Title: Disparities in cancer screening in people with mental illness across the world: prevalence and comparative meta-analysis versus the general population including 4,717,839 people

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Background. Since people with mental illness more likely die from cancer, we assessed whether people with mental illness undergo less cancer screening versus the general population.

Methods. Systematic review and meta-analysis of observational studies. Primary outcome was Odds Ratio (OR) of cancer screening in people with mental illness versus the general population. Secondary outcome was prevalence of cancer screening in mental illness. Sensitivity and subgroup analyses considered specific mental illness, diagnostic criteria, confounder adjustment, country/region, and program vs. opportunistic screening. Newcastle-Ottawa Scale was used to assess study quality. This study is registered with PROSPERO, number CRD42018114781.

Findings. Forty-seven publications provided data from 46 samples including 4,717,839 subjects (female=69.85%), for screening for breast (k=35, mental illness=296,699, general population =1,023,288), cervical (k=29, mental illness=295,688, general population =3,540,408), colorectal (k=12, mental illness=153,283, general population =2,228,966), lung (k=1, mental illness=420, general population =0), gastric (k=1, mental illness=420, general population =0), ovarian (k=1, mental illness=37, general population =0) and prostate (k=6, mental illness=52,803, general population =2,038,916) cancer. Median quality of the included studies was high (7; IQR=2).

Considering any mental illness, screening was significantly lower versus general population for any (k=37, OR=0.757,95%CI=0.722-0.792), breast (k=27,OR=0.652,95%CI=0.603-0.705), cervical (k=23,OR=0.891,95%CI=0.840-0.945), and prostate (k=4,OR=0.777,95%CI=0.701-0.862) cancer, but not for colorectal cancer (k=8,OR=1.02,95%CI=0.903-1.151). In schizophrenia, screening was lower versus general population for any, breast, and cervical cancer. In mood disorders, screening was lower versus general population for any and breast cancer, without differences for cervical cancer, while screening was more frequent for colorectal cancer.

In any mental illness, screening prevalence of any, breast, cervical, colorectal, and prostate cancer were 56.5%(95%CI=51.5-61.3%), 61.9%(95%CI=54.7-68.6%), 59.7%(95%CI=49.4-69.2%), 37.1%(95%CI=28.9-46.1%), and 48.2%(95%CI=31.3-65.5%), respectively.

Interpretation. Despite the increased mortality from cancer in mental illness, this population receives inferior cancer screening versus the general population. Specific approaches should be developed to assist people with mental illness to undergo appropriate cancer screening, especially women with schizophrenia.

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Keywords: Mental illness; disparities; cancer screening; gender medicine; prevention, life expectancy.

Research in context

Evidence before this study

People with mental illness have increased cancer mortality than the general population, which is not explained by differences in cancer risk alone. One potential explanation is inferior medical care, especially low rates of cancer screening, which may lead to a later stage cancer diagnosis. We searched PubMed and PsycInfo from database inception up to May 5th, 2019, using the search "(schizophrenia or schizoaffective or psychos* or depress* or bipolar disorder or mania or eating disorder or anorexia nervosa or bulimia nervosa or binge eating disorder or obsessive or compulsive or post-traumatic stress disorder or anxiety disorder or panic disorder) AND (malignancy OR melanoma OR cancer) AND (screening)". We also hand-searched the reference lists of included studies and previous reviews. We included all published observational studies reporting prevalence rates of cancer screening in subjects suffering from mental illness. To date, individual published studies have provided inconsistent results whether there exists an increase, a decrease, or no difference in cancer screening in subjects with mental illness versus the general population. No previous meta-analysis has pooled data on frequencies of any and specific types of cancer screening across all mental illnesses to provide a comprehensive picture of whether and to what degree a disparity exists between subjects with mental illness and the general population.

Added value of this study

This study is the first comprehensive evidence-synthesis to date and provides a quantitative estimate of disparities in cancer screening in people with multiple mental illnesses vs. the general population. Cancer screening is a key component for decreasing cancer mortality. Given that elevated cancer mortality contributes to the 20-year premature mortality among people with mental illness, whether there exists a gap in cancer screening that could represent a modifiable factor is a clinically relevant question.

The present study provides concerning evidence based on data from over 4.5 million people, from all continents except Africa, showing that subjects (women in particular) experiencing mental illness (schizophrenia in particular) undergo less cancer screening than the general population, after accounting for several confounding factors. Our subgroup analyses shed further light on the specifics of these disparities, showing that disparities occur across countries, but that the extent of such disparities between countries may be different, and that they are particularly pronounced for women with schizophrenia. However, even subjects with mood disorders, conditions that are far more frequent than schizophrenia, suffer from significant cancer screening disparities. Also, we show that the gap is largest where the healthcare has improved the most for the general population, namely in program vs. opportunistic cancer screening. Finally, we show that Asia is the region where the lowest portion of subjects with mental illness undergoes cancer screening, and conversely that Australia is the region where the healthcare system works the best in involving subjects with mental illness in cancer screening.

Implications of all the available evidence

The evidence synthesis provided by this study illustrates consistently inferior cancer screening across mental disorders, which calls for urgent actions to promote cancer screening in subjects suffering from mental illness, and in women in particular, in virtually all regions around the world. Cancer screening programs that have shown to be effective in the general population do not appear to work for as well for people with mental illness, and specific as well as tailored interventions are urgently needed. Primary care and prevention service stakeholders, general practitioners, and psychiatrists should fill this gap in health system organizations and everyday clinical practice. Future, large-scale, multi-center prospective studies should identify what interventions and care structures are most effective and cost-efficient for providing adequate cancer screening to people with mental illness, and investigate how this may improve overall health outcomes and life expectancy among this vulnerable population.

Introduction

People with mental illness die around 15-20 years earlier than the general population, primarily due to physical health conditions (1-3). The disparities in physical health between those with mental illness and the general population is increasing over time, and those with mental illness are seemingly not benefitting from the improvements in health outcomes seen in the general population (1). Cardiovascular diseases are the most common cause of death with a two- to three-fold increase in standardized mortality ratios (4, 5), together with several frequent comorbidities, such as osteoporosis, metabolic syndrome and diabetes (6-8).

In addition to the aforementioned comorbid conditions, cancer is also responsible for increased mortality in mental illness. While the overall incidence of cancer in mental illness is similar to the general population (9), mortality from cancer in both genders is increased 1.4- to 2- fold (4). The incidence of cervical cancer has been reported as slightly less than that in the general population (10) but mortality rates are higher, with a high case fatality ratio for women with cervical (1.98, 95% confidence interval [CI] 1.31-2.92) or breast cancer (1.23, 95% CI 1.01-1.51) and an overall cancer mortality rate ratio in women with mental illness of 1.24 (95% CI 1.17-1.32) (11). Original studies have also described increased mortality in colorectal cancer (12).

Several reasons could explain why cancer mortality differs between subjects with and without mental illness. For instance, increased cancer mortality in mental illness may be due to disparities in care (13), in that people with mental illness are significantly less likely to receive surgical interventions or radiotherapy and to have fewer chemotherapy sessions (10). Additionally, it has been suggested that those with mental illness may be less tolerant of intensive treatment regimens with significant side effect burdens and also that co-morbid physical illness may contribute to the increased mortality rates (14). Another potential explanation, however, is that increased cancer mortality in mental illness may be due to delayed cancer diagnosis (i.e., detection at an advanced stage when the prognosis is already poor) (15).

Despite the fact that few studies have questioned a delayed cancer diagnosis in mental illness(16), others have shown that later stage at diagnosis, including presentation with metastases, is one of the main factors explaining increased cancer mortality in subjects with mental illness compared with non-users of mental health services.(10, 12) Also, previous systematic reviews have suggested that the quality of all preventive services for those with mental illnessis of lower quality (17). Additionally, both narrative reviews and meta-analyses in women with mental illness have shown substantial disparities in cancer screening compared to the general population (18, 19), although only examining female samples, specifically with relation to breast cancer. Thus, there is currently little understanding of the extent to which these disparities persist across sexes and cancer types. Furthermore, the differences in cancer screening between diagnostic categories of mental illness, and across nations, regions and related health care systems, deserve further exploration.

