment and monitored for sufficient time to find shared features between the considered conditions. We performed mass spectrometry-based proteomic and metabolomic investigations of patients with different cancer phenotypes (breast, ovarian, renal, and prostate) and patients with schizophrenia. The resulting vast quantity of proteomic and metabolomic data were then processed using systems biology and one-dimensional (1D) convolutional neural network (1DCNN) machine learning approaches. Traditional systematic approaches permit the segregation of schizophrenia and cancer phenotypes on the level of biological processes, while 1DCNN recognized "signatures" that could segregate distinct cancer phenotypes and schizophrenia at the comorbidity level. The designed network efficiently discriminated unrelated pathologies with a model accuracy of 0.90 and different subtypes of oncophenotypes with an accuracy of 0.94. The proposed strategy integrates systematic analysis of identified compounds and application of 1DCNN model for unidentified ones to reveal the similarity between distinct phenotypes.

Kotze, C. et Roos, J. L. (2020). "End-of-life decision-making capacity in an elderly patient with schizophrenia and terminal cancer." S Afr Fam Pract (2004) **62**(1): e1-e4.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8378126/pdf/SAFP-62-5111.pdf

Medical practitioners are confronted daily with decisions about patients' capacity to consent to interventions. To address some of the pertinent issues with these assessments, the end-of-life decision-making capacity of a 72-year-old female with treatment-resistant schizophrenia and terminal cancer is discussed, as are the role of the treating clinician and the importance of health-related values. There is a recommendation that the focus of these assessments can rather be on practical outcomes, especially when capacity issues arise. This implies that the decision-making capacity of the patient is only practically important when the treatment team is willing to proceed against the patient's wishes. This shifts the focus from a potentially difficult assessment to the simpler question of whether the patient's capacity will change the treatment approach. Clinicians should attend to any possible underlying issues, instead of focusing strictly on capacity. Compared to the general populations people with serious mental illness (SMI) have higher rates of physical illness and die at a younger age, but they do not commonly access palliative care services. Conversations about end-of-life care can occur without fear that a person's

psychiatric symptoms or related vulnerabilities will undermine the process. More research about palliative care and advance care planning for people with SMI is needed. This is even more urgent in light of the coronavirus disease-2019 (COVID-19) pandemic, and South African health services should consider recommendations that advanced care planning should be routinely implemented. These recommendations should not only focus on the general population and should include patients with SMI.

Kredentser, M. S., Martens, P. J., Chochinov, H. M., et al. (2014). "Cause and rate of death in people with schizophrenia across the lifespan: a population-based study in Manitoba, Canada." J Clin Psychiatry **75**(2): 154-161.
https://www.psychiatrist.com/read-pdf/2436/

OBJECTIVE: To compare the causes and rates of death for people with and without schizophrenia in Manitoba, Canada. METHOD: Using de-identified administrative databases at the Manitoba Centre for Health Policy, a population-based analysis was performed to compare age- and sex-adjusted 10-year (1999-2008) mortality rates, overall and by specific cause, of decedents aged 10 years or older who had 1 diagnosis of schizophrenia (ICD-9-CM code 295, ICD-10-CA codes F20, F21, F23.2, F25) over a 12-year period (N = 9,038) to the rest of the population (N = 969,090). RESULTS: The mortality rate for those with schizophrenia was double that of the rest of the population (20.00% vs. 9.37%). The all-cause mortality rate was higher for people with schizophrenia compared to all others (168.9 vs. 99.1 per thousand; relative risk [RR] = 1.70, P < .0001); rates of death due to suicide (RR = 8.67, P < .0001), injury (RR = 2.35, P < .0001), respiratory illness (RR = 2.00, P < .0001), and circulatory illness (RR = 1.64, P < .0001) were also significantly higher in people with schizophrenia. Overall cancer deaths were similar (28.6 vs. 27.3 per thousand, P = .42, NS) except in the middle-aged group (40-59), in which cancer death rates were significantly higher for those with schizophrenia (28.7 vs. 11.6 per thousand; RR = 2.48, P < .01). Mortality rates due to lung cancer were significantly higher in people with schizophrenia (9.4 vs. 6.4 per thousand, RR = 1.45, P < .001). CONCLUSIONS: People with schizophrenia are at increased risk of death compared to the general population, and the majority of these deaths are occurring in older age from physical disease processes. Risk of cancer mortality is significantly higher in middle-aged but not younger or older patients with schizophrenia. Understanding these patients' vulnerabilities to physical illness has important public health implications for prevention, screening, and treatment as the population ages.

Kuppili, P. P. et Nebhinani, N. (2018). "Deciphering the paradoxical incidence of cancer in schizophrenia." Australas Psychiatry: 1039856218797439.
https://journals.sagepub.com/doi/10.1177/1039856218797439

OBJECTIVES: The incidence of cancer in schizophrenia has been an area of controversy. The current article aims to provide a commentary outlining the contradictory findings of incidence of cancer in schizophrenia as well as discuss the available theories linking cancer with schizophrenia and address the methodological issues of the studies which could lead to the discrepant findings. METHOD: A literature search was carried out primarily using the electronic database of MEDLINE through PubMed using the search terms 'cancer' and 'schizophrenia'. Google Scholar was used to supplement the search. RESULTS: The findings were inconclusive, with studies documenting increased, decreased as well as no risk of cancer in patients with schizophrenia, compared with the general population. Several methodological limitations exist with regard to measures of assessment, sample size and selection bias. CONCLUSIONS: The association between cancer and schizophrenia remains controversial. Genetic as well as environmental theories exist explaining the paradoxical incidence of cancer in schizophrenia. The methodological factors could contribute to the discrepant findings.

Levav, I., Kohn, R., Barchana, M., et al. (2009). "The risk for cancer among patients with schizoaffective disorders." J Affect Disord **114**(1-3): 316-320.

BACKGROUND: Several epidemiological studies explored the risk for cancer among both persons with schizophrenia and their first-degree relatives, and among patients with bipolar disorder. No studies have yet explored the risk among persons with schizoaffective disorders. METHOD: Linkage analysis was conducted based on the psychiatric and the cancer national databases. Standardized incidence ratios (SIR) for aggregated cancer sites were calculated by comparing the incidence rates among patients in the psychiatric case register with schizoaffective disorders with the incidence rates in the Jewish-Israeli general population. RESULTS: No significant alteration in cancer risk was found for both genders: males,

SIR=1.11, 95% CI (0.48-1.73) and females, SIR=1.38, 95% CI (0.96-1.80). LIMITATIONS: Our sample was derived from patients with a history of psychiatric hospitalization. Putative factors such as diet, smoking and medications were not investigated. CONCLUSIONS: Our study showed no significant increase in the risk for cancer in schizoaffective disorders. Those results appear to be positioned between the schizophrenia findings that show a lower risk for cancer and the bipolar disorder findings that show an increased risk.

Levav, I., Lipshitz, I., Novikov, I., et al. (2007). "Cancer risk among parents and siblings of patients with schizophrenia." Br J Psychiatry **190**: 156-161.
https://www.cambridge.org/core/services/aop-cambridge-core/content/view/3E6B4B7BAC00C91786A4589011444814/S0007125000233576a.pdf/div-class-title-cancer-risk-among-parents-and-siblings-of-patients-with-schizophrenia-div.pdf

BACKGROUND: A reduced risk of cancer has been noted among people with schizophrenia. Given that genetic causes have been proposed as an explanation of this finding, one would expect that the risk of cancer among first-degree relatives would be equally reduced. AIMS: To investigate the risk of cancer among the biological parents and full siblings of people receiving in-patient care for schizophrenia. METHOD: Linkage analysis was conducted between national population, psychiatric and cancer databases. Standardised incidence ratios for all cancer sites were calculated by comparing the incident rates among first-degree relatives with national incidence rates. RESULTS: A reduced cancer risk was found across all groups examined. Among parents, whose numbers were adequately large, the findings reached statistical significance. For index cases and siblings--a markedly younger population--only a trend was elicited. CONCLUSIONS: The genetic hypothesis--namely, the presence of a gene with the dual effect of reducing the cancer risk and disrupting neurodevelopment--is a plausible explanation for these findings.

Levav, I., Ponizovsky, A. et Grinshpoon, A. (2006). "Cancer and schizophrenia." Br J Psychiatry **188**: 191.
https://www.cambridge.org/core/services/aop-cambridge-core/content/view/363911BCC8E7AA47F8EB1762D1F0E150/S0007125000169715a.pdf/div-class-title-cancer-and-schizophrenia-div.pdf

Li, H., Li, J., Yu, X., et al. (2018). "The incidence rate of cancer in patients with schizophrenia: A meta-analysis of cohort studies." Schizophr Res **195**: 519-528.

BACKGROUND: Numerous studies report that cancer prevalence in patients with schizophrenia might be different from the general population, but findings remain controversial. AIM: Our updated meta-analysis of cohort studies aims to analyze the data from cohort studies concerning the incidence risk of overall cancer and some site-specific cancers in patients with schizophrenia. METHOD: We performed a systemic search through electronic databases. Cohort studies evaluating and describing the cancer incidence among patients with schizophrenia were included. Pooled risk ratios (RRs) were calculated for assessing the incidence risk of cancer. RESULTS: There were 16 cohort studies included in this meta-analysis, which combined a total of 480,356 participants with schizophrenia and 41,999 cases of cancer. Results showed that there was a slight significant decreased overall risk ratio of cancer incidence among patients with schizophrenia (RR=0.90, 95% CI 0.81-0.99). When stratified by cancer site and gender, there were significant decreased incidence risk rates of colorectal cancer (RR=0.82, 95% CI 0.69-0.98) and prostate cancer (RR=0.55, 95% CI 0.42-0.71) in those patients, moreover, the incidence rate of colorectal cancer decreased significantly in male patients (RR=0.89, 95% CI 0.81-0.98), and the incidence rate of lung cancer increased significantly in female patients (RR=1.12, 95% CI 1.01-1.25). CONCLUSIONS: The incidence risk of some cancers was reduced in patients with schizophrenia. Gender and type of cancer were two important confounding factors contributed to the heterogeneity that required adjustment in our cancer incidence meta-analysis.

Lichtermann, D. (2005). "Cancer risk in parents of patients with schizophrenia." Am J Psychiatry **162**(5): 1024; author reply 1024-1026.

Lichtermann, D., Ekelund, J., Pukkala, E., et al. (2001). "Incidence of cancer among persons with schizophrenia and their relatives." Arch Gen Psychiatry **58**(6): 573-578.
https://jamanetwork.com/journals/jamapsychiatry/articlepdf/481785/yoa20101.pdf

BACKGROUND: It has repeatedly been reported that the risk for cancer in patients with schizophrenia is different from that of the general population, specifically a lower risk for lung cancer despite increased smoking. Confirmation of these associations could lead to hypotheses on shared risk or protective factors, either genetic or environmental. METHODS: From Finland's National Hospital Discharge and Disability Pension registers, Helsinki, we identified a cohort of 26 996 individuals born between 1940 and 1969 and treated for schizophrenia between 1969 and 1991. They were followed up for cancer from 1971 to 1996 by record linkage with the Finnish Cancer Registry, yielding 446 653 person-years at risk, and standardized incidence ratios (SIRs) were calculated. Likewise, 39 131 parents and 52 976 siblings of the patients with schizophrenia were followed up to explore familial genetic hypotheses on deviations in cancer risk. RESULTS: In patients with schizophrenia, an increased overall cancer risk was found (724 cases observed vs 619 expected; SIR, 1.17; 95% confidence interval [CI], 1.09-1.25). Half of the excess cases were attributable to lung cancer (SIR, 2.17; 95% CI, 1.78-2.60), and the strongest relative increase in risk was in pharyngeal cancer (SIR, 2.60; 95% CI, 1.25-4.77). Cancer incidence in siblings (SIR, 0.89; 95% CI, 0.83-0.94) and parents (SIR, 0.91; 95% CI, 0.89-0.93) was consistently lower than that in the general population. CONCLUSION: Although specific lifestyle factors, particularly tobacco smoking and alcohol consumption, probably account for the increased cancer risk in patients with schizophrenia, the decreased risk in relatives would be compatible with a postulated genetic risk factor for schizophrenia offering selective advantage to unaffected relatives.

Lin, C. Y., Lane, H. Y., Chen, T. T., et al. (2013). "Inverse association between cancer risks and age in schizophrenic patients: a 12-year nationwide cohort study." Cancer Sci **104**(3): 383-390.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7657149/pdf/CAS-104-383.pdf

The association between schizophrenia and cancer risk is contentious in the clinical and epidemiological literature. Studies from different populations, tumor sites, or health care systems have provided inconsistent findings. In the present study, we examined a less well-investigated hypothesis that age plays a crucial role in cancer risk in schizophrenia. We conducted a nationwide cohort study using Taiwan's National Health Insurance Research Database (NHIRD) between 1995 and 2007. Overall, gender-, and age-stratified standardized incidence ratios (SIR) were used to investigate the pattern of cancer risk by age. Of the 102 202 schizophrenic patients, 1738 developed cancer after a diagnosis of schizophrenia (SIR = 0.92; 95% confidence interval [CI] 0.90-0.96). However, the age-stratified SIR declined with age (e.g. SIR [95% CI] = 1.97 [1.85-2.33], 0.68 [0.65-0.78], and 0.36 [0.34-0.45] for those aged 20-29, 60-69, and >/=70 years, respectively) in both genders and for major cancers. Cancer risks in schizophrenic patients were lower for cancers that are more likely to develop at an older age in the general population (e.g. stomach cancer [SIR = 0.62; 95% CI 0.57-0.80], pancreatic cancer [SIR = 0.49; 95% CI 0.39-0.84], and prostate cancer [SIR = 0.35; 95% CI 0.29-0.58]). In contrast, cancer risks were higher for cancers that have a younger age of onset, such as cancers of the nasopharynx (SIR = 1.18; 95% CI 1.08-1.49), breast (SIR = 1.50; 95% CI 1.44-1.66) and uterine corpus (SIR = 2.15; 95% CI 1.98-2.74). The unique age structures and early aging potential of schizophrenia populations may contribute to the observed inverse relationship between age and cancer risk. Higher cancer comorbidity in young schizophrenic patients deserves more attention.

Lin, G. M., Chen, Y. J., Kuo, D. J., et al. (2013). "Cancer incidence in patients with schizophrenia or bipolar disorder: a nationwide population-based study in Taiwan, 1997-2009." Schizophr Bull **39**(2): 407-416.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3576164/pdf/sbr162.pdf

BACKGROUND: Both genetic and environmental factors have been reasoned for cancer development in schizophrenia patients. However, the influence of age of onset and duration of schizophrenia on cancer incidence has rarely been emphasized. Besides, bipolar disorder tends to resemble schizophrenia from the perspective of multiple rare mutations. Comparing pattern and risk of cancers between schizophrenia and bipolar patients is illuminating. METHODS: This study used the Taiwan National Health Insurance Database. A total of 71,317 schizophrenia and 20,567 bipolar disorder patients from 1997 to 2009 were enrolled. Both cohorts were followed up for cancer during the same period by record linkage with the cancer certification in Taiwan. Age and gender standardized incidence ratios (SIRs) of overall and site-specific cancers were calculated. RESULTS: The SIR for all cancers was 1.17 for the schizophrenia cohort. Increased cancer risk (SIR: 1.31, 95% CI: 1.17-1.48) was observed in females but not males. For the bipolar disorder cohort, the SIR for all cancers was 1.29, but the excess risk was found in males (SIR: 1.42, 95% CI:

1.14-1.77) and not females. Cancer risk decreases as the duration and age of onset of schizophrenia increases. If schizophrenia is diagnosed before 50, the SIRs for colorectal, breast, cervical, and uterine cancers increase but if diagnosed after 50, the SIRs for all cancers decrease except for breast cancer. In bipolar disorder, the SIRs for all site-specific cancers were insignificant. CONCLUSIONS: Among schizophrenia patients, overall cancer risk varies inversely with age at diagnosis and disease duration. Besides, gender-specific cancer risks differ between schizophrenia and bipolar disorder.