Therefore, in order to provide an updated understanding of how disparities in cancer screening may affect people with mental illness, we conducted a systematic review and meta-analysis investigating screening rates across all cancers in subjects with mental illness. We further sought to conduct subgroup analyses to examine differences with regards to cancer screening types, sex, region, and psychiatric diagnoses. We hypothesized that subjects with mental illness would be disadvantaged in cancer screening compared with the general population, that such disparities are most pronounced in people with schizophrenia, but also in patients with mood disorders. Furthermore, we hypothesized that cancer disparities would be relatively universal across all types of cancer, and across all regions.

Methods

Search, inclusion criteria

We followed an a-priori protocol registered in PROSPERO, CRD42018114781. We complied with the procedures outlined by the 2015 update of the Preferred Reporting Items for Systematic review and Meta-Analysis Protocols (PRISMA-P) (http://www.prisma-statement.org/) (20) and the Meta-analysis Of Observational Studies in Epidemiology (MOOSE) guidelines (21), performing an electronic literature search from database inception and without language restriction on May 5th, 2019, using PubMed and PsycInfo. The following search key was used in PubMed, with equivalent/appropriate syntax for PsycInfo "((schizophrenia or schizoaffective or psychos* or depress* or bipolar disorder or mania or eating disorder or anorexia nervosa or bulimia nervosa or binge eating disorder or obsessive or compulsive or post-traumatic stress disorder or anxiety disorder or panic disorder) and (melanoma or malignancy or cancer) and (screening)". In addition to systematic database searches, references of previous reviews on this topic and of included studies were hand-searched for potential additional eligible studies.

Inclusion criteria were: i) observational studies, ii) focusing on any type of cancer screening, iii) in patients with mental illness, defined according to structured criteria, validated scale, or clinical records, and iv) which reported prevalence of cancer screening in patients, or comparative measures between patients and the general population. No restriction was applied to mental illness or cancer type.

Couples of two authors (EF, MF, ED, JF, AK, AM, BS, JS) independently conducted the search and selected eligible papers. Any disagreement was resolved by consensus by a third author (MS).

Data extraction

The following information was extracted into a pre-defined excel spreadsheet. Author, year, diagnostic criteria, specific mental illness, age range of the population, number of patients, number of controls, total population, country, type of cancer participants were screened for, percent females, whether association measures were adjusted or not, which variables the association measures were adjusted for, the percentage or raw number of subjects receiving cancer screening in patients and in controls, and - if available - adjusted association measures quantifying eventual disparities in cancer screening between mental illness patients and controls (OR, RR, together with 95% confidence intervals). Two authors (MS, EF) independently extracted data. Any disagreement was resolved by consensus. No language restriction was applied.

Quality assessment

Two authors (MS, ED) independently assessed the quality of the included studies with the Newcastle-Ottawa Scale (NOS), with a score $\geq$7 (out of 9) indicating high quality (22).

Meta-analysis

Given that we anticipated considerable heterogeneity across included studies, we performed a random-effects meta-analysis (23, 24) using comprehensive meta-analysis (CMA, version 2). We calculated the odds ratio (OR) and 95% CI of any and specific cancer screening in patients with mental illness versus the general population (primary outcome), and the pooled prevalence of cancer screening in patients together with its 95%CI (secondary outcome). Heterogeneity was assessed with the I^2 statistics for each analysis (with significant heterogeneity being indicated by $I^2 \geq 50\%$ (25). Publication bias was assessed via visual inspection of funnel plots and the Begg-Mazumdar Kendall's tau and Egger bias test (26). We also calculated the trim and fill adjusted analysis (27) in case of publication bias (namely Egger's test p-value <0.1), and the fail-safe number (estimated number of studies needed to move the effect size from significant to non-significant).

We also ran sensitivity analyses considering only studies, which defined mental illness according to any version of the DSM or ICD-criteria, and in studies adjusting for confounding factors.

Also, we ran subgroup analyses comparing cancer screening disparities and prevalence in patients with schizophrenia versus patients with mood disorders, comparing studies from different regions, and comparing cancer screening usually implemented in the context of screening programs, based on the available quantitative evidence (breast and cervical) vs. other/opportunistic cancer screening (colon, prostate). Given the different health care system between Canada and United States of America (national health service versus. insurance-based service), we did not pool the two countries together in the "North America" region, but analyzed them separately instead.

Finally, we run random effect meta-regression to test whether and quantify how the gap between subjects with mental illness and the general population increased with increasing screening rates in the general population.

Results

Search results and the study selection process are described in Figure 1. Out of 3,710 initial hits, we screened 3,004 studies at the title/abstract level, selecting 145 studies for full-text assessment. We excluded 98 studies for specific reasons after full-text assessment, and finally included data from 46 samples (reported in 47 publications). The complete list of the 98 studies excluded after full-text assessment, with reasons for exclusion, is reported in Supplementary material, page 17.

Detailed characteristics and references of included studies are reported in Supplementary material, page 2. Overall, this meta-analysis reports data from 4,717,839 subjects (501,559 patients with mental illness, and 4,216,280 controls), who were more than two-thirds female (69.85%). Mental illness was defined in 20 studies according to DSM or ICD diagnostic criteria, 13 with validated scales, 10 according to clinical records, and 3 using different criteria within the same study. The cancer screening period lasted from 1 year (7 studies) to lifetime screening (6 studies). Age ranged from 18-79 years. Concerning mental illness, 14 studies focused on subjects with depression only, 6 with schizophrenia, 14 with mixed mental disorders while reporting screening estimates for specific groups, and 12 included mixed mental disorders without reporting on specific diagnostic groups. All continents except Africa were represented. Specifically, 25 studies were conducted in the USA, 5 in Canada, 3 in the UK, 3 in Australia, 2 in Israel, 2 in Denmark, and one each in Taiwan, Hong Kong, in the European Union (without specifying countries), in Sweden, Japan, and in the USA plus Canada. Overall, 31 studies provided adjusted estimates, while 15 did not consider the influence of confounding factors. Confounding factors considered in the analyses heterogeneously included social, economic, demographic, behavioral, and clinical factors potentially influencing the association between mental illness and low cancer screening. A detailed report on the quality of included studies according to the NOS scale is reported in Supplementary material, page 13. The quality of included studies was high (NOS score $\geq$7) in 26 out of 46 (56.52%) studies, with a median=7 (IQR = 2).

Results of main comparative random-effects meta-analysis together with publication bias, fail-safe number and trim and fill analysis are reported in detail in Table 1. A forest plot is also represented in Figure 2, showing disparities in cancer screening between mental illness and the general population in any, breast, cervical and colorectal cancer.

Screening occurred in significantly fewer people with mental illness than in controls for any (k=37, OR = 0.76, 95%CI 0.72-0.79, p<0.001), breast (k=27, OR = 0.65, 95%CI 0.60-0.70, p<0.001), cervical (k=23, OR = 0.89, 95%CI 0.84-0.94, p<0.001), and prostate cancer (k=4, OR = 0.78, 95%CI 0.70-0.86, p<0.001), but not for colorectal cancer. In schizophrenia, screening was significantly less likely than controls for any, breast, and cervical cancer. In mood disorders, screening was significantly less likely than in controls for any

and breast cancer, without any difference for cervical cancer, while screening was more frequent than in controls for colorectal cancer.

Publication bias emerged only for any cancer screening in any mental illness (one out of 12 comparisons, with fail-safe N equal to 3,117). The trim and fill analysis confirmed that subjects with any mental illness are significantly less likely to receive any cancer screening even when adjusting for indicated publication bias.

Results of comparative sensitivity random-effects meta-analysis together with publication bias, fail-safe number, and trim and fill analyses are reported in detail in Table 1 (together with main analyses). Considering studies using DSM/ICD criteria, compared with the general population, any cancer screening was significantly less likely in any mental illness and in schizophrenia, but not in mood disorders. In patients with any mental illness, schizophrenia, and mood disorders, breast cancer screening rates were the lowest versus the control group compared to all other examined cancers. Prostate cancer screening was also significantly less likely in any mental illness compared with the general population. Conversely, cervical cancer screening rates were not different from the general population in any mental illness, schizophrenia, or mood disorders. Similarly, colorectal cancer screening rates were not different between any mental illness and controls.

Publication bias emerged in four out of 11 comparisons, and results remained significant after a trim and fill analyses.

In studies adjusting for confounding factors, any cancer and breast cancer screening rates were significantly lower versus controls in subjects with any mental illness, schizophrenia, and mood disorders. Cervical cancer screening was less frequent in any mental illness, and schizophrenia compared with controls, but no difference emerged for mood disorders when considering adjusted studies only. Prostate cancer screening rates were lower in any mental illness compared with controls in adjusted studies. Finally, in adjusted studies, colorectal cancer screening did not differ significantly between subjects with any mental illness, or mood disorders, and controls.

Publication bias emerged in three out of 12 comparisons and results remained significant after a trim and fill analyses, with fail-safe numbers ranging from 136 to 7,862 (see Table 1).

Detailed results of subgroup analyses of country/region, diagnostic spectrum, and program versus opportunistic screening, with heterogeneity measures, are reported in Table 2 and Table 3. In regional subgroup analyses, considering any mental illness, no significant differences emerged in terms of disparities in any site cancer screening. When looking at specific cancer sites, differences across countries emerged for breast, cervical, colorectal, and prostate cancer. However, disparities were confirmed in the vast majority of countries. Conversely, any cancer but not site-specific cancer screening disparities differed among regions in schizophrenia and mood disorders (See table 2 and table 3).

In diagnostic spectrum subgroup analyses, any site and breast cancer screening disparities differed between schizophrenia and mood disorders, being consistently lower in schizophrenia. On the other hand, cervical screening disparities did not differ between schizophrenia spectrum and mood disorders.

Finally, disparities in cancer screening were more pronounced in the context of screening programs compared with opportunistic screening.

Detailed results of the prevalence of cancer screening analyses are reported in Table 4. In any mental illness, screening prevalence of any site, breast, cervical, colorectal, and prostate cancer were 56.5% (95%CI=51.5-61.3%), 61.9% (95%CI=54.7-68.6%), 59.7% (95%CI=49.4-69.2%), 37.1% (95%CI=28.9-46.1%), 48.2% (95%CI=31.3-65.5%) respectively, and no differences emerged between people with schizophrenia and mood disorders. Conversely, large regional differences emerged in cancer screening prevalence for all aforementioned cancer sites, with Asia consistently having the lowest prevalence of cancer screening, Europe, Canada and USA being overall in the middle, and Australia providing the highest rates of cancer screening in subjects with mental illness.

Results of meta-regression are reported in Table 5. Result show that considering any cancer, cervical cancer, and colorectal cancer, the gap between subjects with mental illness and the general population increases with increasing participation of the general population in cancer screening (p<0.001 in each group).

Discussion

The current meta-analysis is the first investigating any and specific cancer screening rates among people with any mental illness, including data from over 4.5 million subjects from all parts of the world, except Africa. Results indicate that subjects with mental illness experience disparities in any, breast, cervical and prostate cancer screening compared with the general population, particularly for breast cancer and in females with schizophrenia. Disparities are also apparent across different regions of the world but to a different extent. Given that cancer screening protects from cancer mortality (70% decline in cervical cancer mortality since screening introduction)(28), such disparities may lead to increased cancer mortality in subjects with mental illness.

The results of our meta-analysis extend previous narrative reviews and confirm our hypothesis that subjects with mental illness undergo less cancer screening than the general population. Results are in line with Aggarwal et al. (studies=19, participants=106,905) (18), Lord et al. (studies=19 in total, 18 for mammography, 10 for uterine cance screening, 4 for colonoscopy, participants=1,377,147) (17), and the meta-analysis of breast cancer screening (mammography) by Mitchell et al. (studies=24, participants=715,705) (19), as well as previous studies, which showed an association between psychotic disorder, substance abuse, and utilization of primary/non-psychiatric care.(29) The present data however expand aforementioned previous systematic reviews, including any mental illness and any cancer type in one quantitative evidence synthesis. The underlying reasons that may explain disparities in cancer screening are multiple. First, while many psychiatrists believe that physical examinations should not be performed by other

professionals (30), they rarely perform physical examinations themselves, possibly due to a shortage of time and equipment, due to challenges associated with agitated or uncooperative patients, and, possibly, due to a degree of skill atrophy, especially in more senior psychiatrists (31). Rare physical examination performed by psychiatrists may reflect poor attention to physical health. Second, it has been shown that a negative attitude of general practitioners towards cancer screening is associated with an almost 20% increased likelihood of patients' not undergoing cancer screening procedures (32). If general practitioners have negative attitudes towards mental illness, this may also partly explain our findings. Third, nurses, who have a positive attitude towards promoting physical health in subjects with mental illness, have shown to be more ambivalent when it comes to cancer screening (33). Such ambivalence may be due to lack of training on physical health promotion, and lack of communication between primary and secondary health-care systems (34). Fourth, symptoms and impairment in (social) functioning and in cognition may compromise healthcare access and utilization. Fifth, the lower cancer screening rates in mental illness may also be explained by common risk factors for mental illness, cancer and a reduced likelihood of undergoing cancer screening. Specifically, poverty and low socio-economic status (SES) are known risk factors for psychiatric disorders (35), while women with lower educational level and lower SES have also been reported to know less about cervical cancer and screening (36). Sixth, patients with mental illness may have difficulties in communicating somatic symptoms, or could not be interested in doing so due to depressed mood or negative symptoms. Seventh, while a call for optimizing the synergy between mental health and primary care has been raised by the World Health Organization,(37) and consistently by other authors,(38-40), this strong rationale has only insufficiently translated into any actual change in clinical practice yet. Finally, diagnostic overshadowing, namely clinicians' attributing early somatic symptoms of cancer to underlying mental illness, may also explain why patients with mental illness undergo less medical exams (41).

We also confirmed the hypothesis that subjects with schizophrenia would suffer from more pronounced disparities compared to individuals with mood disorders. Such differences may be due to the persistent functional impairment, which is more frequently present in schizophrenia (42), as opposed to more frequent, yet still often sub-optimal inter-episode improvement of functioning in people with mood disorders (43). Thus, impairment in social functioning, which is closely related to (social) cognition in schizophrenia (44), may be responsible for less effective memory, more severe social withdrawal, less medical care help seeking behavior, and less social contacts, which each contribute to less participation in cancer screening. Nonetheless, we have also shown that any and breast cancer screening is low in people with mood disorders, hence raising public health concerns given the high prevalence of mood disorders compared with schizophrenia.

We also confirmed that cancer screening disparities were universal across different geographical regions, yet to a different extent. Region-wise subgroup analyses showed that the lowest prevalence of cancer screening in subjects with mental illness is found in Asia, and the highest in Australia, with Europe, USA and other regions ranging between these two extremes. However, paradoxically, Australia also had the highest disparities for some cancer sites, and in people with mood disorders in particular (see table 3). This result can

be explained by the fact that disparities are largest where screening in the general population is the highest, as shown by the meta-regression analyses. In other words, if in Australia cancer screening campaigns work brilliantly for the general population, this does not hold true for patients with mental illness, who do not benefit as much from health-care progress as the general population. Differences among regions may also be due to variable measurements healthcare system properties, or cohort-level characteristics.

Despite confirming most of our hypotheses, colorectal cancer screening did not differ between mental illness and controls, although the colorectal cancer screening prevalence was the lowest (37.1% versus 48.2%-61.9% for the other cancer sites). This finding indicates that cancer screening rate disparities also depend on the rates of cancer screening in the general population. For instance, when the general population suffers from low cancer screening coverage (45-47), disparities for the mentally ill might not be evident due to a ceiling effect.