Lin, H. Y., Hsieh, J. G., Hsieh, C. J., et al. (2020). "Differences in the Opioid Consumption of Terminally Ill Schizophrenic and Nonschizophrenic Cancer Patients: Analysis of Secondary National Population Data." J Pain Symptom Manage **59**(6): 1232-1238.
https://www.jpsmjournal.com/article/S0885-3924(19)31065-6/fulltext

CONTEXT: It is uncertain whether terminally ill schizophrenic cancer patients are hypoalgesic or have disparities in pain management. OBJECTIVES: The objective of this study was to analyze the dosage of opioids used in terminally ill cancer patients with and without schizophrenia. METHODS: This is a population-based retrospective cohort study based on data derived from the Taiwan National Health Insurance Research Database. Patients aged >20 years and newly diagnosed between 2000 and 2012 with at least one of the six most common cancers were included. After 1:4 matching, 1001 schizophrenic cancer patients comprised the schizophrenia cohort, while 4004 cancer patients without schizophrenia comprised the nonschizophrenia cohort. The percentage of opioid use, accumulated dose, and average daily dose near the end of life were analyzed for each cohort using multiple logistic and linear regression models. RESULTS: The percentage of opioid use was lower in the schizophrenic cohort than the nonschizophrenic cohort during the last month before death (69.6% vs. 84.8%, odds ratio = 0.40, 95% CI = 0.34-0.48). The accumulated dose of opioid consumption was also lower in the schizophrenic cohort (2407 mg vs. 3694 mg, P value < 0.05). CONCLUSION: Near the end of life, cancer patients with schizophrenia use less opioid than their nonschizophrenic counterparts. Cognitive impairment may be a cause in the disparity in end-of-life care for terminally ill schizophrenic cancer patients. Thus, we should formulate a more accurate pain scale system and pay attention to their need for pain treatment.

Lin, J. R. et Lin, M. L. (2014). "[Nursing experience with a schizophrenic breast cancer patient after mastectomy]." Hu Li Za Zhi **61**(5): 97-103.

This case study used cognitive therapy to improve the life quality of a 46-year-old woman with chronic schizophrenia who had undergone a mastectomy for breast cancer. This case had suffered from schizophrenia for over 24 years and was hospitalized in the chronic ward of our hospital. Breast cancer was revealed during an annual comprehensive physical checkup. In May 2012, this case received a right mastectomy at a local hospital. After the surgery, she was readmitted to the psychiatric acute ward for further care from May 30th to August 28th, 2012. A holistic nursing assessment was conducted that addressed five major aspects. The major nursing problems found during hospitalization were: acute pain, body image disturbance, and low self-esteem. A decline in pain score from 10 to 4 was achieved by developing rapport with the patient, empathizing with her distress, and providing active care to the wound. Her body image changed because of loosing her breast. Her acceptance of the loss improved through helping her to explore her feelings of change. To improve her self-esteem, we offered cognitive therapy to change her negative thinking process. She became more sanguine and cheerful. Moreover, her dependence in terms of activities of daily living decreased. This individualized intervention contributed to the recovery of a post-mastectomy, schizophrenic patient from low self-esteem.

Lindamer, L. A., Wear, E. et Sadler, G. R. (2006). "Mammography stages of change in middle-aged women with schizophrenia: an exploratory analysis." BMC Psychiatry **6**: 49.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1636038/pdf/1471-244X-6-49.pdf

BACKGROUND: Health care providers and educators who seek to create health promotion programs and individualized comprehensive care plans for women with schizophrenia are hindered by the lack of data to guide their efforts. PURPOSE: This study tested the hypothesis that women with schizophrenia adhere to mammography screening guidelines at the same rate as other same-age women. The study also investigated the validity of the Health Belief (HB) and Stages of Change (SOC) models for breast cancer screening among women with schizophrenia. METHODS: Socio-demographic and clinical variables, as well as knowledge, attitudes, and barriers were assessed as a function of stage of change related to

breast cancer screening in 46 women with schizophrenia. RESULTS: Women with schizophrenia were statistically less likely to be adherent to the screening recommendations than those without schizophrenia. Some support was found for the validity of the HB and SOC models for breast cancer screening in women with schizophrenia. Women in the Precontemplation stage had significantly higher negative attitude scores compared to Contemplation and Action/Maintenance stages (59.7, 45.7, and 43.2, respectively), and there was a trend for more barriers in the Precontemplation group (4.6, 2.6, 2.7 respectively). CONCLUSION: Given the small sample size, further research on the rates of breast cancer screening in women with schizophrenia is warranted. Nonetheless, these data suggest that providers who care for women with schizophrenia may need to make take additional measures to ensure that this population receives appropriate screening so as to not put them at greater risk for a late-stage diagnosis of breast cancer. Furthermore, these pilot data suggest that HB and SOC theory-based interventions may be valid for increasing mammography rates in women with schizophrenia.

Lopes, R., Soares, R., Figueiredo-Braga, M., et al. (2014). "Schizophrenia and cancer: is angiogenesis a missed link?" Life Sci **97**(2): 91-95.

Cancer prevalence and risk in schizophrenia (SZ) patients, as well as their implicated molecular pathways, is a debate that has become increasingly appreciated, despite lacking evidence. Since angiogenesis is imbalanced in both conditions, a non-systematic review of the existing literature using the PubMed database was performed to summarize current knowledge and to elucidate hypothesis regarding the reduced incidence of cancer in SZ, exploring possible angiogenesis biology aspects that can be interrelated both with SZ and cancer. Some lines of evidence based in epidemiology, genetic, molecular and biochemical studies suggest a putative interplay between SZ pathophysiology and angiogenesis, involving different molecular pathways and also influencing cancer biology. Studying angiogenesis in SZ and its implications to cancer is an unexplored field that could provide more insightful knowledge regarding its pathophysiology and promote the development of treatment applications.

Lu, D., Song, J., Lu, Y., et al. (2020). "A shared genetic contribution to breast cancer and schizophrenia." Nat Commun **11**(1): 4637.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7492262/pdf/41467_2020_Article_18492.pdf

An association between schizophrenia and subsequent breast cancer has been suggested; however the risk of schizophrenia following a breast cancer is unknown. Moreover, the driving forces of the link are largely unclear. Here, we report the phenotypic and genetic positive associations of schizophrenia with breast cancer and vice versa, based on a Swedish population-based cohort and GWAS data from international consortia. We observe a genetic correlation of 0.14 (95% CI 0.09-0.19) and identify a shared locus at 19p13 (GATAD2A) associated with risks of breast cancer and schizophrenia. The epidemiological bidirectional association between breast cancer and schizophrenia may partly be explained by the genetic overlap between the two phenotypes and, hence, shared biological mechanisms.

Martens, P. J., Chochinov, H. M., Prior, H. J., et al. (2009). "Are cervical cancer screening rates different for women with schizophrenia? A Manitoba population-based study." Schizophr Res **113**(1): 101-106.

CONTEXT: Barriers to cervical cancer screening (Pap tests) may exist for women experiencing schizophrenia. DESIGN: This study analyzed healthcare records of all women in the province of Manitoba, Canada to: (a) compare cervical cancer screening rates of women with and without schizophrenia; and (b) determine factors associated with screening uptake. SETTING: This study took place in Manitoba, Canada, utilizing anonymized universal administrative data in the Population Health Research Data Repository at the Manitoba Centre for Health Policy. PARTICIPANTS: All females aged 18-69 living in Manitoba December 31, 2002, excluding those diagnosed with invasive or in situ cervical cancer in the study period or previous 5 years. MAIN OUTCOME: To determine factors associated with Papanicolaou (Pap) test uptake (1+ Pap test in 3 years, 2001/02-2003/04), logistic regression modeling included: diagnosis of schizophrenia, age, region, average household income, continuity of care (COC), presence of major physical comorbidity. Good COC was defined as at least 50% of ambulatory physician visits from the same general/family practitioner within two years. RESULTS: Women with schizophrenia (n=3220) were less likely to have a Pap test (58.8% vs. 67.8%, p<.0001) compared to all other women (n=335 294). In the logistic regression, a diagnosis of schizophrenia (aOR=0.70, 95% CI 0.65-0.75); aged 50+, and living in a low-income area or the North decreased likelihood; good continuity of care (aOR 1.88, 95% CI 1.85-1.91)

and greater physical comorbidity (1.21, 95% CI 1.04-1.41) increased likelihood. CONCLUSION: Women with schizophrenia are less likely to receive appropriate cervical cancer screening. Since good continuity of care by primary care physicians may mitigate this, psychiatrists should consider assisting in ensuring screening uptake.

Mateen, F. J., Jatoi, A., Lineberry, T. W., et al. (2008). "Do patients with schizophrenia receive state-of-the-art lung cancer therapy? A brief report." Psychooncology **17**(7): 721-725.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2715919/pdf/nihms121776.pdf

OBJECTIVE: Patients with schizophrenia sometimes receive substandard medical care. This study explored such disparities among lung cancer patients with underlying schizophrenia. METHODS: This retrospective study focused on patients with pre-existing schizophrenia (or in some instances schizoaffective disorder) and a lung cancer diagnosis made between 1980 and 2004. 'Disparity' was defined as a patient's having been prescribed less aggressive therapy for a potentially curable cancer based on state-of-the-art treatment standards for the time and for the cancer stage. Qualitative methods were used to assess healthcare providers' decision-making. RESULTS: 29 patients were included. The median age was 59 years; 38% were men. Twenty-three had non-small cell lung cancer and 6 small cell lung cancer; 17 had potentially curable cancers. Five of 17 had a 'disparity' in cancer care: (1) no cancer therapy was prescribed because of chronic obstructive pulmonary disease; (2) no cancer therapy was prescribed because of infection; (3) no chemotherapy was prescribed because the patient declined it; radiation was provided; (4) no chemotherapy was prescribed because of the patient's schizophrenia symptoms; radiation was administered; and (5) no surgery was performed because of disorientation from a lobotomy; radiation was prescribed. Comments from healthcare providers suggest reflection and ethical adjudication in decision-making. CONCLUSION: Schizophrenia was never the sole reason for no cancer treatment in patients with potentially curable lung cancer. This study provides the impetus for others to begin to assess the effect of schizophrenia on lung cancer management in other healthcare settings.

Meyer, A. A., Hwang, M., Farasatpour, M., et al. (2013). "Metastatic breast cancer in patients with schizophrenia." Mol Clin Oncol **1**(2): 359-364.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3956275/pdf/mco-01-02-0359.pdf

Breast cancer is a major health problem worldwide. The median survival duration for patients with metastatic breast cancer is two to three years. Approximately 1% of populations worldwide have schizophrenia. The manner in which schizophrenic patients fare when diagnosed with metastatic breast carcinoma (MBC) was evaluated. We queried the National Department of Veterans Affairs (DVA) datasets using computer codes for a pre-existing diagnosis of schizophrenia and a later diagnosis of breast carcinoma. Chart-based data concerning the identified subjects were then requested. Previously determined inclusion and exclusion criteria were applied to select evaluable patients from the medical records, prior to extracting demographic details and data concerning the treatment course in each subject. Ten patients had distant metastases at initial diagnosis, while seven developed MBC following prior curative-intent treatment. Two patients refused therapy. Ten did not comply with recommended management. Five harmed or threatened physicians, other caregivers or themselves. Schizophrenic patients with MBC often fail to understand the nature of their illnesses. Often they do not accept palliative treatment, while a number of them do not comply with therapy, once initiated. They often exhibit behaviors that are detrimental to themselves or others. Formal psychiatric consultation is therefore necessary in patients. Several detrimental behaviors may be predicted reliably by history alone.

Modrzewska, K. et Book, J. A. (1979). "Schizophrenia and malignant neoplasms in a North Swedish population." Lancet **1**(8110): 275-276.
https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(79)90806-7/fulltext

Mortensen, P. B. (1987). "Neuroleptic treatment and other factors modifying cancer risk in schizophrenic patients." Acta Psychiatr Scand **75**(6): 585-590.

https://onlinelibrary.wiley.com/doi/abs/10.1111/j.1600-0447.1987.tb02839.x?sid=nlm%3Apubmed

In a Danish cohort of schizophrenics consisting of 6,168 patients followed during 1957-1980, the incidence of certain types of cancer has been shown to be significantly decreased (5). From this cohort 30 males with lung cancer, 21 males with bladder cancer, 17 females with cancer of the uterine cervix and 40

females with breast cancer, were each matched to two "healthy" schizophrenic controls from the same cohort. A range of social, demographic and nosocomial factors were registered from the individual case files, and statistical analysis was carried out, using Cox's regression model. Neuroleptic treatment with various drugs other than reserpine reduced the risk of developing all four cancer types studied. In contrast reserpine treatment increased the risk of developing cancer of the breast and uterine cervix. Furthermore, cancer risk was found to be modified by other well-known risk factors.

Mortensen, P. B. (1989). "The incidence of cancer in schizophrenic patients." J Epidemiol Community Health **43**(1): 43-47.
https://jech.bmj.com/content/jech/43/1/43.full.pdf

A cohort of 6168 schizophrenic patients was followed from 1957 to 1984 to determine the incidence of cancer in these patients. In the male schizophrenic patients the incidence of cancer was found to be significantly reduced in comparison with the general Danish population. This reduction was especially marked for cancer in the respiratory system, cancer of the prostate and cancer of the bladder. In the female patients the overall incidence of cancer did not differ from that of the general Danish population, but there was an increased risk of cancer of the digestive tract, especially cancer of the pancreas and a slight increase of the risk of breast cancer. In the female patients the risk of respiratory cancers and cancer of the female genital organs, especially cancer of the uterine cervix, was reduced. These alterations of the incidence of cancer in schizophrenic patients cannot be ascribed to differences in diagnostic accuracy. As a possible explanation of these findings a reduced exposure to well known carcinogens such as cigarette smoke may be relevant. We speculate that exposure to neuroleptics such as phenothiazines and reserpine may also be part of the explanation for the findings.

Mortensen, P. B. (1992). "Neuroleptic medication and reduced risk of prostate cancer in schizophrenic patients." Acta Psychiatr Scand **85**(5): 390-393.
https://onlinelibrary.wiley.com/doi/abs/10.1111/j.1600-0447.1992.tb10325.x?sid=nlm%3Apubmed

A decreased incidence of cancer of the prostate has been demonstrated in a cohort of 6168 chronic schizophrenic patients followed up from 1957 to 1984. A case-control study was performed based on this cohort to determine the possible influence of neuroleptic treatment and other factors on the risk of developing prostate cancer. Thirty-eight male schizophrenic patients who had developed prostate cancer during the observation period were compared with 76 age- and sex-matched controls from the same cohort. The only significant association was that of a reduced risk of prostate cancer among those who had been treated with a cumulative dose of high-dose phenothiazines (primarily chlorpromazine) of 15 g or more. These patients had been treated with an average daily dose of 145 mg chlorpromazine for an average of 12.5 years. No other significant risk factors were identified.

Mortensen, P. B. (1994). "The occurrence of cancer in first admitted schizophrenic patients." Schizophr Res **12**(3): 185-194.

The incidence of cancer was studied in a cohort of all first admitted 9156 patients in Denmark with a diagnosis of schizophrenia in the period 1970-1987. The overall incidence of cancer was reduced particularly in the males. Adjustment for the smoking habits of psychiatric patients enhanced this risk reduction. Fewer than expected had been diagnosed with cancer prior to the first schizophrenia admission. This tendency was limited to the female patients. The reduced cancer incidence was particularly marked for genital cancers, in particular testicular cancer, and skin cancers including malignant melanoma. Breast cancer risk was not increased, thus not substantiating concerns that neuroleptics would increase breast cancer risk through the elevation of serum prolactin levels. Some available evidence in the literature supports the hypothesis of an antineoplastic effect of neuroleptics as an explanation for the low occurrence of cancer in schizophrenic patients. Further large sample studies including an extension of the follow-up of this cohort are needed to establish the reduced risk of cancer in schizophrenic patients as well as exploring the causes for this reduction.