The present work has several implications, given that cancer screening disparities are highest for those cancers where universal programs usually exist around the world (i.e., breast, cervical), compared with other cancer sites (i.e., colon), for which opportunistic screening procedures are performed. In other words, while cancer screening campaigns work well in preventing cancer in the general population in several countries with national screening programmes, such as in the UK, Italy, and Sweden, among others, apparently this benefit does not generalize to people with mental illness. For instance, while a meta-analysis from 2001 (48) showed that more women who received a reminder letter attended cancer screening (OR=1.64, 95% CI=1.49-1.80), and while other strategies seem to promote cancer screening in the general population, (49-52) approaches generally working with subjects not affected by mental illness might not work for subjects with mental illness. Therefore, such interventions should likely involve awareness among mental health specialists, and facilitation of communication between primary and tertiary care as well as between specialists in mental health and physical health care, aiming for a close collaborations between mental health and primary care.(37-40, 53)

The present work has several limitations. First, results were virtually always heterogeneous, calling for cautious interpretations, especially of some of the marginally significant findings. More specifically, the studies included in the present meta-analysis reported on studies from countries with different screening guidelines and with different follow-up durations. Second, in subgroup analyses, some regions were under-represented (i.e., Asia versus USA). Hence, results on differences among these under-represented countries and others should be considered exploratory. Third, we relied on published data and were only able to report results that were adjusted for a limited number of potential confounders, namely those that the authors of the original papers had adjusted their analyses for. Furthermore, based on the more limited data, there remains controversy about the value of screening for prostate cancer (54). However, prostate cancer screening was included in our analyses, as reduced uptake in people with mental illness may serve as a marker of reduced access to preventive care in general. By definition, our results only apply to cancer sites for which widespread screening exists. Due to very limited data on lung cancer, despite high smoking frequencies in

the mentally ill (55, 56), our results cannot explain disparities in survival for lung cancer (or other cancers), yet, likely similar barriers to screening and health care access and quality for mental illness will be at play there too. Furthermore, since too few studies were available that differentiated between unipolar vs bipolar mood disorder, we were unable to conduct subgroup analyses of cancer screening across these two subgroups. Additionally, studies adjusting for potentially confounding factors considered heterogeneous types and numbers of covariates. Finally, we did not find any studies on melanoma, although screening for this cancer is common in several countries, including Australia.

In conclusion, subjects with mental illness, including mood disorders, and in particular women with schizophrenia, undergo cancer screening significantly less frequently compared with the general population. Such a gap is most pronounced for those cancers for which the general population often receives universal screening based on national programs. Such disparity may contribute to the life expectancy gap between subjects with psychiatric disorders and the general population. Asia has the lowest screening rates, and Australia has the highest, and disparities seem to be the highest where the general population is best involved in cancer screening programs. More studies are needed on lung cancer screening, given the high rates of smoking in people with mental illness. Specific strategies, which should ideally involve mental health departments, general practitioners, and prevention as well as primary care departments, should be tested and implemented in order to fill this important health care gap and to avoid subjects with mental illness being left behind in cancer prevention.

Authors' contributions

MS and BS designed the protocol of the study. MS, EF, AK, JF, MF, ED, AM, JIS, BS conducted the screening and data extraction. MS, CUC run the analyses. MS, AFC, PFP, SK, CUC drafted the manuscript. All authors read, modified, and approved the final version of the submitted manuscript.

Conflict of interest statements

Authors declare no conflict of interest

Role of funding source

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Figure 1.

Title. PRISMA flow-chart of study selection process

Figure 1. PRISMA flow-chart of study selection process

Identification	
Records identified through database searching (n = 3710)	Additional records identified through other sources (n = 23)

Records after duplicates removed (n = 3004)

Screening

Records screened (n = 3004) → Records excluded at title/abstract assessment (n = 2859)

Elegibility

Full-text articles assessed for eligibility (n = 145) → Full-text articles excluded, with reasons (n = 98)

no cancer screening (n=68)

no data available (n=16)

no mental illness (n=6)

valid diagnosis (n=4)

pdf not found (n=4)

Included

Studies included in quantitative synthesis (meta-analysis) (n = 47 publications; 46 studies)

Figure 2.

Title. Forest plot with estimates of disparities in cancer screening between subjects with mental illness and the general population: main and sensitivity analyses

Legend. MI, mental illness

Legend. MI, mental illness.

Table 1. Comparative random effect meta-analysis of cancer screening (breast, cervical, colorectal, prostate) in patients with mental illness compared with general population, and sensitivity analysis on studies using ICD/DSM diagnosis, and adjusted studies.

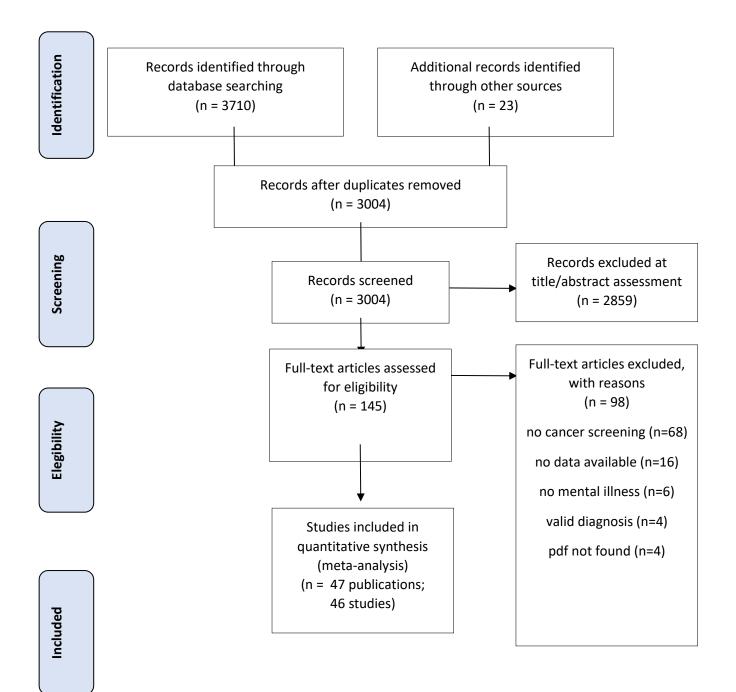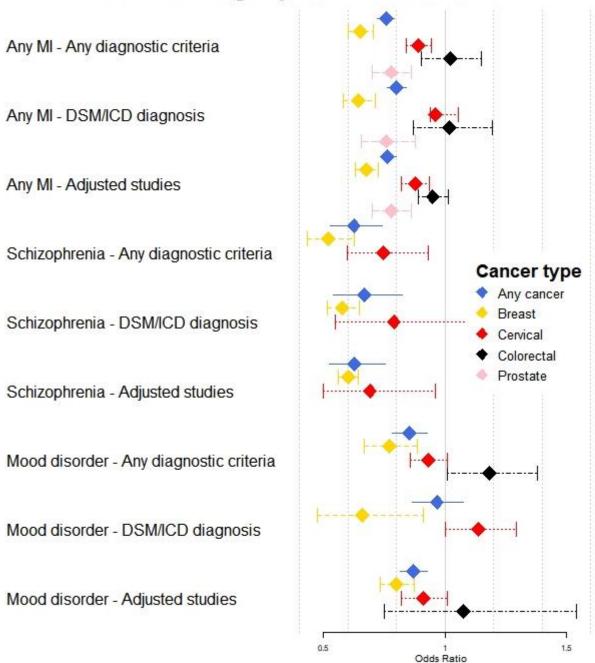| Cancer screening	Publications/samples	OR (95%CI)*	p value	I²	Egger's test p value / Fail safe N / Effect size after trim and fill (in case of publication bias)
Any mental illness#					
Any diagnostic criteria					
Any cancer	37/149	0.757 (0.722-0.792)	<0.001	98.53%	0.025 /5174 / 0.905 (0.862-0.951) 39 studies trimmed looking for missing studies to right of mean
Breast	27/85	0.652 (0.603-0.705)	<0.001	97.58%	0.878 /7920
Cervical	23/44	0.891 (0.840-0.945)	<0.001	98.47%	0.811 / 2820
Colorectal	8/11	1.02 (0.903-1.151)	0.753	97.84%	0.463 / NA /
prostate	4/9	0.777 (0.701-0.862)	<0.001	79.68%	0.493 / 457
DSM or ICD diagnosis					
Any cancer	14/78	0.800 (0.762-0.839)	<0.001	97.16%	0.002 / 8808 / 0.948 (0.903-0.996) 20 studies trimmed looking for missing studies to right of mean
Breast	8/44	0.642 (0.579-0.711)	<0.001	96.44%	0.006 / 7798 / 0.674 (0.609-0.745) 4 studies trimmed looking for missing studies to right of mean
Cervical	9/25	0.959 (0.939-1.055)	0.876	97.61%	0.742 / NA
Colorectal	3/5	1.018 (0.869-1.193)	0.821	82.08%	0.481 / NA
Prostate	2/4	0.757 (0.653-0.878)	<0.001	54.72%	0.042 / 49 / 0.813 (0.687-0.962) 2 studies trimmed looking for missing studies to right of mean
Adjusted studies*					
Any cancer	31/121	0.763 (0.731-0.797)	<0.001	97.82%	0.004 / 7846 / 0.898 (0.861-0.938) 30 studies trimmed looking for missing studies to right of mean
Breast	21/69	0.674 (0.628-0.724)	<0.001	96.18%	0.039 / 4057 / 0.799 (0.743-0.859) 17 studies trimmed looking for missing studies to right of mean
Cervical	19/35	0.876 (0.821-0.936)	<0.001	98.67%	0.111 / 153
Colorectal	5/7	0.949 (0.889-1.012)	0.111	70.26%	0.530 / NA
Prostate	4/9	0.777 (0.701-0.862)	<0.001	79.68%	0.494 / 457
Schizophrenia and other non-affective psychoses					
Any diagnostic criteria					
Any cancer	13/24	0.624 (0.525-0.742)	<0.001	98.78%	0.540 / 4696
Breast	8/12	0.518 (0.431-0.624)	<0.001	91.99%	0.604 / 2232
Cervical	7/10	0.746 (0.597-0.932)	0.010	98.59%	0.622 / 163
DSM or ICD diagnosis					
Any cancer	8/14	0.666 (0.539-0.822)	<0.001	98.12%	0.280 / 494
Breast	4/7	0.578 (0.516-0.647)	<0.001	26.62%	0.020 / 249 / 0.621 (0.548-0.704) 4 studies trimmed looking for missing studies to right of mean
Cervical	4/6	0.789 (0.549-1.135)	0.202	99.09%	0.919 / NA
Adjusted studies*					
Any cancer	10/15	0.627 (0.521-0.754)	<0.001	98.09%	0.160 / 1421
Breast	5/8	0.601 (0.561-0.644)	<0.001	15.58%	0.029 / 517 / 0.617 (0.566-0.672) 4 studies trimmed looking for missing studies to right of mean
Cervical	5/6	0.690 (0.497-0.958)	0.027	99.10%	0.614 / 136
Mood disorders					
Any diagnostic criteria					