Mortensen, P. B. et Juel, K. (1990). "Mortality and causes of death in schizophrenic patients in Denmark." Acta Psychiatr Scand **81**(4): 372-377.
https://onlinelibrary.wiley.com/doi/abs/10.1111/j.1600-0447.1990.tb05466.x?sid=nlm%3Apubmed

A cohort consisting of 6178 people that were psychiatric inpatients with a clinical schizophrenia diagnosis in 1957 were followed up from 1957 through 1986, and their cause-specific mortality was determined. Mortality from cardiovascular diseases, lung diseases, gastrointestinal and urogenital disorders, accidents and suicide was increased, whereas mortality from cerebrovascular disorders was reduced. In the male patients cancer mortality was reduced whereas cancer mortality in the female patients was increased. Mortality from a number of causes that theoretically could be associated with side effects from neuroleptics was increased. Mortality from some causes of death used as a measurement of the quality of medical care was found to be slightly increased. Further studies of the quality of the medical care provided to schizophrenic patients and of the association between neuroleptic medication and mortality are needed.

Ni, L., Wu, J., Long, Y., et al. (2019). "Mortality of site-specific cancer in patients with schizophrenia: a systematic review and meta-analysis." BMC Psychiatry **19**(1): 323.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6816203/pdf/12888_2019_Article_2332.pdf

BACKGROUND: Numerous studies have reported contradicting results on the relationship between cancer mortality and schizophrenia. Our aim is to quantify the mortality rate of common site-specific cancers among patients with schizophrenia and to synthesize the available research evidence. METHODS: We performed a systemic search of the PubMed, EMBASE and Web of Science databases. Studies reporting the mortality rate of different cancer in patients with schizophrenia were included. A random-effects model was applied to calculate the pooled relative risks (RRs) with 95% confidence intervals (95%CIs). RESULTS: Seven studies consisting of 1,162,971 participants with schizophrenia were included in this meta-analysis. Data regarding mortality risk of breast, colon, lung and prostate cancer among schizophrenia patients were subjected to quantitative analysis. Pooled results showed significant increases in mortality risk of breast cancer (RR = 1.97, 95%CI 1.38-2.83), lung cancer (RR = 1.93, 95%CI 1.46-2.54) and colon cancer (RR = 1.69, 95%CI 1.60-1.80) in patients with schizophrenia compared with those in the general population or control group. The mortality risk of prostate cancer increased in male patients, although no significant difference was detected (RR = 1.58, 95% CI 0.79-3.15). Increased risks of mortality from lung and colon cancer were observed in female patients (RR = 2.49, 95%CI 2.40-2.59 and RR = 2.42, 95%CI 1.39-4.22, respectively) and elevated risks of mortality from lung and colon cancer in male patients (RR = 2.40, 95%CI 2.30-2.50 and RR = 1.90, 95%CI 1.71-2.11, respectively) were detected. CONCLUSIONS: Individuals with schizophrenia have a significantly high risk of mortality from breast, colon, and lung cancer.

Nordentoft, M., Plana-Ripoll, O. et Laursen, T. M. (2021). "Cancer and schizophrenia." Curr Opin Psychiatry **34**(3): 260-265.

PURPOSE OF REVIEW: On the basis of articles published in 2018, 2019 and 2020, the first aim of this review is to present estimates of incidence rates and excess mortality of overall cancer and organ-specific cancers for patients with schizophrenia compared with the general population.The second aim is to explore if underdiagnosis and undertreatment can explain - at least partly - the increased mortality of cancer in patients with schizophrenia compared with the general population. RECENT FINDINGS: Patients diagnosed with schizophrenia have an approximately 50% increased risk of death by cancer compared to age and sex-matched people in the general population. Studies have confirmed an increased mortality from breast, lung and colon cancer in patients with schizophrenia.Analyses of incidence of cancer revealed contradicting results, with some studies showing no increase in incidence and others a modestly increased incidence in overall cancer. Studies of incidence of specific types of cancers showed modestly increased risk of pancreas, oesophagus, breast cancer and contradicting results regarding lung cancer.In studies identified that compared to the general population, patients with schizophrenia were at an increased risk of not being diagnosed or treated for cancer before death of cancer. In addition, patients with schizophrenia had lower chances of getting optimal treatment for colon cancer after diagnosis. SUMMARY: This review indicates that patients with schizophrenia are at increased risk of dying of cancer and of several specific types of cancer. This increased mortality can be reduced if the price of tobacco is increased, if smoking cessation programmes are offered systematically, screening programs better implemented in this highly vulnerable group, and if procedures to facilitate access to early diagnosis and effective treatment are implemented.

Obuchi, T., Okabayashi, K., Imakiire, T., et al. (2014). "Outcomes of surgery in lung cancer patients with schizophrenia." Surg Today **44**(5): 855-858.
https://link.springer.com/article/10.1007/s00595-013-0599-0

PURPOSE: There are very few reports regarding the outcome of lung cancer surgery in patients with schizophrenia, and the clinical features of such patients are still unclear. METHODS: From 2004 to 2012, 11 lung cancer patients (six male, five female; mean age, 62.7 years) with schizophrenia underwent lung resections at our institutions. All patients had been institutionalized because they were unable to live independently at home. We retrospectively evaluated their postoperative clinical outcomes and long-term results. RESULTS: Ten of the 11 patients had comorbidities, such as diabetes mellitus and chronic obstructive pulmonary disease. Preoperatively, two patients had a history of treatment for other primary cancers in other organs, and one was on hemodialysis. A lobectomy was performed in nine patients, a segmentectomy in one, and a partial resection in one. There were no hospital deaths. The postoperative morbidity included two cases of pneumonia, one of atelectasis, and one of prolonged air leakage lasting more than 7 days. Wandering was postoperatively observed in two patients; one of these fell and fractured the left femur. At the time of our investigation, two patients were deceased, and the overall 5-year survival rate was 74.1 %. CONCLUSIONS: The postoperative morbidity and long-term results of schizophrenic patients with lung cancer were acceptable. Therefore, even in patients with schizophrenia, surgical treatment for lung cancer should be recommended when deemed to be necessary.

Oksbjerg Dalton, S., Munk Laursen, T., Mellemkjaer, L., et al. (2003). "Schizophrenia and the risk for breast cancer." Schizophr Res **62**(1-2): 89-92.

The authors investigated the risk for breast cancer in schizophrenia in a cohort of 1336313 Danish women born after 1935, including information on reproductive factors. In all, 7541 had been hospitalized for schizophrenia in 1970-1997 and the overall relative risk for breast cancer adjusted for age, period, age at first birth and number of births was not increased (RR, 0.91; 95% confidence interval, 0.71-1.12). Studies not taking parity into account may overestimate the risk for breast cancer in schizophrenic women.

Overall, J. E. (1978). "Prior psychiatric treatment and the development of breast cancer." Arch Gen Psychiatry **35**(7): 898-899.
https://jamanetwork.com/journals/jamapsychiatry/article-abstract/491955

Computerized records of a large university hospital were searched to identify all women from 1967 to 1976 whose conditions had been diagnosed as breast cancer or primary cancer of another site. The records for those women with diagnoses of cancer were then examined to identify any prior psychiatric diagnoses. The rationale was that most patients treated in this hospital setting for psychiatric disorders received neuroleptic drugs, and patients with a diagnosis of schizophrenia are almost certain to be treated with major neuroleptic drugs over a prolonged period of time. No substantial difference in the relative frequency of prior psychiatric treatment was observed between breast cancer and other cancer groups.

Pettersson, D., Gissler, M., Hällgren, J., et al. (2020). "The overall and sex- and age-group specific incidence rates of cancer in people with schizophrenia: a population-based cohort study." Epidemiol Psychiatr Sci **29**: e132.
https://www.cambridge.org/core/services/aop-cambridge-core/content/view/72C90089E86067EDE4237A0532CF8F2B/S204579602000044Xa.pdf/div-class-title-the-overall-and-sex-and-age-group-specific-incidence-rates-of-cancer-in-people-with-schizophrenia-a-population-based-cohort-study-div.pdf

AIMS: Decades of research show that people with schizophrenia have an increased risk of death from cancer; however, the relationship between schizophrenia and cancer incidence remains less clear. This population-based study investigates the incidence of seven common types of cancer among people with a hospital diagnosis of schizophrenia and accounting for the effects of age, sex and calendar time. METHODS: This population-based study used 1990-2013 data from three nationwide Swedish registries to calculate the incidence (in total, by age group and by sex) of any cancer and of lung, oesophageal, pancreatic, stomach, colon, (in men) prostate and (in women) breast cancer in 111 306 people with a hospital diagnosis of schizophrenia. The incidence in people with diagnosed schizophrenia was

compared with the incidence in the general population. Risk estimates accounted for the effects of calendar time. RESULTS: In 1 424 829 person-years of follow-up, schizophrenia did not confer an overall higher cancer risk (IRR 1.02, 95% CI 0.91-1.13) but was associated with a higher risk for female breast (IRR 1.19, 95% CI 1.12-1.26), lung (IRR 1.42, 95% CI 1.28-1.58), oesophageal (IRR 1.25, 95% CI 1.07-1.46) and pancreatic (IRR 1.10, 95% CI 1.01-1.21) and a lower risk of prostate (IRR 0.66, 95% CI 0.55-0.79) cancer. Some age- and sex-specific differences in risk were observed. CONCLUSIONS: People with schizophrenia do not have a higher overall incidence of cancer than people in the general population. However, there are significant differences in the risk of specific cancer types overall and by sex calling for efforts to develop disease-specific prevention programmes. In people with schizophrenia, higher risk generally occurs in those <75 years.

Polednak, A. P. (2014). "Trend in rates for deaths with mention of schizophrenia on death certificates of US residents, 1999-2010." Soc Psychiatry Psychiatr Epidemiol **49**(7): 1083-1091.
https://link.springer.com/article/10.1007/s00127-014-0846-8

BACKGROUND: Trends in mortality rates for schizophrenia using multiple causes of death (including contributory causes) coded on death certificates in the US resident population apparently have not been reported. METHODS: Age-standardized rates for deaths per 100,000 in 1999-2010 at age 15+ years (and for 15-64 and 65+ years) with mention of schizophrenia were examined for the US resident population, including variation by age, gender, race (blacks/African Americans and whites) and region. RESULTS: Deaths at age 15+ years coded with schizophrenia as underlying cause were only 12 % of all deaths with mention of schizophrenia, for which the rate declined from 1.58 in 1999 (3,407 deaths) to 1.32 in 2010 (3,422 deaths) (percentage change or PC = -16 %). Declines were larger in females than males, in whites than blacks, and occurred in the Northeast, Midwest and South but not the West. The rate increased for age 15-64 years (PC = +28 %) (mainly in males), however, while declining for age 65+ years (PC = -35 %). For deaths at age 15-64 years with schizophrenia coded as other than the underlying cause, the largest continuous increase was for endocrine-metabolic diseases (predominantly diabetes mellitus) as underlying cause, with smaller increases in males for cardiovascular diseases, external causes and neoplasms. CONCLUSION: Trends in the US rate for deaths with mention of schizophrenia varied among the sociodemographic groups examined. The lack of decline for age 15-64 years requires further study especially with regard to mediators (e.g., obesity) of excess mortality in schizophrenia identified from cohort studies.

Preti, A. (2008). "Reduced risk of cancer in schizophrenia: a role for obstetric complications?" Acta Psychiatr Scand **118**(3): 251-253; author reply 253.
https://onlinelibrary.wiley.com/doi/10.1111/j.1600-0447.2008.01235.x

Preti, A. et Wilson, D. R. (2011). "Schizophrenia, cancer and obstetric complications in an evolutionary perspective-an empirically based hypothesis." Psychiatry Investig **8**(2): 77-88.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3149115/pdf/pi-8-77.pdf

OBJECTIVE: Patients diagnosed with schizophrenia have reduced fecundity and premature mortality (both accidental and violent) with no obvious compensatory advantages among kin. The prevalence of the disorder is around 0.7/1%, higher than the expected prevalence of spontaneous mutations. Genes favoring schizophrenia may have been positively selected in the environment of evolutionary adaptation. Literature on potential adaptive genes is reviewed within an evolutionary framework. METHODS: Literature search on major scientific search engine (PubMed/Medline, Ovid/PsychInfo) on papers aimed at investigating potential pathways justifying a mutation-selection balanced model. Findings are presented with a narrative touch to favor readability and understanding. RESULTS: Reduced incidence of cancer in both patients diagnosed with schizophrenia and their siblings was reported worldwide. Such findings are notable given higher cancer risk factors in schizophrenia, i.e., smoking, alcohol abuse, obesity, poor diet, and poor adherence to therapy. Some genes involved in cancer proliferation might as well confer protective advantage in immune-surveillance, inflammation, vascular proliferation or apoptosis that otherwise will adversely affect early neurodevelopment. CONCLUSION: Evidence that reduced risk of certain somatic diseases is associated with schizophrenia is quite significant to progress in the evolutionary epidemiological analysis of psychopathology.

Raviv, G., Laufer, M., Baruch, Y., et al. (2014). "Risk of prostate cancer in patients with schizophrenia." Compr Psychiatry **55**(7): 1639-1642.

OBJECTIVES: To examine the rate of prostate cancer in a cohort of schizophrenia in-patients in the PSA-era as compared to expected rates. There is conflicting evidence on the relative risk of prostate cancer in men with schizophrenia. METHODS: the study sample was comprised of schizophrenia patients who had been admitted to a tertiary care mental health center between 1990 and 2011. The data for the sample was cross-referenced with the National Cancer Registry. Analyses of Standardized Incidence Rates (SIR) for prostate cancer and for lung cancer (representing an organ system not sensitive to sex hormones) were performed. RESULTS: Of 4,326 schizophrenia patients included in the present study, 181 (4.2%) were diagnosed with cancer at any site. Only 10 of these patients were diagnosed with prostate cancer. This reflects a reduced risk; SIR of 0.56 (95% CI 0.27-1.03). In the same cohort, 33 schizophrenia patients were diagnosed with lung cancer presenting a SIR of 1.43 (95% CI 0.98-2.01) in this sample. CONCLUSIONS: The present study suggests a reduced rate of prostate cancer in patients admitted for schizophrenia. There are several possible explanations for this finding including chronic state of hyperprolactinemia induced by antipsychotic drugs.

Rhondali, W., Ledoux, M., Sahraoui, F., et al. (2013). "[Management of psychiatric inpatients with advanced cancer: a pilot study]." Bull Cancer **100**(9): 819-827.

The prevalence of cancer is not well established and probably underestimated in long-stay psychiatric inpatients. Psychiatric patients do not have the same access for cancer screening and care. Therapeutic decision-making is a real ethical problem. In this context, access to medical care should be provided by the establishment of guidelines and/or recommendations for this specific population. The aim of our study was to assess how cancer was managed among long term psychiatric inpatients. For this pilot study, we used a mixed methodology: a quantitative part with a retrospective chart review of cancer patients in a psychiatric institution and a qualitative part based on semi-structured interviews with psychiatrists with discourse analysis. Delay in cancer diagnosis can be explained by communication and behavior disorders, inadequate screening, and additional tests often refused by patients. Compliance and ethical issues (i.e. obtaining informed consent) are many pitfalls to optimal cancer care that should be explored in further research.

Rice, D. (1979). "No lung cancer in schizophrenics?" Br J Psychiatry **134**: 128.
https://www.cambridge.org/core/services/aop-cambridge-core/content/view/724891512271BF86F5A932F9C00EB103/S0007125000199404a.pdf/div-class-title-no-lung-cancer-in-schizophrenics-div.pdf

Rizos, E., Siafakas, N., Koumarianou, A., et al. (2012). "miR-183 as a molecular and protective biomarker for cancer in schizophrenic subjects." Oncol Rep **28**(6): 2200-2204.
https://www.spandidos-publications.com/10.3892/or.2012.2052/download

Previous studies have suggested that schizophrenia is associ-ated with a reduced risk of cancer. Genes that are involved in cell cycle regulation seem to have additional functions in post-mitotic neurons involved in neuronal migration and synaptic plasticity. MicroRNAs (miRNAs) play a dominant role in the regulation of gene expression in the central nervous system (CNS). Due to their involvement in a large number of CNS pathways, miRNAs pose as appealing molecules for further investigation, with potential diagnostic, prognostic and therapeutic value. In the present study, we investigated the potential association between cancer and schizophrenia in 2 patient sample groups. We analyzed a large number of miRNAs in a control group of 6 schizophrenic patients and a study group of 8 schizophrenic patients with a solid tumor. A comparison between the control and study groups showed that only miR-183 was differentially expressed. Specifically, a significant downregulation of miR-183 in the samples of the study group was observed. Although a larger sample size is required to validate this result for the general patient population, our findings provide a first indication that miR-183 may play a role in regulating the expression of other genes with onco-suppressor activity. Our results are in agreement with the theory that patients with schizophrenia may have a tumor suppressor gene or enhanced neuronal apoptotic activities. Further studies are required in order to shed light on the role of miRNAs and particularly, on the suppressive role of miR-183 in the neurobiological pathways involved in schizophrenia.

Rizos, E., Siafakas, N., Skourti, E., et al. (2016). "miRNAs and their role in the correlation between schizophrenia and cancer (Review)." Mol Med Rep **14**(6): 4942-4946.
https://www.spandidos-publications.com/10.3892/mmr.2016.5853/download

Schizophrenia (SZ) and cancer (Ca) have a broad spectrum of clinical phenotypes and a complex biological background, implicating a large number of genetic and epigenetic factors. SZ is a chronic neurodevelopmental disorder signified by an increase in the expression of apoptotic molecular signals, whereas Ca is conversely characterized by an increase in appropriate molecular signaling that stimulates uncontrolled cell proliferation. The rather low risk of developing Ca in patients suffering from SZ is a hypothesis that is still under debate. Recent evidence has indicated that microRNAs (miRNAs or miRs), a large group of small noncoding oligonoucleotides, may play a significant role in the development of Ca and major psychiatric disorders, such as SZ, bipolar disorder, autism spectrum disorders, suicidality and depression, through their interference with the expression of multiple genes. For instance, the possible role of let7, miR98 and miR183 as biomarkers for Ca and SZ was investigated in our previous research studies. Therefore, further investigations on the expression profiles of these regulatory, small RNA molecules and the molecular pathways through which they exert their control may provide a plausible explanation as to whether there is a correlation between psychiatric disorders and low risk of developing Ca.

Roppel, R. M. (1978). "The cancer-schizophrenia linkage." Agressologie **19**(4): 239-245.

Saku, M., Tokudome, S., Ikeda, M., et al. (1995). "Mortality in psychiatric patients, with a specific focus on cancer mortality associated with schizophrenia." Int J Epidemiol **24**(2): 366-372.
https://academic.oup.com/ije/article-abstract/24/2/366/636822?redirectedFrom=fulltext

BACKGROUND: Higher mortality rates among psychiatric patients compared with the general population have been widely reported. On the other hand, lower cancer mortality for schizophrenics has been occasionally pointed out. Few studies from Japan have investigated mortality among psychiatric patients, and this study is the first large-scale follow-up in this country. METHODS: A total of 4980 patients admitted to a national mental hospital from 1948 through 1982 were followed up until 31 August 1985. The standardized mortality ratios (SMR) were calculated in comparison to the general population, using the person-years method. RESULTS: The SMR for total deaths and those for malignancy were as follows for males/females respectively: 2.55/3.02 and 0.84/1.37 for schizophrenia, 1.76/2.37 and 1.44/2.10 for depression, 2.45/3.04 and 1.18/1.82 for mania, 1.81/1.90 and 0.27/1.07 for neurosis, 5.55/4.33 and 1.85/3.34 for alcohol/drug abuse, and 3.65/3.57 and 1.01/0.72 for organic brain syndrome. CONCLUSIONS: The SMR for total deaths were significantly elevated in schizophrenia, depression, mania, neurosis, alcohol/drug abuse, and organic brain syndrome, respectively. The SMR for malignancy were not elevated nor lowered significantly in any of these disease categories. The SMR for stomach cancer in male schizophrenics was significantly lower (0.27; $P < 0.05$).

Schyve, P. M., Smithline, F. et Meltzer, H. Y. (1978). "Neuroleptic-induced prolactin level elevation and breast cancer: an emerging clinical issue." Arch Gen Psychiatry **35**(11): 1291-1301.
https://jamanetwork.com/journals/jamapsychiatry/article-abstract/492004

This article reviews the evidence that neuroleptics may increase the risk of breast cancer via their effects on prolactin secretion. All available neuroleptics, including reserpine, raise serum prolactin levels. Elevated serum prolactin level increases the incidence of spontaneously occurring mammary tumors in mice, and increases the growth of established carcinogen-induced mammary tumors in rats. Caution is necessary in extrapolating this relationship to human mammary tumors because human and rodent tumors differ in some important characteristics, including hormone responsiveness. Serum prolactin levels in women with, or at risk for, breast cancer have generally been normal, and only a minority of human mammary tumors respond to changes in serum prolactin levels. Epidemiologic studies have failed to demonstrate an increased risk of breast cancer associated with the use of neuroleptics or reserpine. Thus, although some human mammary tumors are prolactin dependent, the available evidence does not demonstrate an increased risk of breast cancer in women receiving neuroleptics. We conclude that (1) additional epidemiologic studies of the incidence of mammary tumors in women treated with neuroleptics are desirable; (2) it is premature to mandate warning patients of an unknown and

undemonstrated increase in the risk of developing breast cancer associated with neuroleptic treatment; (3) detection of existing mammary tumors by breast examination prior to administration of neuroleptics is desirable; and (4) development of antipsychotic drugs that do not increase serum prolactin level may be indicated.

Seeman, M. V. (2011). "Preventing breast cancer in women with schizophrenia." Acta Psychiatr Scand **123**(2): 107-117.
https://onlinelibrary.wiley.com/doi/10.1111/j.1600-0447.2010.01626.x

OBJECTIVE: To record risk factors for breast cancer in women with schizophrenia and recommend preventive actions. METHOD: A PubMed literature search (from 2005 to 2010) was conducted, using the search terms 'schizophrenia', 'antipsychotics', 'breast cancer' and 'risk factors'. RESULTS: Several risk factors of relevance to schizophrenia were identified: obesity, elevated prolactin levels, low participation in mammography screening, high prevalence of diabetes, comparatively low parity, low incidence of breastfeeding, social disadvantage, high levels of smoking and alcohol consumption, low activity levels. CONCLUSION: Awareness of breast cancer risk should lead to more accurate risk ascertainment, stronger linkage with primary care, regular monitoring and screening, judicious choice and low dose of antipsychotic treatment, concomitant use of adjunctive cognitive and psychosocial therapies, referral to diet and exercise programmes as well as smoking and drinking cessation programmes, avoidance of hormonal treatment and discussion with patient and family about the pros and cons of preventive measures in high-risk women. Psychiatrists are in a position to reverse many of the identified risk factors.

Shah, H. A., Lee, H. B. et Nunery, W. R. (2008). "Neglected basal cell carcinoma in a schizophrenic patient." Ophthalmic Plast Reconstr Surg **24**(6): 495-497.

Obtaining informed consent from patients with mental disorders can be a complicated and involved process, potentially resulting in decisions contrary to the advice of physicians. We present a schizophrenic patient with an invasive basal cell carcinoma involving the periocular structures and the right orbit. Exenteration was recommended with en bloc resection of the tumor. The ethical and legal committees decided against surgical intervention. Rather, the patient was admitted for medical treatment of his mental illness. A multidisciplinary approach with consultation of a psychiatrist, social worker, and ethical and legal committees is often necessary in the care of patients with mental illness.

Sharma, A., Ngan, S., Nandoskar, A., et al. (2010). "Schizophrenia does not adversely affect the treatment of women with breast cancer: a cohort study." Breast **19**(5): 410-412.
https://www.thebreastonline.com/article/S0960-9776(10)00108-6/pdf

BACKGROUND: Data on the natural course of patients with breast cancer and schizophrenia are limited. Although there have been studies in assessing the incidence of breast cancer in the setting of schizophrenia, there is very little information concerning the clinical profile of these women. METHODS: We analyzed the data from our electronic notes system by searching for the terms 'schizophrenia' or 'schizophrenic' and 'breast cancer' or 'tumour' between 1993 and 2009. Information was collected on demographics, clinico-pathologic disease variables, treatment including anti-emetic use, chemotherapy delivery and outcomes. RESULTS: From 90,676 patients screened, we identified 37 individuals who had breast cancer and a pre-existing underlying diagnosis of schizophrenia. Of these, 30 (81%) presented with early breast cancer and 7 (19%) presented with metastatic disease. Node positivity was observed in 14 individuals (38%). The average interval between diagnosis of schizophrenia and breast cancer was more than 20 years in the majority of the patients. Treatment outcomes, trial involvement, compliance and ability to provide informed consent were similar to our previously published cohort data. CONCLUSIONS: Schizophrenia does not affect treatment delivery or outcomes in women with breast cancer. The presence of schizophrenia should not be a limiting factor for entry into clinical trials. Breast cancer patients with this illness should be offered standard treatment without discrimination, including entry into clinical trials.

Soni, S. M. et Gill, J. (1979). "Malignancies in schizophrenic patients." Br J Psychiatry **134**: 447-448.
https://www.cambridge.org/core/services/aop-cambridge-core/content/view/3A9A34E43502DDB397CF864B44801CC9/S0007125000058748a.pdf/div-class-title-malignancies-in-schizophrenic-patients-div.pdf

Steinert, T., Breier, A. et Flammer, E. (2011). "[Preventive medical checkups and consultations in people with schizophrenia and a comparison group of similar social status]." Psychiatr Prax **38**(2): 87-90. https://www.thieme-connect.com/products/ejournals/abstract/10.1055/s-0030-1248553

OBJECTIVE: To examine whether the utilisation of preventive medical checkups and contacts to doctors differs between people with schizophrenia and a comparison group of comparable social status in Germany. METHOD: 120 patients, each 40 from a hospital, an out-patient clinic and a residential home, were interviewed as well as 118 attendants of a social welfare office as a comparison group. RESULTS: Cancer screenings were realised less frequently than in the general population both among the patients and the controls. Contacts with doctors of somatic disciplines were more frequent among patients than among controls and the general population. CONCLUSION: The health behaviour of patients with schizophrenia was not significantly different from a comparison group with similar social status.

Taipale, H., Solmi, M., Lähteenvuo, M., et al. (2021). "Antipsychotic use and risk of breast cancer in women with schizophrenia: a nationwide nested case-control study in Finland." Lancet Psychiatry **8**(10): 883-891. https://www.thelancet.com/journals/lanpsy/article/PIIS2215-0366(21)00241-8/fulltext

BACKGROUND: Breast cancer is more common in female patients with schizophrenia than in the general population. It is not known whether treatment with prolactin-increasing antipsychotics contributes to increased odds of breast cancer. METHODS: We used Finnish nationwide registers of hospital treatment, prescription drug purchases, and cancer diagnoses to do a nested case-control study. Of women with schizophrenia, those with breast cancer (cases) were matched by age and duration of illness with five women without cancer (controls). Cases and controls were aged 18-85 years and exclusion criteria were any previous cancer diagnoses, receipt of organ transplant, mastectomy, or diagnosis of HIV. The main analysis was the association between cumulative exposure to prolactin-increasing drugs and breast cancer. The analyses were done with conditional logistic regression, by adjusting for comorbid conditions and concomitant medications. Ethnicity data were not available. FINDINGS: Of 30 785 women diagnosed with schizophrenia between 1972 and 2014, 1069 were diagnosed with breast cancer between Jan 1, 2000, and Dec 31, 2017. Compared with 5339 matched controls, 1-4 years cumulative exposure (adjusted odds ratio [OR] 0·95, 95% CI 0·73-1·25) or 5 or more years exposure (adjusted OR 1·19, 0·90-1·58) to prolactin-sparing antipsychotics (including clozapine, quetiapine, or aripiprazole) was not associated with an increased risk of breast cancer in comparison with minimal exposure (<1 year). When compared with less than 1 year of exposure to prolactin-increasing antipsychotics (all other antipsychotics), 1-4 years of exposure was not associated with an increased risk, but exposure for 5 or more years was associated with an increased risk (adjusted OR 1·56 [1·27-1·92], p<0·001). The risk for developing lobular adenocarcinoma associated with long-term use of prolactin-increasing antipsychotics (adjusted OR 2·36 [95% CI 1·46-3·82]) was higher than that of developing ductal adenocarcinoma (adjusted OR 1·42 [95% CI 1·12-1·80]). INTERPRETATION: Long-term exposure to prolactin-increasing, but not to prolactin-sparing, antipsychotics is significantly associated with increased odds of breast cancer. Monitoring prolactinemia and addressing hyperprolactinemia is paramount in women with schizophrenia being treated with prolactin-increasing antipsychotics. FUNDING: Finnish Ministry of Social Affairs and Health.

Tanskanen, A., Tiihonen, J. et Taipale, H. (2018). "Mortality in schizophrenia: 30-year nationwide follow-up study." Acta Psychiatr Scand **138**(6): 492-499. https://onlinelibrary.wiley.com/doi/10.1111/acps.12913

OBJECTIVE: Recent reports suggest that the mortality gap between persons with schizophrenia and the general population is increasing. We investigated the mortality, age at death, and causes of death among persons diagnosed with schizophrenia and the general population in Finland during 1984-2014. METHODS: All persons with schizophrenia in Finland were identified from hospital discharge register, and compared with the Finnish population aged 16 years and older during 1984-2014, based on data from Statistics Finland. Age at death and standardized mortality ratio (SMR) were calculated for each follow-up year. RESULTS: Mean age at death increased from 57.6 years in 1984 to 70.1 years in 2014 in persons with schizophrenia, and from 70.9 to 77.5 years in the general population. All-cause SMR remained stable during the follow-up (2.6 in 1984 and 2.7 in 2014). A major change was observed in SMR for suicides which decreased from 11.0 in 1984 to 6.6 in 2014 (-40%). The SMRs for cardiovascular and cancer deaths showed increasing trends. CONCLUSION: The longevity of persons with schizophrenia is improving at

approximately the same rate as the general population but suicide rates have declined substantially. However, there is still a major disparity in mortality compared with general population.