Table 2. Region subgroup random effect meta-analysis of cancer screening (breast, cervical, colorectal, prostate) in patients with mental illness #

Country/region	Publications/samples	OR (95%CI)*	p value	I²	Subgroup difference across different regions p value
Any mental illness					
Any cancer					
Israel	2/2	0.807(0.750-0.869)	<0.001	39.50%	0.085
Europe	6/25	0.777(0.728-0.829)	<0.001	97.87%	
USA*	21/105	0.769(0.717-0.825)	<0.001	98.41%	
Australia	2 / 5	0.762(0.697-0.834)	<0.001	94.90%	
Canada*	6/9	0.729(0.587-0.905)	0.004	88.55%	
Asia	1/3	0.302(0.157-0.581)	<0.001	NA	
Breast cancer					
Canada*	4/4	0.929(0.523-1.650)	0.8	63.73%	0.016
Israel	1/1	0.767(0.691-0.851)	<0.001	NA	
USA*	18/65	0.667(0.608-0.732)	<0.001	97.97%	
Europe	4/12	0.655(0.573-0.749)	<0.001	91.82%	
Asia	1/3	0.302(0.157-0.581)	<0.001	NA	
Cervical cancer					
USA*	14/24	0.980(0.880-1.092)	0.714	96.98%	<0.001
Europe	3/12	0.880(0.822-0.941)	<0.001	97.97%	
Australia	2 / 3	0.728(0.674-0.787)	<0.001	8.14%	
Canada*	5/5	0.670(0.491-0.914)	0.012	92.73%	
Colorectal cancer					
Europe	1/1	1.300(1.095-1.543)	0.003	NA	<0.001
USA	6/9	1.011(0.879-1.163)	0.878	98.05%	
Australia	1/1	0.900(0.861-0.941)	<0.001	NA	
Prostate cancer					
Israel	1/1	0.830(0.781-0.882)	<0.001	NA	<0.001
USA	2/7	0.772(0.638-0.935)	0.008	69.38%	
Australia	1/1	0.720(0.700-0.740)	<0.001	NA	
Schizophrenia spectrum disorders					
Any cancer					
Israel	1 / 1	0.830(0.781-0.882)	<0.001	NA	<0.001
Canada	2/6	0.674(0.618-0.735)	<0.001	50.26%	
USA	5/13	0.619(0.449-0.852)	0.003	99.16%	
Europe	5/8	0.545(0.409-0.727)	<0.001	98.36%	
Breast cancer					
Canada	1 / 1	0.640(0.578-0.708)	<0.001	NA	0.090
Europe	3/4	0.576(0.504-0.659)	<0.001	41.03%	
USA	4/7	0.463(0.345-0.623)	<0.001	67.29%	

Table 3. Subgroup meta-analysis of disparities in any cancer screening between schizophrenia spectrum disorder and mood disorders, and in program vs opportunistic screening

Mental illness	Cancer	Publications/samples	Odds ratio and p value	Heterogeneity	Subgroup difference between schizophrenia and mood disorders p value
Diagnostic spectrum					
Schizophrenia spectrum disorders	Any cancer	13/24	0.624 (0.525-0.742); p < 0.001	98.78%	0.002
Mood disorders	Any cancer	25/49	0.851 (0.783-0.926); p < 0.001	98.84%	
Schizophrenia spectrum disorders	Breast cancer	8/12	0.518 (0.431-0.624); p < 0.001	91.99%	0.001
Mood disorders	Breast cancer	18/24	0.770 (0.658-0.886); p < 0.001	98.09%	
Schizophrenia spectrum disorders	Cervical cancer	7/10	0.746 (0.597-0.932); p = 0.010	98.59%	0.069
Mood disorders	Cervical cancer	16/19	0.930 (0.856-1.011); p = 0.090	96.84%	
Program vs opportunistic					
Program	Breast and cervical cancer	28/131	0.734 (0.698-0.772); p<0.001	98.53%	0.002
Opportunistic	Colon and prostate cancer	2/18	0.905 (0.803-1.019), p=0.1	98.35%	

Table 4. Meta-analysis of prevalence of cancer screening (breast, cervical, colorectal, prostate, gastric, lung, ovarian) in patients with mental illness (defined according to any criteria), and subgroup analysis across countries and between schizophrenia and mood disorders.