Taylor-Desir, M. J., Sawchuk, C. N., Crane, S. J., et al. (2022). "Integration of mental health and supportive care in individuals with schizophrenia and cancer: Assertive community treatment model." Psychooncology. https://onlinelibrary.wiley.com/doi/10.1002/pon.5911

Tiihonen, J., Tanskanen, A., Bell, J. S., et al. (2022). "Long-term treatment with clozapine and other antipsychotic drugs and the risk of haematological malignancies in people with schizophrenia: a nationwide case-control and cohort study in Finland." Lancet Psychiatry **9**(5): 353-362. https://www.thelancet.com/journals/lanpsy/article/PIIS2215-0366(22)00044-X/fulltext

BACKGROUND: Clozapine is the most efficacious treatment for schizophrenia and is associated with lower overall mortality than are other antipsychotic drugs, despite the risk of agranulocytosis. Preliminary reports over the past 10 years suggest a possible risk of haematological malignancies, but the issue has remained unsettled. We aimed to study the risk of haematological malignancies associated with use of clozapine and other antipsychotics. METHODS: We did a nationwide case-control (and cohort) study of people with schizophrenia, using prospectively gathered data from Finnish national registers. A nested case-control study was constructed by individually matching cases of lymphoid and haematopoietic tissue malignancy with up to ten controls without cancer by age, sex, and time since first schizophrenia diagnosis. For the case-control study, we restricted inclusion criteria to malignancies diagnosed on a histological basis, and excluded individuals outside of the age range 18-85 years, and any patients that had a previous malignancy. Analyses were done using conditional logistic regression adjusting for comorbid conditions. FINDINGS: For the case-control study 516 patients with a first-time diagnosis of lymphoid and haematopoietic tissue malignancy during years 2000-17 and diagnosed after their first diagnosis of schizophrenia were identified. 102 patients were excluded due to diagnosis that was without a histological basis, five patients were excluded because of their age, and 34 were excluded for a previous malignancy, resulting in 375 patients being matched to controls. We selected up to ten controls without cancer (3734 in total) for each case from the base cohort of people with schizophrenia. For the cohort study, data for 55 949 people were included for analysis. Cumulative incidence of haematological malignancies during the mean follow-up of 12·3 years (SD 6·5) was 102 (0·7%) cases among 13 712 patients who had used clozapine (corresponding to event rate of 61 cases per 100 000 person-years), and during mean follow-up of 12·9 years (SD 7·2) was 235 (0·5%) malignancies among 44 171 patients having used other antipsychotic medication than clozapine (corresponding to 41 cases per 100 000 person-years). Of the 375 individuals with haematological malignancies (305 lymphomas, 42 leukaemia, 22 myelomas, 6 unspecified) observed from 2000-17, 208 (55%) were males and 167 (45%) were female. Ethnicity data were not available. Compared with non-use of clozapine (most had used other antipsychotics and a few had used no antipsychotics), clozapine use was associated with increased odds of haematological malignancies in a dose-response manner (adjusted odds ratio 3·35, [95% CI 2·22-5·05] for ≥5000 defined daily dose cumulative exposure, p<0·0001). Exposure to other antipsychotic drugs was not associated with increased odds. A complementary analysis showed that the clozapine-related risk increase was specific for haematological malignancies, because no such finding was observed for other malignancies. Over 17 years of follow-up of the base cohort, 37 deaths occurred due to haematological malignancy among patients exposed to clozapine (26 with ongoing use at time of haematological malignancy diagnosis, and 11 in patients who did not use clozapine at the exact time of their cancer diagnosis), whereas only three deaths occurred due to agranulocytosis. INTERPRETATION: Unlike other antipsychotics, long-term clozapine use is associated with increased odds of haematological malignancies. Long-term clozapine use has a higher effect on mortality due to lymphoma and leukaemia than due to agranulocytosis. However, acknowledging that the absolute risk is small compared with the previously observed absolute risk reduction in all-cause mortality is important. Our results suggest that patients and caregivers should be informed about warning signs of haematological malignancies, and mental health clinicians should be vigilant for signs and symptoms of haematological malignancy in patients treated with clozapine. FUNDING: The Finnish Ministry of Social Affairs and Health and Academy of Finland.

Torrey, E. F. (2006). "Prostate cancer and schizophrenia." Urology **68**(6): 1280-1283. https://www.goldjournal.net/article/S0090-4295(06)01965-0/fulltext

OBJECTIVES: To assess the incidence of prostate cancer in individuals with schizophrenia. METHODS: A MEDLINE search was performed for all studies of "prostate cancer" or "cancer" and "schizophrenia." RESULTS: Five studies had age-standardized, site-specific cancer data. All five had a lower standardized incidence ratio for prostate cancer, ranging from 0.49 to 0.76. The incidence of cancer at other sites varied among the studies. Possible explanations included ascertainment bias; genetic factors; antipsychotic drug effects, either by being cancer protective or decreasing testosterone, or both; and lifestyle differences, such as prolonged hospitalization resulting in a decreased opportunity for heterosexual intercourse. CONCLUSIONS: The results of this study have revealed that the incidence of prostate cancer in individuals with schizophrenia is significantly lower than expected.

Tran, E., Rouillon, F., Loze, J. Y., et al. (2009). "Cancer mortality in patients with schizophrenia: an 11-year prospective cohort study." Cancer **115**(15): 3555-3562.
https://acsjournals.onlinelibrary.wiley.com/doi/pdfdirect/10.1002/cncr.24383?download=true

BACKGROUND: Schizophrenia has been associated with a rate of premature mortality that is 2 to 3 times higher than that in the general population. Although the role of cancer in this excess mortality remains unclear, previous incidence or mortality studies found contradictory results. METHODS: In 1993, a large prospective study was initiated in a cohort of 3470 patients with schizophrenia to examine cancer-related mortality and predictors. Standardized mortality ratios (SMRs) were calculated, adjusting for age and sex relative to a representative sample of the French general population. RESULTS: During the 11-year follow-up, 476 (14%) patients died; the mortality rate was thus nearly 4-fold higher than in the general population. Cancer was the second most frequent cause of mortality (n=74), with a global SMR of 1.5 (95% confidence interval [95% CI], 1.2-1.9). For all cancers, the SMRs were 1.4 (not significant) for men and 1.9 (95% CI, 1.4-2.8) for women. For men, lung cancer was the most frequent localization (n=23; 50%), with an SMR of 2.2 (95% CI, 1.6-3.3). For women, breast cancer was the most frequent localization (n=11; 39%), with an SMR of 2.8 (95% CI, 1.6-4.9). In comparison with patients who did not die of cancer, there were 2 significant baseline predictors of death by lung cancer in the final logistic regression model: duration of smoking and age>38 years. CONCLUSIONS: The results of the current study demonstrated an increased risk of mortality by cancer in patients with schizophrenia, especially for women from breast cancer and for men from lung cancer.

Trevizol, A. P., Cerqueira, R. O., Brietzke, E., et al. (2019). "New-onset psychiatric symptoms following intracranial meningioma in a patient with schizophrenia: a case study." Braz J Psychiatry **41**(1): 91-92.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6781699/pdf/bjp-41-01-91.pdf

Tsuang, M. T., Perkins, K. et Simpson, J. C. (1983). "Physical diseases in schizophrenia and affective disorder." J Clin Psychiatry **44**(2): 42-46.

Studies of the increased or decreased risk of specific physical diseases in patients with schizophrenia and affective disorder are reviewed. Existing data suggest further examination of the following relationships: (1) the presence in schizophrenics of increased incidence of gastrointestinal cancer and of cardiovascular and infectious diseases, and of decreased incidence of lung cancer and rheumatoid arthritis; and (2) the increased incidence of circulatory, respiratory, and atopic diseases, and of diabetes mellitus among patients with major affective disorder. A majority of the studies reviewed failed to meet methodologic standards necessary to provide conclusive evidence. An ongoing research project which generally meets these standards, the Oxford Record Linkage Study, is described.

Tsuang, M. T., Woolson, R. F. et Fleming, J. A. (1980). "Causes of death in schizophrenia and manic-depression." Br J Psychiatry **136**: 239-242.
https://www.cambridge.org/core/journals/the-british-journal-of-psychiatry/article/abs/causes-of-death-in-schizophrenia-and-manicdepression/6C7C2720FB127B2C72F7642575F8E8FB

Causes of death were studied in a cohort of 200 schizophrenic, 100 manic, and 225 depressive patients who were followed in a historical prospective study. These patients were admitted between 1934 and 1944 and were studied 30 to 40 years later. Five cause of death categories were considered in this analysis: (1) unnatural deaths, (2) neoplasms, (3) diseases of the circulatory system, (4) infective and parasitic diseases, and (5) other causes. For each cause of death, the expected number of deaths was calculated from vital statistics for the State of Iowa for the time period of follow-up. Observed numbers

of deaths were contrasted with expected numbers of deaths to assess statistical significance for each diagnostic group. There was a significant excess of unnatural deaths in all diagnostic groups in both sexes, with the exception of female manics. This group, however, did show a significant excess of circulatory system deaths. Both male and female schizophrenics showed a substantial excess of infective disorder deaths.

Tsuang, M. T., Woolson, R. F. et Fleming, J. A. (1980). "Schizophrenia and cancer death." Lancet **1**(8166): 480-481. https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(80)91019-3/fulltext

Tylec, A., Dubas-Slemp, H., Wojcicka, A., et al. (2018). "The difficulties of secondary prophylaxis of cervical cancer in women suffering from paranoid schizophrenia - a case study." Psychiatr Pol **52**(2): 251-259.

Cervical cancer constitutes 5.32% of all malignant neoplasm cases, it is the sixth most common condition of the cancer type and it is an important problem because of its medical, epidemiological and social implications. The aim of primary prophylaxis is to reduce the number of new cases, while secondary prophylaxis is to provide early diagnoses and treatment of cancer cases. The aim of this work is to present the case of 55-year-old woman treated with chronic paranoid schizophrenia whose gynecologist refused to collect biological material for cytological evaluation. The patient was diagnosed with carcinoma planoepitheliale (G2), then treated surgically and qualified for adjuvant-radiological treatment. Despite the good mental state and a psychiatrists' statement (treating the patient for many years) of the absence of contraindications for hospitalization, a gynecologist-oncologist refused to admit the patient to the ward in fear of a threat to other patients and decided on outpatient palliative treatment of the patient. Finally, radiologist-oncologist performed the complete cycle of irradiation in order to cure the patient. While looking for possible reasons of cervical cancer development in individuals with psychotic disorders, all the possible carcinogenic factors have to be taken into account. Nulliparous women and virgins treated for mental illness must not be denied screening examinations related to cervical cancer. Despite the changes, also related to the implementation of the mental health program, people with mental disorders with underlying physical illness are still stigmatized, even by a higher medical personnel. Moreover, mentally ill patients are denied proper treatment in accordance with the current state of medical knowledge.

Viprey, M., Pauly, V., Salas, S., et al. (2021). "Palliative and high-intensity end-of-life care in schizophrenia patients with lung cancer: results from a French national population-based study." Eur Arch Psychiatry Clin Neurosci **271**(8): 1571-1578.
https://link.springer.com/article/10.1007/s00406-020-01186-z

Schizophrenia is marked by inequities in cancer treatment and associated with high smoking rates. Lung cancer patients with schizophrenia may thus be at risk of receiving poorer end-of-life care compared to those without mental disorder. The objective was to compare end-of-life care delivered to patients with schizophrenia and lung cancer with patients without severe mental disorder. This population-based cohort study included all patients aged 15 and older who died from their terminal lung cancer in hospital in France (2014-2016). Schizophrenia patients and controls without severe mental disorder were selected and indicators of palliative care and high-intensity end-of-life care were compared. Multivariable generalized log-linear models were performed, adjusted for sex, age, year of death, social deprivation, time between cancer diagnosis and death, metastases, comorbidity, smoking addiction and hospital category. The analysis included 633 schizophrenia patients and 66,469 controls. The schizophrenia patients died 6 years earlier, had almost twice more frequently smoking addiction (38.1%), had more frequently chronic pulmonary disease (32.5%) and a shorter duration from cancer diagnosis to death. In multivariate analysis, they were found to have more and earlier palliative care (adjusted Odds Ratio 1.27 [1.03;1.56]; p = 0.04), and less high-intensity end-of-life care (e.g., chemotherapy 0.53 [0.41;0.70]; p < 0.0001; surgery 0.73 [0.59;0.90]; p < 0.01) than controls. Although the use and/or continuation of high-intensity end-of-life care is less important in schizophrenia patients with lung cancer, some findings suggest a loss of chance. Future studies should explore the expectations of patients with schizophrenia and lung cancer to define the optimal end-of-life care.

Viprey, M., Pauly, V., Salas, S., et al. (2021). "Palliative and high-intensity end-of-life care in schizophrenia patients with lung cancer: Results from a French national population-based study." Eur Arch Psychiatry Clin Neurosci **271**(8): 1571-1578.
https://link.springer.com/article/10.1007/s00406-020-01186-z

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Wang, K. S., Zuo, L., Owusu, D., et al. (2014). "Prostate Cancer Related JAZF1 Gene is Associated with Schizophrenia." J Schizophr Res **1**(1).

BACKGROUND: Epidemiological studies have shown that there is a reduced risk of prostate cancer among persons diagnosed with schizophrenia (SCZ). However, the mechanism of such relationship is not clear. The reduced incidence of cancer observed in SCZ patients may be related to differences in genetic background. Recently, the JAZF1 gene is found to be associated with prostate cancer and type 2 diabetes. However, no study has focused on the association of JAZF1 with the risk of SCZ. METHODS: We examined genetic associations of 118 single-nucleotide polymorphisms (SNPs) within the JAZF1 gene with SCZ using one European American (EA) sample of 1,149 cases and 1,347 controls. Logistic regression analysis of SCZ as a binary trait was performed using PLINK software. RESULTS: The most significant association with SCZ was observed with rs10258132 (p = 0.0011); while the next best signal was rs17156259 (p = 0.0031). The third best associated SNP was rs7791865 (p = 0.00889). In addition, haplotype analyses revealed that the A-C haplotype from rs10244184 and rs10258132 was associated with SCZ (p = 0.00093); and the G-G haplotype from rs17156238 and rs17156259 was associated with SCZ (p = 0.00455). CONCLUSION: These findings provide evidence of several genetic variants in JAZF1 gene influencing the risk of SCZ and will serve as a resource for replication in other populations.

Wang, Y., He, G., He, L., et al. (2011). "Do shared mechanisms underlying cell cycle regulation and synaptic plasticity underlie the reduced incidence of cancer in schizophrenia?" Schizophr Res **130**(1-3): 282-284.

Evidence from epidemiology suggests that the incidence of cancer is reduced in those with schizophrenia. Clues that could explain this finding have recently emerged from neuroscience--genes that were previously thought only to be involved in cell cycle regulation have additional functions in post-mitotic neurons related to neuronal migration and synaptic plasticity. This brief communication provides a concise summary of this evidence. We propose that this convergence between epidemiology and neuroscience will provide a more tractable search space for candidate genes, and provide clues for etiopathogenesis of schizophrenia.

Wu Chou, A. I., Wang, Y. C., Lin, C. L., et al. (2017). "Female schizophrenia patients and risk of breast cancer: A population-based cohort study." Schizophr Res **188**: 165-171.

OBJECTIVE: Breast cancer is the most common type of cancer in women. This population-based cohort study aimed to examine the association between breast cancer in female schizophrenia patients and its association with the use of antipsychotics drugs. METHODS: All study subjects were selected from the Taiwan Insurance Claims Data (1998-2008). We compared the risk for breast cancer between female schizophrenia patients receiving antipsychotics (n=29,641) with female patients without any serious mental illnesses nor receiving antipsychotic drugs (n=59,282). We also compared between patients on 1) first-generation antipsychotics (FGAs) alone; 2) combination of first and second generation antipsychotics (SGAs); and 3) SGAs alone. We then stratified those on SGAs into two subgroups according to their prolactin-elevating properties: risperidone (RIS), paliperidone (PAL) or amisulpride (AMI) and all other SGAs. RESULTS: After adjusting for confounding factors, the risk of breast cancer in female schizophrenia patients was 1.94 higher than the non-schizophrenia cohort (aHR: 1.94, 95% CI: 1.43-2.63). Schizophrenia patients receiving a combination of FGAs and SGAs had a slightly higher risk of breast cancer than non-schizophrenic patients (aHR: 2.17, 95% CI: 1.56-3.01). Patients on RIS, PAL, and AMI had a 1.96-fold risk of breast cancer compared to the non-schizophrenic cohort (95% CI: 1.36-2.82). CONCLUSIONS: This study raises awareness among both clinicians and patients about the importance of breast cancer screening and the promotion of healthy lifestyle choices. Due to the nature of our database, confounding factors - such as parity, obesity, hormone therapy, and smoking - could not be controlled for.

Xiping, Z., Shuai, Z., Feijiang, Y., et al. (2019). "Meta-analysis of the Correlation Between Schizophrenia and Breast Cancer." Clin Breast Cancer **19**(1): e172-e185.
https://www.clinical-breast-cancer.com/article/S1526-8209(18)30090-9/fulltext

PURPOSE: To determine the correlation between schizophrenia and breast cancer (BC). METHODS: We searched relevant articles indexed in the PubMed, Embase, and Cochrane Library databases; managed the data in Endnote X7 software; evaluated literature quality by Newcastle-Ottawa quality evaluation criteria; designed tables; and extracted relevant data. The main outcome measure was BC incidence. Effect values were risk ratio and 95% confidence intervals. We used Stata 13.1 software to perform the meta-analysis, choosing a corresponding combination model according to heterogeneity test results and carrying out subgroup analyses in order to better understand the stability of results through sensitivity analysis. RESULTS: On the basis of 15 studies that assessed patients in different geographic regions, meta-analysis results showed that BC incidence between the exposure group (patients with schizophrenia) and the control group (nonschizophrenia population or general population) had statistical difference (risk ratio = 1.18; 95% confidence interval, 1.05, 1.32), thus showing that BC incidence in patients with schizophrenia is higher than in the nonschizophrenia or general population. Subgroup analysis indicated that gender and geographic region may be sources of the assessed studies' heterogeneity. CONCLUSION: The incidence of schizophrenia is positively correlated with BC, and the incidence of BC in patients with schizophrenia is increased to a certain degree. Because of the effects of potential and publication bias, this conclusion needs more high-quality studies to increase the strength of evidence.

Xu, D., Chen, G., Kong, L., et al. (2017). "Lower risk of liver cancer in patients with schizophrenia: a systematic review and meta-analysis of cohort studies." Oncotarget **8**(60): 102328-102335.
https://www.oncotarget.com/article/21679/pdf/

Previous studies regarding the association between schizophrenia and the subsequent risk of liver cancer have shown inconsistent results. We aimed to perform a systematic review and meta-analysis to evaluate the association between schizophrenia and liver cancer incidence. We systematically searched the PubMed and Embase electronic databases for cohort studies reporting the standardized incidence ratio (SIR) for the risk of liver cancer in patents with schizophrenia as compared with the general population. A random-effects model was used to analyze the data. Stratified analyses were performed according to the gender of the patients. Seven studies comprising 312,834 patients with schizophrenia were included. During follow-up, 581 liver cancer cases were confirmed. The meta-analysis results showed that schizophrenia was associated with a trend of a lower liver cancer incidence (SIR: 0.83, 95% confidence interval [CI]: 0.66-1.04, p = 0.10) with significant heterogeneity (I(2) = 81%). Sensitivity analysis of five cohorts of patients with cancer events before the diagnosis of schizophrenia indicated that schizophrenia was associated with a significantly lower incidence of liver cancer (SIR: 0.76, 95% CI: 0.61-0.96, p = 0.02; I(2) = 84%). The reduction of a subsequent incidence of liver cancer was significant in male patients with schizophrenia (SIR: 0.71, p = 0.005), and a trend of a reduced risk of liver cancer was also detected in

female patients (SIR: 0.83, p = 0.12). Significant publication bias was detected. However, "trim and fill" analyses by including the imputed unpublished studies showed similar results. In summary, schizophrenia may be protective against the incidence of liver cancer.

Xu, L., Qi, X., Zhu, C., et al. (2018). "Activation of IL-8 and its participation in cancer in schizophrenia patients: new evidence for the autoimmune hypothesis of schizophrenia." Neuropsychiatr Dis Treat **14**: 3393-3403.
https://www.dovepress.com/getfile.php?fileID=46922

To investigate the autoimmune mechanisms of schizophrenia, we explored the relationship between schizophrenia and cancer using gene expression data of peripheral blood mononuclear cells from GSE27383 datasets. Gene screening and enrichment analysis using Gene Set Enrichment Analysis were applied to identify possible connections between schizophrenia and cancer. Real-time PCR (quantitative PCR), Western blotting and immunohistochemistry were performed on the brain tissue from both schizophrenia patients and normal controls. The genes for IL-8, as well as PTGS2, TPR, JUN, CXCL1, CXCL3, CXCL5 and PARD3 were highly expressed in schizophrenia patients. Cancer and chemokine signaling pathways were enriched in the schizophrenic group, related to the high expression of IL-8. Increased expression of IL-8 was further confirmed by quantitative PCR, Western blotting and immunohistochemistry results. Our results suggest that IL-8 may participate specifically in the pathophysiological changes that occur in schizophrenia. Additionally, our findings provide novel evidence supporting the autoimmune hypothesis of schizophrenia.

Yung, A. R. et Firth, J. (2018). "Women with schizophrenia are at increased risk of breast cancer." Evid Based Ment Health **21**(3): e13.
https://ebmh.bmj.com/content/21/3/e13.long

Zhuo, C., Tao, R., Jiang, R., et al. (2017). "Cancer mortality in patients with schizophrenia: systematic review and meta-analysis." Br J Psychiatry **211**(1): 7-13.
https://www.cambridge.org/core/services/aop-cambridge-core/content/view/10D02A0902F60CEE7ED4AE357D73E692/S0007125000279907a.pdf/div-class-title-cancer-mortality-in-patients-with-schizophrenia-systematic-review-and-meta-analysis-div.pdf

BackgroundPrevious studies have reported conflicting results on the association between schizophrenia and cancer mortality.AimsTo summarise available evidence and quantify the association between schizophrenia and cancer mortality using meta-analysis.MethodWe systematically searched literature in the PubMed and Embase databases. Risk estimates and 95% confidence intervals reported in individual studies were pooled using the DerSimonian-Laird random-effects model.ResultsWe included 19 studies in the meta-analysis. Among them, 15 studies reported standardised mortality ratios (SMRs) comparing patients with schizophrenia with the general population, and the pooled SMR was 1.40 (95% CI 1.29-1.52, P < 0.001). The other four studies reported hazard ratios (HRs) comparing individuals with schizophrenia with those without schizophrenia; the pooled HR was 1.51 (95% CI 1.13-2.03, P = 0.006).ConclusionsPatients with schizophrenia are at a significantly increased risk of cancer mortality compared with the general population or individuals without schizophrenia.

Zhuo, C. et Triplett, P. T. (2018). "Association of Schizophrenia With the Risk of Breast Cancer Incidence: A Meta-analysis." JAMA Psychiatry **75**(4): 363-369.

Importance: Patients with schizophrenia are considered to have many risk factors for the development of cancer. However, the incidence of breast cancer in women with schizophrenia compared with the general population remains uncertain. Objective: To perform an updated meta-analysis to evaluate the association between schizophrenia and the risk of breast cancer. Data Sources: A systematic search of the PubMed and EMBASE databases was conducted using the search terms schizophrenia, schizophrenic, psychosis, combined with breast and cancer, tumor, neoplasm, or carcinoma. The final literature search was performed on August 15, 2017. Study Selection: Cohort studies reporting the standardized incidence ratio (SIR) for the risk of breast cancer in women with schizophrenia compared with the general population. Data Extraction and Synthesis: The meta-analysis adhered to Meta-analysis of Observational Studies in Epidemiology and the Cochrane Handbook for Systematic Reviews of Interventions. Data extraction was performed independently. A random-effects model was used to pool the results, and a recently proposed prediction interval was calculated to describe the heterogeneity. Main Outcomes and

Measures: The SIR for the risk of breast cancer in women with schizophrenia compared with the general population or those without schizophrenia. Results: Twelve cohorts including 125760 women were included in this meta-analysis. The results of the meta-analysis showed that schizophrenia was associated with a significantly increased risk of breast cancer incidence in women (SIR, 1.31; 95% CI, 1.14-1.50; P < .001), with significant heterogeneity (P < .001; I2 = 89%). Substantial between-study variance was also suggested by the wide prediction interval (0.81-2.10), which indicated that it is possible that a future study will show a decreased breast cancer risk in women with schizophrenia compared with the general population. The subgroup analysis results showed that the association was not significantly affected by whether breast cancer cases were excluded at baseline or the sample size of the included studies. Conclusions and Relevance: The incidence of breast cancer in women with schizophrenia is higher than that of the general female population. However, significant heterogeneity exists among the included studies. Women with schizophrenia deserve intensive prevention and treatment of breast cancer.

Zuber, V., Jonsson, E. G., Frei, O., et al. (2018). "Identification of shared genetic variants between schizophrenia and lung cancer." Sci Rep **8**(1): 674.
https://escholarship.org/content/qt8fc5685v/qt8fc5685v.pdf?t=pakge5

Epidemiology studies suggest associations between schizophrenia and cancer. However, the underlying genetic mechanisms are not well understood, and difficult to identify from epidemiological data. We investigated if there is a shared genetic architecture between schizophrenia and cancer, with the aim to identify specific overlapping genetic loci. First, we performed genome-wide enrichment analysis and second, we analyzed specific loci jointly associated with schizophrenia and cancer by the conjunction false discovery rate. We analyzed the largest genome-wide association studies of schizophrenia and lung, breast, prostate, ovary, and colon-rectum cancer including more than 220,000 subjects, and included genetic association with smoking behavior. Polygenic enrichment of associations with lung cancer was observed in schizophrenia, and weak enrichment for the remaining cancer sites. After excluding the major histocompatibility complex region, we identified three independent loci jointly associated with schizophrenia and lung cancer. The strongest association included nicotinic acetylcholine receptors and is an established pleiotropic locus shared between lung cancer and smoking. The two other loci were independent of genetic association with smoking. Functional analysis identified downstream pleiotropic effects on epigenetics and gene-expression in lung and brain tissue. These findings suggest that genetic factors may explain partly the observed epidemiological association of lung cancer and schizophrenia.

Cancers et troubles bipolaires

ÉTUDES FRANÇAISES

Bendjema, Z. (2021). "Construction et évaluation d'un parcours de prévention somatique destiné aux patients psychotiques et bipolaires suivis par un secteur de santé mentale." L'information psychiatrique **98**(8): 727-728.
https://www.cairn.info/revue-l-information-psychiatrique-2021-8-page-727.htm

Les patients souffrant de troubles mentaux sévères ont un excès de mortalité imputable au risque cardiovasculaire, métabolique et de cancer réduisant leur espérance de vie de 20 %. Ces facteurs de risque sont similaires à ceux de la population générale dans leur nature, mais sont surreprésentés. Les pathologies qui en découlent sont accessibles à la prévention et au dépistage. Néanmoins les études suggèrent un défaut de prévention et de suivi.

Fond, G., Baumstarck, K., Auquier, P., et al. (2020). "End-of-Life Care Among Patients With Bipolar Disorder and Cancer: A Nationwide Cohort Study." Psychosom Med **82**(7): 722-732.

OBJECTIVE: This study aimed to describe end-of-life (EOL) care in individuals with bipolar disorder (BD) who died of cancer compared with mentally healthy individuals. METHODS: This was a nationwide cohort study of all adult individuals who died of cancer in hospitals in France between 2013 and 2016. Outcomes were compared between individuals with BD and mentally healthy individuals in the last month of life including palliative care and high-intensity EOL care (chemotherapy, artificial nutrition, and other interventions). A subanalysis explored differences between patients with BD and patients

with schizophrenia. RESULTS: The study included 2015 individuals with BD and 222,477 mentally healthy controls. Compared with the controls, individuals with BD died 5 years earlier, more often had comorbidities and thoracic cancer, and had fewer metastases, but did not have shorter delays from cancer diagnosis to death. After matching and adjustment for covariates, individuals with BD more often received palliative care in the last 3 days of life (25% versus 13%, p < .001) and less high-intensity care (e.g., chemotherapy 12% versus 15%, p = .004), but more artificial nutrition (6% versus 4.6%, p = .003). Compared with the schizophrenia comparison group, chemotherapy was received more by individuals with BD in the last 14 days of life (12.5% for BD versus 9.4%, p < .001). CONCLUSIONS: Individuals with BD were more likely to receive palliative care and less likely to receive high-intensity EOL care, except for artificial nutrition. These results may not be specific to BD, as no difference was found between patients with BD and schizophrenia except for chemotherapy.

Mallet, J., Huillard, O., Goldwasser, F., et al. (2018). "Mental disorders associated with recent cancer diagnosis: Results from a nationally representative survey." Eur J Cancer **105**: 10-18.
https://www.ejcancer.com/article/S0959-8049(18)31408-4/fulltext

BACKGROUND: Receiving a diagnosis of cancer may be associated with increased risk of mental disorders. Yet, in this context, no factor predicts the onset of a mental disorder besides the diagnosis of cancer itself. If patients with a history of mental disorder are at particular risk is unknown. METHODS: Data were derived from a large national sample of the US population. Face-to-face surveys were conducted on 36309 adults during 2012-2013 period. Data were used to examine the associations among the past-year prevalence of mental disorders (according to the Diagnostic and Statistical Manual of Mental Disorders-5), the treatment-seeking rates and a recent cancer diagnosis. Data were analysed according to the antecedents of mental disorder in participants and according the presence of a recent cancer diagnosis. RESULTS: Participants recently diagnosed with cancer (n = 1300) were significantly at higher risk to present suicide attempt (adjusted odds ratio [AOR] = 3.52; 95% confidence interval [CI] = 1.23-10.04), post-traumatic stress disorder (AOR = 2.25; 95% CI = 1.71-2.96), bipolar disorder (AOR = 2.22; 95% CI = 1.46-3.38) and drug use disorder (AOR = 1.64; 95% CI = 1.13-3.39). The prevalence of most of the mental disorders considered was significantly higher for participants with a history of mental disorder compared with participants without such a history. Conversely, a recent diagnosis of cancer was not associated with significant differences in the incidence of mental disorders in participants with no history of mental disorder. CONCLUSIONS: Patients with a history of mental disorder receiving a cancer diagnosis are at high risk of relapse and should be closely monitored.

ÉTUDES ETRANGERES

Almeida, O. P., Hankey, G. J., Yeap, B. B., et al. (2018). "Older men with bipolar disorder diagnosed in early and later life: Physical health morbidity and general hospital service use." J Affect Disord **241**: 269-274.
https://api.research-repository.uwa.edu.au/ws/files/33790187/Almeida_et_al_2018_Older_men_with.pdf

BACKGROUND: Bipolar disorder (BD) has been associated with greater health morbidity burden, but it is unclear if this association is affected by age at the time of diagnosis and how this might impact on the use of general hospital services. METHODS: Cross-sectional study investigating the prevalence of common medical morbidities among participants with early (EOBD) and late onset diagnosis of BD (LOBD - age at diagnosis >/=60 years) derived from a community-representative sample of 37,183 men aged 65-85 years. Cohort study over a follow up period of up to 17.7 years investigating the hazard of general hospital use among older men associated with EOBD and LOBD taking into account age and prevalent medical morbidities. RESULTS: 250 older men had a recorded diagnosis of BD, 75 of whom had LOBD. Diabetes, stroke and diseases of the respiratory and digestive systems were more frequent in men with than without BD. There were no differences in the distribution of medical morbidities between men with EOBD and LOBD. The adjusted hazard ratio (HR) of contact with general hospital services was significantly higher among men with EOBD (HR=1.33; 95%CI=1.14, 1.54) and LOBD (HR=1.27, 95%CI=1.06, 1.51) compared with older men without BD. Older men with EOBD had the highest number of contacts with general hospital services during follow up, although men with EOBD

and LOBD did not differ in the number of contacts due to episodes of mania or depression. The medical reasons for contact with general hospital services of men with EOBD and LOBD overlapped but were not identical. CONCLUSIONS: Older men with BD experience greater health morbidity than men without BD. Older men with BD access hospital services for the management of physical morbidities earlier and more frequently than men without BD. Age at the time of diagnosis of BD has limited impact on the risk of contact with general medical services, although subtle differences in the physical morbidity of men with EOBD and LOBD warrant further investigation.

Anmella, G., Fico, G., Lotfaliany, M., et al. (2021). "Risk of cancer in bipolar disorder and the potential role of lithium: International collaborative systematic review and meta-analyses." Neurosci Biobehav Rev **126**: 529-541.

We examined bipolar disorder (BD) as a risk factor for developing cancer and the role of lithium on cancer incidence. We conducted two systematic review and meta-analyses of population-based studies providing data on these associations. We screened articles indexed in MEDLINE, Scopus, Embase, and PsycINFO up to August 2020. The first random-effects meta-analysis, based on 4,910,661 individuals from nine studies estimated an increased risk of cancer of any kind [RR = 1.24 (1.05-1.46); p < 0.01], especially breast cancer [RR = 1.33 (1.15-1.55); p < 0.01] in BD. The second random-effects meta-analysis, based on 2,606,187 individuals from five studies did not show increased risk of cancer in people with BD using lithium, and even suggested a small protective effect both in overall [RR = 0.94 (0.72-1.22); p = 0.66] and urinary cancer [RR = 0.93 (0.75-1.14); p = 0.48] although these findings did not reach statistical significance. The current evidence highlights that cancer risk is increased in individuals with BD, particularly breast cancer in women. Lithium may have a potential protective effect on cancer, including urinary cancer. The role of lithium as a mainstay of treatment for BD is reinforced by this study.