Country/region and Mental illness	Cancer	Publications/samples	Prevalence	Heterogeneity	Subgroup comparison between schizophrenia and mood disorders
Any cancer					
Any mental illness	Any cancer	34/155	56.5% (51.5-61.3)	99.91%	
Australia	Any cancer	1/2	87.6% (78-93.4)	NA	<0.001
Europe	Any cancer	6/23	69.5% (64.1-74.4)	99.54%	
Canada	Any cancer	3/3	61.7% (43.4-77.2)	99.46%	
USA	Any cancer	19/111	58.8% (53.4-64)	99.9%	
Israel	Any cancer	2/2	34.4% (19.6-53)	99.74%	
Asia	Any cancer	3/14	18% (11.9-26.4)	96.83%	
Mood disorders	Any cancer	19/35	50.6% (41.4-59.8)	99.94%	0.408
Schizophrenia spectrum disorders	Any cancer	16/36	44.5% (33.9-55.6)	99.87%	
Breast cancer					
Any mental illness	Breast cancer	25/81	61.9% (54.7-68.6)	99.89%	
Australia	Breast cancer	1/1	91.5% (83.2-95.9)	NA	<0.001
USA	Breast cancer	16/65	65.6% (57.9-72.6)	99.89%	
Europe	Breast cancer	3/9	56.9% (50.5-63.1)	96.16%	
Canada	Breast cancer	1/1	44.8% (42.3-47.4)	NA	
Israel	Breast cancer	1/1	43.7% (42.2-45.2)	NA	
Asia	Breast cancer	1 /4	15.4% (8.7-26)	NA	
Mood disorders	Breast cancer	13/16	57.9% (41.4-7.28)	99.92%	0.570
Schizophrenia spectrum disorders	Breast cancer	12/17	52.3% (41.8-62.5)	99.53%	
Cervical cancer					
Any mental illness	Cervical cancer	20/42	59.7% (49.4-69.2)	99.94%	
Australia	Cervical cancer	1/1	84% (75.5-90)	NA	<0.001
Canada	Cervical cancer	2/2	69.4% (47.7-84.9)	99.48%	
Europe	Cervical cancer	3/12	81.4% (78.1-84.3)	99.62%	
USA	Cervical cancer	12/25	47% (38.3-55.9)	99.9%	
Asia	Cervical cancer	2/2	19.3% (2.8-66.4)	96.39%	
Mood disorders	Cervical cancer	11/12	52.9% (31.1-73.6)	99.97%	0.654
Schizophrenia spectrum disorders	Cervical cancer	10/14	46.7% (32.8-61.1)	99.74%	
Colorectal cancer					
Any mental illness	Colorectal cancer	10/18	37.1% (28.9-46.1)	99.79%	
USA	Colorectal cancer	7/12	46.7% (35.8-57.9)	99.86%	<0.001
Europe	Colorectal cancer	1/1	27% (15.2-43.3)	NA	
Asia	Colorectal cancer	2 /5	19.3% (13.1-27.6)	7%	
Mood disorders	Colorectal cancer	5/5	34.0% (19.4-52.4)	99.89%	0.525

Table 5. Meta-regression between the gap in screeing rates between the general population and subjects with mental illness, and the screening rates in the general population.

Cancer	Publications/samples	Beta	95%CI	P value
Any cancer	35/143	-0.79	-1.18 - -0.39	<0.001
Breast cancer	26/84	0.35	-0.21 – 0.91	0.223
Cervical cancer	21/42	-1.46	-2.12 - -0.80	<0.001
Colorectal cancer	6/9	-0.76	-1.13 - -0.39	<0.001
Prostate cancer	3/8	-0.51	-1.68 - -0.68	0.404

Disparities in cancer screening in people with mental illness across the world: prevalence and comparative meta-analysis versus the general population including 4,717,839 people

Supplementary material content

Supplementary table 1. Characteristics of studies reporting on disparities or prevalence of cancer screening in subjects suffering from mental illness

Author	Diagnostic criteria	Screening period (years)	Age	Psychiatric disorder	N patients	N controls	N total	Country	Female %	Cancer	Screening procedure	Adjusted (Y/N)	which variables are analyses adjusted for	Association measure	Prevalence
Abrams, 2012 (1)	ICD-9	1	41,00	substance use disorder	6122	85375	105 681	USA	100,00%	cervical	pap smear	Y	age, region, comorbidity, diagnosis, race.	Y	Y
			46,00	psychosis	4747										
			42,00	psychosis and substance use disorder	1104										
			41,00	bipolar disorder or mania	3319										
			43,00	depression	5014										
Aggarwal, 2008 (2)	CES-D	1	57(50-79)	depressive symptoms	12621	67368	79 989	USA	100,00%	breast	mammography	N		Y	Y
										colon	colonscopy				
Blackwell, 2008 (3)	Composite International Diagnostic Interview	2	18 - 69	major depressive episodes	496	4358	4 854	USA/Canada	100,00%	breast	mammography	Y	demographic, socio-economic, health staus and other variables	Y	N
										cervical	pap smear				
Carney, 2006 (4)	DSM-IV	5	48,30	mood disorder	22512	131683	191 356	USA	100,00%	breast	mammography	Y	age, rural location, utilization of nonmental health services, and severity and type of the mental disorder.	Y	Y
				psychotic disorders	525										
				adjustment disorders	8656										
				anxiety disorders	9340										
				low severity other mental disorder	2113										

	Coding	Score	Age	Disorder	Cases	Controls	Total	Country	%	Cancer	Screening		Adjustment		
				sexual disorder	3175										
				sleep disorder	3454										
				somatoform disorder	3121										
				substance disorder	6777										
Chochinov, 2009 (5)	ICD-9	2	50-69	schizophrenia	1448	108792	110 240	Canada	100,00%	breast	mammography	Y	age, region, average household income, continuity of care, and physical comorbid-Ities.	Y	Y
Domino, 2014 (6)	clinical records	3	≥50	schizophrenia	15636	106555	188 531	USA	66,00%	colon	colon screening	Y	inpatient hospital days	Y	Y
			≥45						100,00%	breast	mammography				
			21-65						100,00%	cervical	cervical screening				
			≥50	depression	66340				66,00%	colon	colon screening				
			≥40						100,00%	breast	mammography				
			21-65						100,00%	cervical	cervical screening				
Druss, 2002 (7)	ICD-9	3	<=65	psychiatric disorder only (ICD-9 codes 290 –302 and 306 – 319)	3 000 all	4 030	7 030	USA	100,00%	cervical	pap smear	Y	demographic, health status, and facility-level characteristics.	Y	Y
		2	50-69						100,00%	breast	mammography				
		1	>=50						0,00%	prostate	PSA				
		1	>=50						21,00%	colon	fecal occult blood				
		3	<=65	substance use disorder					100,00%	cervical	pap smear				
		2	50-69						100,00%	breast	mammography				
		1	>=50						0,00%	prostate	PSA				
		1	>=50						21,00%	colon	fecal occult blood				
		3	<=65	dual diagnosis (co-morbid psychiatric and substance use disorders).					100,00%	cervical	pap smear				

Author	Criteria	n	Age	Disorder	Cases	Controls	Total	Country	%	Site	Test	Adj?	Adjustment variables		
		2	50-69						100,00%	breast	mammography				
		1	>=50						0,00%	prostate	PSA				
		1	>=50						21,00%	colon	fecal occult blood				
Druss, 2008 (8)	CIDI-SF>=3 (DSM-III)	1	>50	major depressive disorder	2220	27861	30 081	USA	69,80%	colon	fecal occult blood	Y	gender, race, age, poverty status, insurance coverage and number of chronic medical conditions.	Y	N
			>40						100,00%	breast	mammography				
			<65						100,00%	cervical	pap smear				
Eriksson, 2019(9)	ICD-10	5	23-60	Schizophrenia spectrum disorders	2364	275879	341 171	Sweden	100%	cervical	Pap smear	Y	age	Y	Y
				Mood disorders	43832										
				Phobia, anxiety, stress-related disorders	19096										
Folsom, 2002(10)	DSM-IV	1	51,5(≥45)	schizophrenia or schizoaffective disorders	47	NA	94	USA	47,00%	colon	fecal occult blood	N		N	Y
									100,00%	breast	mammography				
									100,00%	cervical	pelvic examination				
			51,3(≥45)	major depressive disorder	47				47,00%	colon	fecal occult blood				
									100,00%	breast	mammography				
									100,00%	cervical	pelvic examination				
Fujiwara AND Inagaki, 2017, 2018 (11, 12)	DSM-5	1	44,8 (40-69)	schizophrenia or schizoaffective disorders	420	NA	420	japan	51,30%	colon	colon screening	N		N	Y
		1	44,8 (40-69)						51,10%	gastric	gastric screening				
		1	44,8 (40-69)						51,30%	lung	lung screening				
		2	44,8 (40-69)						100,00%	breast	mammography				
		2	20-69						100,00%	cervical	pap smear				