BarChana, M., Levav, I., Lipshitz, I., et al. (2008). "Enhanced cancer risk among patients with bipolar disorder." J Affect Disord **108**(1-2): 43-48.

BACKGROUND: In contrast to numerous epidemiological studies that explored the risk for cancer among persons with schizophrenic psychoses, analogous studies conducted on people with bipolar disorder are rarer, despite some commonalities in biological, treatment-related variables and unhealthy lifestyles. This study investigates the risk for cancer among psychiatric inpatients diagnosed with bipolar disorder. METHODS: Linkage analysis was conducted based on the psychiatric and the cancer national databases. Standardized incidence ratios (SIR) for both aggregated sites and for breast cancer were calculated by comparing the incidence rates among hospitalized patients with bipolar disorder with the incidence rates in the Jewish-Israeli general population. RESULTS: An enhanced cancer risk was found for bipolar disorder in both genders: men, SIR 1.59 (95% CI 1.01-2.17); women, SIR 1.75 (95% CI 1.31-2.18). The risk for breast cancer was higher, but not significantly, than in the general female population, SIR 1.70 (95% CI 0.99-2.41). LIMITATIONS: Our sample was derived from psychiatric inpatients, thus it is likely that the bipolar disorder cases had greater severity. Putative factors such as diet, smoking and medications were not investigated. CONCLUSIONS: Our study showed an enhanced risk for cancer among patients with bipolar disorder. Clinicians might note this risk for timely diagnosis and treatment.

Carmassi, C., Pardini, F., Dell'Oste, V., et al. (2021). "Suicidality and Illness Course Worsening in a Male Patient with Bipolar Disorder during Tamoxifen Treatment for ER+/HER2+ Breast Cancer." Case Rep Psychiatry **2021**: 5547649.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8012138/pdf/CRIPS2021-5547649.pdf

PURPOSE: Tamoxifen is a selective estrogenic receptor modulator (SERM) drug. In addition to its common use in breast cancer ER+, Tamoxifen has been object of growing interest in psychiatry as antimanic drug. At the same time, clinical concerns about Tamoxifen's depressogenic effect have been repeatedly raised even without reaching univocal conclusions. We discuss the case of a 45-year-old-male with a diagnosis of Bipolar Disorder type II, treated with Tamoxifen as relapse prevention treatment after surgery for a ER+/HER2+ breast cancer. The patient required two psychiatric admissions in a few-month time span since he showed a progressive worsening of both depressive and

anxiety symptoms, with the onset of delusional ideas of hopelessness and failure up to suicidal thoughts. The clinical picture showed poor response to treatment trials based on various associations of mood-stabilising, antidepressants, and antipsychotic drugs. During the second hospitalization, after a multidisciplinary evaluation, the oncologists agreed on Tamoxifen discontinuation upon the severity of the psychiatric condition. The patient underwent a close oncological and psychiatric follow-up during the following 12 months. METHODS: Psychiatric assessments included the Montgomery-Asberg Depression Rating Scale (MADRS), the Hamilton Depression Scale (HAM-D), the Columbia Suicide Severity Rating Scale (C-SSRS), and the Quality of Life Enjoyment and Satisfaction Questionnaire Short Form (Q-LES-Q-SF). All questionnaires were administered at the time of the second hospitalization and in a one-year follow-up. RESULTS: Suicidal ideation fully remitted and depressive symptoms markedly and rapidly improved in the aftermath of Tamoxifen discontinuation. The symptomatological improvement remained stable across one-year follow-up. CONCLUSIONS: Male patients with a mood disorder history constitute a high-risk group as to Tamoxifen psychiatric side effects. The onset or worsening of depressive symptoms or suicidality should be carefully addressed and promptly treated, and clinicians should be encouraged to consider the possibility of discontinue or reduce Tamoxifen therapy after a multidisciplinary evaluation.

Chen, M. H., Tsai, S. J., Su, T. P., et al. (2022). "Cancer risk in patients with bipolar disorder and unaffected siblings of such patients: A nationwide population-based study." Int J Cancer **150**(10): 1579-1586.
https://onlinelibrary.wiley.com/doi/10.1002/ijc.33914

Increasing evidence suggests that patients with bipolar disorder are more likely to develop malignant cancer than in the general population. However, the overall cancer risk in the unaffected siblings of such patients remains unknown. From the National Health Insurance Research Database of Taiwan, 25 356 patients with bipolar disorder, 25 356 age-matched unaffected siblings of patients with bipolar disorder and 101 422 age-matched controls without severe mental disorders between 1996 and 2010 were enrolled in our study. Patients who developed cancer between the time of enrollment and the end of 2011 were identified. Cancers were divided into three subgroups based on the related layer of embryonic development: ectodermal, mesodermal and endodermal cancers. Patients with bipolar disorder (odds ratio [OR] = 1.22, 95% confidence interval [CI]: [1.06, 1.40]) and unaffected siblings of such patients (OR = 1.17, 95% CI [1.02, 1.34]) had greater risk of developing malignant cancer than did controls. Furthermore, only those aged <50 years, for both patients with bipolar disorder (OR = 1.90, 95% CI [1.38, 2.61]) and unaffected siblings (OR = 1.65, 95% CI [1.19, 2.28]), were more likely to develop the ectodermal cancer, especially breast cancer, than the control group. The associations of bipolar disorder and susceptibility to bipolar disorder with increased cancer risk in the younger population may imply a genetic overlap in neurodevelopment and malignancy pathogenesis. Our findings may encourage clinicians to monitor cancer risk factors and warning signs closely in patients with bipolar disorder and unaffected siblings of such patients.

Cole, M. et Padmanabhan, A. (2012). "Breast cancer treatment of women with schizophrenia and bipolar disorder from Philadelphia, PA: lessons learned and suggestions for improvement." J Cancer Educ **27**(4): 774-779.
https://link.springer.com/article/10.1007/s13187-012-0391-7

Treating cancer in patients with concurrent severe mental illness is complex and challenging for patients, families, and health care providers. Two such illnesses include schizophrenia and bipolar disorder. In this review, cases of women with breast cancer and severe mental illness from Philadelphia, PA illustrate the obstacles these women face in maintaining adequate cancer care. Barriers to receiving cancer treatment include understanding their disease, continuing medications and appointments, and experiencing complications of their psychiatric disorders. Learning from these cases is critical for health care providers and allows for innovation in treating and educating this difficult population. Increasing patient visit time, using social support services, and psychiatrist and psychiatrist-liaisons are necessary to improve care. In addition, family or caregivers should be included in discussions when possible. These techniques will assist in educating patients, improve insight into their disease and treatment, and allow them to benefit from cancer therapy.

Conell, J., Lewitzka, U., Ritter, P., et al. (2015). "[Is there an increased risk for renal tumors during long-term treatment with lithium?]." Nervenarzt **86**(9): 1157-1161.
https://link.springer.com/article/10.1007/s00115-015-4413-7

> Lithium salts are the recommended first-line treatment (gold standard) in national and international treatment guidelines for acute and maintenance treatment of affective disorders, such as bipolar disorders. Lithium has also been shown to have a unique protective effect against suicide in patients suffering from affective disorders. Despite the well-known acute and long-term adverse effects lithium therapy can be safely administered if patients are properly educated and carefully monitored. A recent study from France now shows that patients with severely impaired renal function who had been treated with lithium salts for more than 10 years could have an increased risk for kidney tumors (benign and malignant). This resulted in an adjustment concerning information within the package leaflet by European authorities. The authors of this article reflect the currently available data in order to better understand and handle this new finding and to warn about uncritical reactions including withdrawal of lithium in successfully treated patients. This article provides clinical recommendations to provide further insight relating to the risk of kidney cancer in long-term lithium therapy.

Dai, W., Liu, J., Qiu, Y., et al. (2022). "Shared postulations between bipolar disorder and polycystic ovary syndrome pathologies." Prog Neuropsychopharmacol Biol Psychiatry **115**: 110498.

> INTRODUCTION: Women with bipolar disorder (BD) present a high prevalence of polycystic ovary syndrome (PCOS) and other reproductive disorders even before diagnosis or treatment of the disease. Postulations on the potential molecular mechanisms of comorbid PCOS in women with BD remain limited to influence of medications and need further extension. OBJECTIVES: This review focuses on evidence suggesting that common metabolic and immune disorders may play an important role in the development of BD and PCOS. RESULTS: The literature covered in this review suggests that metabolic and immune disorders, including the dysfunction of the hypothalamic-pituitary-adrenal axis, chronic inflammatory state, gut microbial alterations, adipokine alterations and circadian rhythm disturbance, are observed in patients with BD and PCOS. Such disorders may be responsible for the increased prevalence of PCOS in the BD population and indicate a susceptibility gene overlap between the two diseases. Current evidence supports postulations of common metabolic and immune disorders as endophenotype in BD as well as in PCOS. CONCLUSIONS: Metabolic and immune disorders may be responsible for the comorbid PCOS in the BD population. The identification of hallmark metabolic and immune features common to these two diseases will contribute to the clarification of the effect of BD on the reproductive endocrine function and development of symptomatic treatments targeting the biomarkers of the two diseases.

Haskins, C. B., Neuner, J. M., McDowell, B. D., et al. (2020). "Effects of Previous Medication Regimen Factors and Bipolar and Psychotic Disorders on Breast Cancer Endocrine Therapy Adherence." Clin Breast Cancer **20**(3): e261-e280.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7103521/pdf/nihms-1543639.pdf

> BACKGROUND: Endocrine therapy adherence remains a barrier to optimal estrogen receptor-positive breast cancer outcomes. We theorized that experience navigating difficult medication regimen factors, such as route of administration complexity, might improve subsequent adherence after stressful cancer diagnoses but not for patients with bipolar and psychotic disorders at risk of poor access and nonadherence. MATERIALS AND METHODS: We included 21,894 women aged ≥ 68 years at their first surgically treated stage I-IV estrogen receptor-positive breast cancer (2007-2013) from the Surveillance, Epidemiology, and End Results-Medicare data set, of whom 5.8% had bipolar or psychotic disorders. We required continuous fee-for-service Medicare (parts A and B) data for ≥ 36 months before and 18 months after the cancer diagnosis. The medication regimen factors in the part D claims for 4 months before included the number of all medications used, pharmacy visits, and administration complexity (medication regimen complexity index subscale). Cox regression analysis was used to model the time to initiation and discontinuation, with longitudinal linear regression for adherence to endocrine therapy. RESULTS: Women with more frequent previous medication use and pharmacy visits were more likely to initiate, 4+ medications and 2+ visits versus no medication (hazard ratio [HR], 1.47; 95% confidence interval [CI], 1.33-1.63), to adhere (6.0%; 95% CI, 4.3-7.6), and to continuously

use their endocrine therapy (discontinuation HR, 0.48; 95% CI, 0.39-0.59). Medication administration complexity had modest effects. Difficult medication regimens were more common for patients with bipolar and psychotic disorders but had no statistically significant effects. CONCLUSIONS: Experience with frequent previous medication use and pharmacy visits might increase the likelihood of endocrine therapy use for most patients but not for those with bipolar and psychotic disorders.

Hippisley-Cox, J., Vinogradova, Y., Coupland, C., et al. (2007). "Risk of malignancy in patients with schizophrenia or bipolar disorder: nested case-control study." Arch Gen Psychiatry **64**(12): 1368-1376.
https://jamanetwork.com/journals/jamapsychiatry/articlepdf/482503/yoa70040_1368_1376.pdf

CONTEXT: There is conflicting evidence on whether people with schizophrenia have a different risk of cancer from that of the general population. OBJECTIVE: To determine the risk of 6 common cancers in patients with schizophrenia or bipolar disorder. DESIGN: Population-based, nested, case-control study. SETTING: A total of 454 practices contributing to the QRESEARCH general practice database. PARTICIPANTS: We analyzed 40,441 incident cases of 6 cancers (breast, colon, rectal, gastroesophageal, prostate, and respiratory) and up to 5 controls per case matched by single year of age, sex, general practice, and calendar time. MAIN OUTCOME MEASURES: Odds ratios (ORs) for cancer risk associated with schizophrenia and bipolar disorder, adjusting for smoking, body mass index, socioeconomic status, comorbidities, and prescribed medications, including antipsychotics. RESULTS: For breast cancer, we identified 10,535/50,074 cases/controls; colon cancer, 5108/24,458; rectal cancer, 3248/15,552; gastroesophageal cancer, 3854/18,477; prostate cancer, 10,190/48,748; and respiratory cancer, 7506/35,981. After adjustment, patients with schizophrenia had a 190% increased colon cancer risk (adjusted OR, 2.90; 95% confidence interval [CI], 1.85-4.57), a marginal increased breast cancer risk (adjusted OR, 1.52; 95% CI, 1.10-2.11), and a 47% decreased respiratory cancer risk (adjusted OR, 0.53, 95% CI, 0.34-0.85). Patients with schizophrenia taking antipsychotics had a 308% increased colon cancer risk (adjusted OR, 4.08; 95% CI, 2.43-6.84). Patients with bipolar disorder had cancer risks similar to patients with neither condition after adjustment. CONCLUSIONS: Patients with schizophrenia have a significantly higher risk of colon cancer and a lower risk of respiratory cancer compared with patients without schizophrenia after adjustment for confounders. In contrast, the risks of cancer in patients with and without bipolar disorder are similar, suggesting that residual confounding is unlikely to explain the findings. The increased risk of colon cancer is particularly marked in patients with schizophrenia who take antipsychotic medications.

Huang, R. Y., Hsieh, K. P., Huang, W. W., et al. (2016). "Use of lithium and cancer risk in patients with bipolar disorder: population-based cohort study." Br J Psychiatry **209**(5): 393-399.
https://www.cambridge.org/core/services/aop-cambridge-core/content/view/08451A678FED03FEC5A7638C47866CD2/S000712500024542Xa.pdf/div-class-title-use-of-lithium-and-cancer-risk-in-patients-with-bipolar-disorder-population-based-cohort-study-div.pdf

BACKGROUND: Lithium inhibits glycogen synthase kinase-3, which is an enzyme involved in the pathogenesis of cancer. AIMS: To investigate the association between lithium and cancer risk in patients with bipolar disorder. METHOD: A retrospective cohort study was designed using the National Health Insurance Research Database (NHIRD) in Taiwan. Patients using lithium comprised the index drug group and patients using anticonvulsants only comprised the control group. Time-dependent Cox regression was used to evaluate the hazard ratios (HRs) for risk of cancer. RESULTS: Compared with anticonvulsant-only exposure, lithium exposure was associated with significantly lower cancer risk (HR = 0.735, 95% CI 0.554-0.974). The hazard ratios for the first, second and third tertiles of the cumulative defined daily dose were 0.762 (95% CI 0.516-1.125), 0.919 (95% CI 0.640-1.318) and 0.552 (95% CI 0.367-0.831), respectively. CONCLUSIONS: Lithium is associated with reduced overall cancer risk in patients with bipolar disorder. A dose-response relationship for cancer risk reduction was observed.

Kahan, N. R., Silverman, B., Liphshitz, I., et al. (2018). "No apparent association between bipolar disorder and cancer in a large epidemiological study of outpatients in a managed care population." Int Clin Psychopharmacol **33**(2): 73-78.
https://www.ingentaconnect.com/content/wk/incps/2018/00000033/00000002/art00003

An association between bipolar disorder (BD) and cancer risk has been reported. The purpose of this study was to investigate this association through linkage analysis of a national HMO database and a national cancer registry. All members of the Leumit Health Services (LHS) HMO of Israel from 2000 to 2012 were included. Members with a recorded diagnosis of BD and a record of at least one written or dispensed prescription for pharmacotherapy for treatment of BD were classified as patients with BD. We linked the LHS population with the Israel National Cancer Registry database to capture all cases of cancer reported. Standardized incidence ratios (SIRs) for cancer in the BD population as compared with non-BD LHS members were calculated. A total of 870 323 LHS members were included in the analysis; 3304 of whom met the criteria for inclusion in the BD arm. We identified 24 515 and 110 cancer cases among members without BD and with BD, respectively. Persons with BD were no more likely than other HMO members to be diagnosed with cancer during the follow-up period [SIR, males=0.91, 95% confidence interval (CI): 0.66-1.22; SIR, females=1.15, 95% CI: 0.89-1.47]. Sensitivity analysis using different criteria for positive BD classification (lithium treatment alone or registered physician diagnosis) had no effect on the estimate of cancer risk. A nonstatistically significant association between breast cancer and BD among women was observed (SIR=1.24, 95% CI: 0.79-1.86). These findings do not corroborate previously reported associations between BD and elevated cancer risk.

Lin, C. C., Hsieh, T. C. et Wu, L. S. (2018). "Long-term use of valproic acid and the prevalence of cancers in bipolar disorder patients in a Taiwanese population: An association analysis using the National Health Insurance Research Database (NHIRD)." J Affect Disord **232**: 103-108.

BACKGROUND: Epigenetic events play a major role in the carcinogenesis of many cancers. A retrospective cohort study had been performed to evaluate the effects of exposure to the anticonvulsant agent valproic acid (VPA), a histone deacetylase inhibitor, on the risk of developing cancers. METHODS: The study was based on the 1998 through 2009 National Health Insurance Research Database (NHIRD), provided by the Taiwan National Health Research Institute. Patients with a diagnosis of bipolar disorder (ICD-9-CM codes 296.0, 296.1, 296.4-8) from 1998 to 2009 were identified. VPA and lithium were the primary index drugs. Patients treated with anticonvulsants who did not use VPA or lithium were selected as the control group. Competing risk regression analysis were used to estimate hazards ratios (HR) and 95% confidence intervals (95% CI) reflecting the association between use of VPA and cancer incidence. RESULTS: The cancer incidence of bipolar disorder patients treated with VPA was no significant difference than treated with lithium and other anticonvulsants. In subgroup analysis, VPA associated to higher risk of genitourinary cancer in the duration <1 year group (HR: 3.49; 95%CI: 1.04, 11.67). No significant differences in other cancers incidence in any duration of VPA treatment. LIMITATIONS: The cancer prevalence in selected bipolar disorder patients was still low. The sample size was not enough for some types of cancer. CONCLUSIONS: A role of VPA in cancer prevention was not found in this study. An increased subgroup risk of genitourinary cancer was observed.

Lin, G. M., Chen, Y. J., Kuo, D. J., et al. (2013). "Cancer incidence in patients with schizophrenia or bipolar disorder: a nationwide population-based study in Taiwan, 1997-2009." Schizophr Bull **39**(2): 407-416. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3576164/pdf/sbr162.pdf

BACKGROUND: Both genetic and environmental factors have been reasoned for cancer development in schizophrenia patients. However, the influence of age of onset and duration of schizophrenia on cancer incidence has rarely been emphasized. Besides, bipolar disorder tends to resemble schizophrenia from the perspective of multiple rare mutations. Comparing pattern and risk of cancers between schizophrenia and bipolar patients is illuminating. METHODS: This study used the Taiwan National Health Insurance Database. A total of 71,317 schizophrenia and 20,567 bipolar disorder patients from 1997 to 2009 were enrolled. Both cohorts were followed up for cancer during the same period by record linkage with the cancer certification in Taiwan. Age and gender standardized incidence ratios (SIRs) of overall and site-specific cancers were calculated. RESULTS: The SIR for all cancers was 1.17 for the schizophrenia cohort. Increased cancer risk (SIR: 1.31, 95% CI: 1.17-1.48) was observed in females but not males. For the bipolar disorder cohort, the SIR for all cancers was 1.29, but the excess risk was found in males (SIR: 1.42, 95% CI: 1.14-1.77) and not females. Cancer risk decreases as the duration and age of onset of schizophrenia increases. If schizophrenia is diagnosed

before 50, the SIRs for colorectal, breast, cervical, and uterine cancers increase but if diagnosed after 50, the SIRs for all cancers decrease except for breast cancer. In bipolar disorder, the SIRs for all site-specific cancers were insignificant. CONCLUSIONS: Among schizophrenia patients, overall cancer risk varies inversely with age at diagnosis and disease duration. Besides, gender-specific cancer risks differ between schizophrenia and bipolar disorder.

Magalhaes, P. V., Kapczinski, F., Nierenberg, A. A., et al. (2012). "Illness burden and medical comorbidity in the Systematic Treatment Enhancement Program for Bipolar Disorder." Acta Psychiatr Scand **125**(4): 303-308. https://onlinelibrary.wiley.com/doi/pdfdirect/10.1111/j.1600-0447.2011.01794.x?download=true

OBJECTIVE: Coexisting chronic medical conditions are common in bipolar disorder. Here, we report the prevalence and correlates of medical comorbidity in patients enrolled in the Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD). We were particularly interested in associations between variables reflecting illness chronicity and burden with comorbid medical conditions. METHOD: We used intake data from the open-label component of the STEP-BD. History of medical comorbidity was obtained from the affective disorders evaluation, and its presence was the outcome of interest. The sample size in analyses varied from 3399 to 3534. We used multiple Poisson regression to obtain prevalence ratios. RESULTS: The prevalence of any medical comorbidity in the sample was 58.8%. In addition to demographic variable, several clinical characteristics were associated with the frequency of medical comorbidity. Having more than 10 previous mood episodes, childhood onset, smoking, lifetime comorbidity with anxiety, and substance use disorders were independently associated with having a medical comorbidity in the final multivariate model. CONCLUSION: The results presented here reveal strong associations between variables related to illness chronicity and medical burden in bipolar disorder. This lends further support to recent multidimensional models incorporating medical morbidity as a core feature of bipolar disorder.

Miniati, M., Conversano, C., Palagini, L., et al. (2020). "Bipolar Disorder Treatments and Ovarian Cancer: A Systematic Review." Clin Neuropsychiatry **17**(5): 300-313. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8629050/pdf/cn-17-300.pdf

We reviewed literature on drugs for bipolar disorders (BD), utilized in ovarian cancer (OC). METHOD: We adhered to the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) guidelines in completion of this systematic review. RESULTS: We identified 73 papers. Thirty-two studies were finally included. BD is rarely diagnosed in OC patients. Limited finding from case reports is available. Drugs used to treat BD (mainly lithium and valproic acid) have been extensively studied in add-on to chemotherapy for treatment-resistant OC cells or in animal models, with promising results in vitro but not in vivo. CONCLUSIONS: The clinical underestimation of BD in OC has leaded to the almost complete absence of evidences for a soundly based clinical guidance in this field. There is a urgent need for a systematic multi-disciplinary approach to OC.

Park, S. J. et Hwang, I. C. (2019). "Cancer risk in people with bipolar disorder: Perspectives for future study." Psychiatry Res **279**: 391-392.

Peng, H., Wu, X., Ge, F., et al. (2021). "Genetically predicted bipolar disorder is causally associated with an increased risk of breast cancer: a two-sample Mendelian randomization analysis." Ann Transl Med **9**(5): 401. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8033315/pdf/atm-09-05-401.pdf

BACKGROUND: Epidemiologic findings suggested that bipolar disorder (BD) may be associated with an increased risk of breast cancer. However, there are few studies that comprehensively evaluating their correlation and the causal effect remains unknown. With a two-sample Mendelian randomization (MR) approach, we were able to investigate the causal relationship between genetically predicted BD and breast cancer risk. METHODS: Utilizing 14 BD-related single nucleotide polymorphisms (SNPs) as instrumental variables (IVs) identified by the latest genome-wide association studies (GWASs), we investigated the correlation between genetically predicted BD and breast cancer risk using summary statistics from the Breast Cancer Association Consortium, with a total of 122,977 cases and 105,974 controls. Study-specific estimates were summarized using inverse variance weighted (IVW) method. To further evaluate the pleiotropy, the weighted median and the MR-Egger regression method were

implemented. Subgroup analyses according to different immunohistochemical types of breast cancer were also conducted. RESULTS: MR analyses demonstrated that genetically predicted BD was causally associated with an increased risk of breast cancer (OR =1.059; 95% CI: 1.008-1.112, P=0.0229). When results were examined by immunohistochemical type, no causal effects between genetically predicted BD and estrogen receptor (ER)-positive breast cancer (OR =1.049, 95% CI: 0.999-1.102 P=0.0556) and ER-negative breast cancer (OR =1.032, 95% CI: 0.953-1.116 P=0.4407) were observed. Additionally, the results demonstrated the absence of the horizontal pleiotropy. CONCLUSIONS: Our findings provided evidence for a causal relationship between genetically predicted BD and an increased risk of breast cancer overall. Further studies are warranted to investigate the underlying mechanism.

Reich, M. et Kotecki, N. (2017). "[Bipolar disorders in oncology: Characteristics and management]." Bull Cancer **104**(5): 442-451.

Bipolar disorders belong to the spectrum of mood disorders and represent a serious psychiatric comorbidity. Behaviors adopted by bipolar patients can foster cancer occurrence but also impact its management, especially during acute depressive or manic episode. Oncologists must adapt their protocols in order to obtain the best compliance for treatment and avoid any possible mood destabilization, with the inherent risk of suicidal attempt. Potential interactions between mood-stabilizing agents (lithium, divalproate, atypical antipsychotics, and anticonvulsivants) and oncologic treatment (chemotherapy, targeted therapy, immunotherapy, corticotherapy) will be particularly watched. To do so, a closely collaboration with the oncopsychiatrist but also with the referent or liaison psychiatry team is necessary during the patient's oncologic care. Some clinical vignettes will illustrate the modalities of care of bipolar disorders in oncology.

Shen, S. H. et Lee, S. H. (2021). "A Case of Lung Cancer with Brain Metastasis following Late-Onset Bipolar Disorder." Behav Neurol **2021**: 8880539.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8034995/pdf/BN2021-8880539.pdf

OBJECTIVE: To describe a case of lung cancer with brain metastasis in a patient who developed new late-onset bipolar disorder 2 years previously. BACKGROUND: The typical onset age of bipolar disorder is approximately 20, and the first episode is usually a depressive episode. It is still not clear which age-specific factors contribute to the underlying risk. MATERIALS AND METHODS: A 65-year-old male patient presented with a new-onset manic episode characterized by labile mood, impulsivity, decreased need for sleep, and grandiosity. He was diagnosed with late-onset bipolar disorder after excluding other possible physiological conditions. He was hospitalized in the acute psychiatric ward, and a combination of mood stabilizers and antipsychotics was prescribed. His mental condition improved, and he remained stable for 2 years. However, he experienced abrupt cognitive decline for 2 months and was referred to the emergency room for physiological examination. RESULTS: The patient was diagnosed with lung cancer with brain metastasis by brain magnetic resonance imaging and whole-body positron emission tomography. CONCLUSION: In geriatric patients, who are at high risk of multiple medical conditions, excluding secondary causes of bipolar disorder is important.

Sylvia, L. G., Shelton, R. C., Kemp, D. E., et al. (2015). "Medical burden in bipolar disorder: findings from the Clinical and Health Outcomes Initiative in Comparative Effectiveness for Bipolar Disorder study (Bipolar CHOICE)." Bipolar Disord **17**(2): 212-223.
https://deepblue.lib.umich.edu/bitstream/handle/2027.42/110852/bdi12243.pdf?sequence=1

OBJECTIVES: Individuals with bipolar disorder have high rates of other medical comorbidity, which is associated with higher mortality rates and worse course of illness. The present study examined common predictors of medical comorbidity. METHODS: The Clinical and Health Outcomes Initiative in Comparative Effectiveness for Bipolar Disorder study (Bipolar CHOICE) enrolled 482 participants with bipolar I or bipolar II disorder in a six-month, randomized comparative effectiveness trial. Baseline assessments included current and lifetime DSM-IV-TR diagnoses, demographic information, psychiatric and medical history, severity of psychiatric symptoms, level of functioning, and a fasting blood draw. Medical comorbidities were categorized into two groups: cardiometabolic (e.g., diabetes, hyperlipidemia, and metabolic syndrome) and non-cardiovascular (e.g., seizures, asthma, and cancer). Additionally, we looked at comorbid substance use (e.g., smoking and drug dependence). RESULTS:

We found that 96.3% of participants had at least one other medical comorbidity. Older age predicted a greater likelihood of having a cardiometabolic condition. Early age of onset of bipolar symptoms was associated with a lower chance of having a cardiometabolic condition, but a greater chance of having other types of medical comorbidity. Additional predictors of other medical comorbidities in bipolar disorder included more time spent depressed, less time spent manic/hypomanic, and longer duration of illness. Medications associated with weight gain were associated with low high-density lipoprotein and abnormal triglycerides. CONCLUSIONS: There appears to be a substantial medical burden associated with bipolar disorder, highlighting the need for collaborative care among psychiatric and general medical providers to address both psychiatric and other medical needs concomitantly in this group of patients.

Weeke, A. et Vaeth, M. (1986). "Excess mortality of bipolar and unipolar manic-depressive patients." J Affect Disord **11**(3): 227-234.

To compare mortality in bipolar and unipolar manic-depressive patients, 2168 manic-depressive first admissions reported to the Danish Psychiatric Central Register were divided into a bipolar group (19%), i.e., patients with at least one admission for mania during an average observation period of six years, and a unipolar group. When compared with the general population, the total group had an increased mortality by suicide and accidents in both sexes and by non-violent causes in men. The bipolar group had a higher non-violent mortality than the unipolar group, but the violent mortality was not different. Statistical problems introduced by patients switching from the unipolar to the bipolar group during the period of observation are discussed.

Wichowicz, H. (2003). "[A manic episode as a result of information about breast cancer diagnosis in a patient suffering from bipolar affective disorder]." Psychiatr Pol **37**(5): 845-850.

The paper describes a patient who suffered from bipolar affective disorder for 22 years and the following manic episode appeared after getting information about a diagnosis of breast cancer. During mania the patient presented delusions of being healthy which caused a marked delay in introducing the necessary treatment of the tumour. Besides, we discuss different authors' views about the possibility of evoking manic episodes by psychological factors. Same authors agree, that such an event may happen but others do not. This matter requires further studies, but any doctor who takes care of a patient with bipolar affective illness should always remember about the possibility of being evoked manic episode by harmful stress events.

Zaidan, M., Stucker, F., Stengel, B., et al. (2014). "Increased risk of solid renal tumors in lithium-treated patients." Kidney Int **86**(1): 184-190.
https://www.kidney-international.org/article/S0085-2538(15)30234-9/pdf

Cystic kidney diseases and toxic interstitial nephritis may be complicated by renal tumors. Long-term lithium intake is associated with tubulointerstitial nephritis and renal cysts but to date such an association with tumors has not been determined. We evaluated this in a retrospective study to determine whether lithium-treated patients were at higher risk of renal tumors compared with lithium-free patients with chronic kidney disease (CKD), and to the general population. Over a 16-year period, 14 of 170 lithium-treated patients had renal tumors, including seven malignant and seven benign tumors. The mean duration of lithium exposure at diagnosis was 21.4 years. The renal cancers included three clear-cell and two papillary renal cell carcinomas, one hybrid tumor with chromophobe and oncocytoma characteristics, and one clear-cell carcinoma with leiomyomatous stroma. The benign tumors included four oncocytomas, one mixed epithelial and stromal tumor, and two angiomyolipomas. The percentage of renal tumors, particularly cancers and oncocytomas, was significantly higher in lithium-treated patients compared with 340 gender-, age-, and estimated glomerular filtration rate (eGFR)-matched lithium-free patients. Additionally, the Standardized Incidence Ratio of renal cancer was significantly higher in lithium-treated patients compared with the general population: 7.51 (95% confidence interval (CI) (1.51-21.95)) and 13.69 (95% CI (3.68-35.06)) in men and women, respectively. Thus, there is an increased risk of renal tumors in lithium-treated patients.