Study	Tool	Yrs	Age	Disorder	Cases	Comparison	Total	Country	%	Cancer	Screening		Adjustment		
Gal,2014 (13)	ICD-10	8	61,00	schizophrenia	8285	16570	24 855	Israel	0,00%	prostate	PSA	Y	sum of PSA tests	Y	Y
Green, 2000 (14)	SF-36	lifetime	52,9(18-102)	Depression	1173	2299	3 472	USA	100,00%	breast	mammography	Y	income, self-reported social-class, health status.	Y	N
										cervical	pap smear				
Harder, 2018 (15)	ICD-10	2	23-49	Intoxicant abuse	3188	419552	466 419	Denmark	100%	cervical	pap smear	Y	age, country of origin, marital status, educational level, income	Y	Y
				schizophrenia and other psychoses	4454										
				affective disorders	13927										
				anxiety and Obsessive-compulsive disorders	21641										
				eating disorders	3657										
Holden, 2015 (16)	CES-D	na	na	depression	37	NA	37	UK	100%	Ovarian	na	N	-	N	Y
										colorectal	na				
Iezzoni, 2001 (17)	NHIS-D	2	>50	serious mental health problem	1944	75818	77 762	USA	100,00%	breast	mammography	Y	age	Y	N
			42,4(18-65)							cervical	pap smear				
			>30							breast	breast examination				
Jensen, 2016 (18)	clinical records	10	50 - 69	Schizophrenia	1 022	137 692	144 264	Denmark		breast	mammography	Y	age, marital status, ethnicity, education, psychiatric comorbidity	Y	Y
				Affective disorders	3 453										
				Anxiety disorders	670										
				Substance abuse	1 427										

Study	Diagnostic	N	Age	Disorder	Cases	Controls	Total	Country	%	Cancer	Screening		Adjustments		
Kaida, 2008 (19)	DSM-IV, ICD-10	3	18-69	depression	1831	23521	25 352	Canada	100,00%	cervical	pap smear	Y	age, education, income, marital status, ethnicity, healthcare utilization	Y	Y
Katz,2018 (20)	clinical records	6	50-74	depression	4354	39964	44,318	Israeli	100%	breast	mammography	Y	Socio-demographic factors and comorbidities	Y	Y
Kempe, 2013 (21)	clinical records	2	52-69	depression	9269	38677	47 946	USA	100,00%	breast	mammography	Y	socioeconomic and health status variable	Y	Y
Koroukian, 2012 (22)	ICD-9-CM	6	50-64	mental illness and/or alcohol/substance abuse	61661	68427	130 088	USA	100,00%	breast	mammography	Y	comorbid conditions and length of enrollment in Medicaid	Y	N
Kotwal, 2012(23)	CES-D, HADS, PSS-4	1	57-85	depression	120	1 049	1 169	USA	0%	prostate	PSA	Y	Age, ethnicity, marital status, education, income	Y	Y
				anxiety											
Lasser, 2003 (24)	modified version of PRIME-MD	2	40-70	anxiety disorders	103	293	672	USA	100,00%	breast	mammography	N		Y	Y
				eating disorders	28										
				mood disorders	84										
				PTSD	27										
				substance abuse	46										
				somatisation	79										
				psychotic disorders	12										
Lindamer, 2003 (25)	clinical records, PANSS, HAM-D	2	57,6(50-79)	schizophrenia	65	51	116	USA	100,00%	breast	mammography	N		Y	Y
		3								cervical	pap smear				
		2	57,6 (50-79)	schizophrenia or schizoaffective disorders					100%	cervical	pelvic examination and pap test				
										breast	mammography				

Study	Source	Period	Age	Disorder	Cases	Controls	Total	Country	%	Cancer	Screening	Adj?	Adjustment variables		
Lindamer, 2006(26)	DSM-IV	lifetime	52,9 (44-72)	schizophrenia or schizoaffective disorders	46	NA	46	USA	100,00%	breast	mammography	N		N	Y
Long, 1998 (27)	clinical records	lifetime	49,1(41-50)	mental health treatment, hospitalization	43	62	105	USA	100,00%	breast	mammography	N		Y	Y
		1	41,70							breast	breast examination				
		1	39,90							cervical	pap smear				
Ludman, 2010 (28)	PHQ-9	2	51-65	depression	755	3904	4 659	USA	100,00%	breast	mammography	Y	age, ethnicity, marital status, education, current smoker, comorbidity, body dissatisfaction	Y	Y
		3	40-65							cervical	pap smear				
Martens, 2009 (29)	clinical records	3	18-69	schizophrenia	3220	335294	338 514	Canada	100%	cervical	pap smear	Y	age, region, income, continuity of care, physical comorbidities	Y	Y
Masterson, 2010 (30)	Kentucky 2002 BRFSS	lifetime	≥40	low depression	543	2818	5 101	USA	100,00%	breast	mammography	Y	age, race, marital status, education, income, and health insurance status	Y	N
				high depression	192										
				very high depression	307										
				low anxiety	622										
				high anxiety	238										
				very high anxiety	381										
Mo, 2014 (31)	clinical records	lifetime	21-65	Severe mental illness	591	NA	591	Hong kong	100,00%	cervical	pap smear	N		N	Y
			>=40						100,00%	breast	mammography				
			>=40						100,00%	breast	breast examination				
			>=50						54,00%	colon	fecal occult blood				
			>=50						54,00%	colon	flexible sigmoidoscopy				
			>=50						54,00%	colon	colonscopy				

Study	Instrument	Period	Age	Mental disorder	Cases	Controls	Total	Country	%	Cancer	Screening	Y/N	Covariates	Y/N	Y/N
			>=50						54,00%	colon	double contrast barium enema				
			>=50						0,00%	prostate	digital rectal exam				
Olesen, 2012 (32)	Goldberg anxiety scale >7	2	44-68	anxiety	295	1657	2 095	Australia	100,00%	cervical	pap smear	Y	age	Y	N
	Goldberg depression scale >7			depression	143										
Owen, 2002 (33)	clinical records	lifetime	46,30	mood disorders, schizophrenia, primary anxiety disorder, other mental disorders	100	NA	100	Australia	100,00%	cervical	pap smear	N		N	Y
										breast	breast examination				
Patten, 2009 (34)	CIDI-SF	2	50-69	major depression	2651	3631	6 282	Canada	100,00%	breast	mammography	Y	age, sex, rural place of residence, education level, a diagnosis of hypertension, other chronic conditions, income and employment status	Y	N
			≥18							cervical	pap smear				
Peytremann-Bridevaux, 2008 (35)	EURO-D>3	10	67,6(≥50)	depressive symptoms	10335	5045	15 380	UE	70,50%	colorectal	colonscopy or flexible sigmoidoscpy	Y	age, gender, socioeconomic status, behavioral risk, chronic disease, disability, country	Y	N
		2	67,6(≥50)						100,00%	breast	breast screening				

Study	Criteria		Age	Condition	n		Total	Country	%	Cancer	Screening		Covariates		
Pirraglia, 2004 (36)	CES-D_=21	1	42-52	high depressive symptoms	492	2 493	3 297	USA	100,00%	breast	mammography	Y	age, race/ethnicity, health insurance, medical history and use, smoking, obesity, and socioeconomic status	Y	N
										cervical	pap smear				
				moderate depressive symptoms	312					breast	mammography				
										cervical	pap smear				
Salsberry, 2005 (37)	ICD-9-CM	3	≥18	schizophrenic disorders	158	NA	669	USA	100,00%	cervical	pap smear	N		N	Y
			≥40							breast	mammography				
			≥18	paranoid disorders	72					cervical	pap smear				
			≥40							breast	mammography				
			≥18	affective disorders	379					cervical	pap smear				
			≥40							breast	mammography				
			≥18	anxiety disorders	60					cervical	pap smear				
			≥40							breast	mammography				
Stecker, 2007 (38)	DSM	5	41,40	depression	270	590	860	USA	100,00%	breast	mammography	N		Y	Y
										cervical	pap smear				
										colon	colonscopy				
Thomas, 2018 (39)	DSM-IV-TR	1	48-67	anxiety disorders	641	NA	14 651	USA	100%	breast	mammography	N		N	Y
				bipolar disorders	2115										
				major depressive disorder	4806										
				other psychiatric disorders	754										
				schizophrenia	6335										
Tuesley, 2018 (40)	clinical records	7.5 to 11	18-69	Schizophrenia or bipolar disorder	41169	2017267	2 058 436	Australia	50%	colorectal	Fecal occult blood	Y	Age, gender, state, number visits with general practitioner per year	Y	N

Study	Criteria	Score	Age	Condition	n		Total	Country	%	Site	Screening		Adjustment variables		
										Cervical	Pap smear				
										prostate	PSA				
Vigod, 2011(41)	DSM-IV	2	56,30	major depressive disorder	67	840	1 398	Canada	100,00%	breast	mammography	Y	Age, income level, level of education, geograph-ical variability (urban/rural), body mass index, and medical and psychiatric comorbidity	Y	N
	Kessler 6-item >8		58(40-70)	clinically significant depressive symptoms	491					cervical	pap smear				
Werneke, 2006 (42)	ICD-10	3	50-64	any psychiatric condition	1048	53340	54 388	UK	100,00%	breast	breast screening	Y	mental health variable including level of psychiatric care, number of inpatient episodes and detention, diagnosis, and the total lenght of time a patient had been seen by the psychiatric service.	Y	Y
Weitlauf, 2013 (43)	ICD-9	5	18-65	PTSD	5668	16828	34 123	USA	100,00%	cervical	pap smear	Y	age, income, physical comorbidities	Y	Y
				depression	11627										
Woodhead, 2016 (44)	ICD-10	3	50-70	schizophrenia	406	132293	133 184	UK	100,00%	breast	mammography	Y	age, ethnicity, deprvation, primary-care consultation frequency	Y	Y
			25-64							cervical	pap smear				
			50-70	bipolar affective disorder	298					breast	mammography				
			25-64							cervical	pap smear				

Study	Criteria		Age	Illness	N	N2	Total	Country	%	Cancer	Screening	Col1	Adjustment	Col2	Col3
			50-70	Other non-organic psychoses	187					breast	mammography				
			25-64							cervical	pap smear				
Xiong, 2008 (45)	DSM-IV-TR	lifetime	40,10	Severe mental illness	229	NA	229	USA	100,00%	cervical	pap smear	N		N	Y
			40,10						100,00%	breast	mammography				
			40,10						100,00%	breast	breast examination				
			>50						0,00%	prostate	PSA				
			>50						0,00%	prostate	digital rectal exam				
			>50						54,00%	colorectal	fecal occult blood				
			>50						54,00%	colorectal	flexible sigmoidoscopy				
Yee, 2011 (46)	ICD-9	3	57,2(50-65)	Anxiety, depressed mood, dissociative symptoms, eating disorders, impulse control disorders, manic symptoms, personality disorders, psychosis, somatoform disorders, and substance use disorders.	321	250	571	USA	100,00%	cervical	pap smear	Y	age, insurance, service connection, and primary care and women's clinic visits.	Y	Y
										colorectal	Fecal occult blood, flexible sigmoidoscopy, colonscopy				
										breast	mammography				

Yen, 2014 (47)	clinical records	2	50-69	delusional disorders, affective disorders, schizophrenia, childhood-onset mental disorder, senile and presenile mental disorders, other organic and nonorganic mental disorders	13089	4154	17 243	Taiwan	100%	breast	mammography	N		Y	Y
46studies (47 publications)	20 DSM/ICD 13 scale 10 clinical records 3 mixed	7 1 year, 11 2 years, 6 3 years, 9 4 years and more, 6 mixed, 6 lifetime, 1 NA	Range 18-79	14 depression, 6 schizophrenia, 14 mixed with specific diagnoses, 12 mixed without specific diagnosis	501 559	4 216 280	4 717 839	25 USA, 3 UK, 1 Taiwan, 1 Hong Kong, 5 Canada, 1 EU, 2 Denmark,1 Sweden, 2 Israel, 1Japan, 3 Australia, 1 USA/Canada	35 Only women, 2 only men 9 mixed	12 breast only, 6 cervical only, 2 prostate only, 26 mixed	11 Mammography, 1 breast examination, 6 pap smear, 2 PSA, 25 mixed, 1 NA	31 Adjusted, 15 non adjusted		37 with association measure, 9 without association measure	34 with prevalence measure, 12 without prevalence measure

Supplementary table 2. Quality of included studies according to Newcastle-Ottawa Scale.

Study	Selection				Comparability	Outcome			Total
	Representativeness of the exposed cohort	Selection of the non exposed cohort	Ascertainment of exposure	Demonstration that outcome of interest was not present at start of study	Comparability of cohorts on the basis of the design or analysis	Assessment of outcome	Was follow-up long enough for outcomes to occur	Adequacy of follow up of cohorts	
Abrams, 2012 (1)	*	*	*	-	**	*	*	-	7
Aggarwal, 2008 (2)	*	*	*	*	**	*	*	*	9
Blackwell, 2008 (3)	*	*	-	*	**	*	*	-	7
Carney, 2006 (4)	*	*	*	*	**	*	*	*	9
Chochinov, 2009 (5)	*	*	*	*	**	*	*	-	8
Domino, 2014 (6)	*	*	*	*	*	*	*	-	7
Druss, 2002 (7)	*	*	*	-	*	*	*	-	6
Druss, 2008 (8)	*	*	*	-	*	*	*	-	6
Eriksson, 2019(9)	*	*	*	*	*	*	*	*	8
Folsom, 2002(10)	*	-	*	*	-	*	*	-	5

Study	Selection				Comparability	Outcome			Total
	Representativeness of the exposed cohort	Selection of the non exposed cohort	Ascertainment of exposure	Demonstration that outcome of interest was not present at start of study	Comparability of cohorts on the basis of the design or analysis	Assessment of outcome	Was follow-up long enough for outcomes to occur	Adequacy of follow up of cohorts	
Fujiwara AND Inagaki, 2017, 2018 (11, 12)	*	-	*	-	-	*	-	-	3
Gal,2014 (13)	*	*	*	-	*	*	*	*	7
Green, 2000 (14)	*	-	-	*	**	*	-	*	6
Harder, 2018 (15)	*	*	*	*	**	*	*	-	8
Holden, 2015 (16)	*	-	-	*	-	*	*	-	4
Iezzoni, 2001 (17)	*	-	*	*	*	*	*	*	7
Jensen, 2016 (18)	*	*	*	*	**	*	*	*	9
Kaida, 2008 (19)	*	-	*	-	**	*	-	-	5
Katz,2018 (20)	*	*	*	*	**	*	*	*	9
Kempe, 2013 (21)	*	*	*	*	**	*	*	*	9
Koroukian, 2012 (22)	*	*	*	*	**	*	*	*	9
Kotwal, 2012(23)	*	-	-	*	**	-	*	-	5

Study	Selection				Comparability	Outcome			Total
	Representativeness of the exposed cohort	Selection of the non exposed cohort	Ascertainment of exposure	Demonstration that outcome of interest was not present at start of study	Comparability of cohorts on the basis of the design or analysis	Assessment of outcome	Was follow-up long enough for outcomes to occur	Adequacy of follow up of cohorts	
Lasser, 2003 (24)	*	-	*	*	-	*	*	*	6
Lindamer, 2003 (25)	-	-	*	*	-	*	*	*	5
Lindamer, 2006(26)	-	-	*	*	-	*	*	*	5
Long, 1998 (27)	*	-	*	*	-	*	-	*	4
Ludman, 2010 (28)	*	*	-	*	**	*	-	*	7
Martens, 2009 (29)	*	*	*	*	**	*	*	-	8
Masterson, 2010 (30)	*	-	-	*	**	*	-	*	6
Mo, 2014 (31)	*	-	*	*	-	*	-	*	5
Olesen, 2012 (32)	*	-	*	*	*	*	*	*	7
Owen, 2002 (33)	*	-	*	*	-	*	*	*	6
Patten, 2009 (34)	*	*	*	*	**	*	*	-	8
Peytremann-Bridevaux, 2008 (35)	*	*	*	*	**	*	*	-	8
Pirraglia, 2004 (36)	*	*	-	*	**	-	*	*	7

Study	Selection				Comparability	Outcome			Total
	Representativeness of the exposed cohort	Selection of the non exposed cohort	Ascertainment of exposure	Demonstration that outcome of interest was not present at start of study	Comparability of cohorts on the basis of the design or analysis	Assessment of outcome	Was follow-up long enough for outcomes to occur	Adequacy of follow up of cohorts	
Salsberry, 2005 (37)	*	-	*	*	-	*	*	*	6
Stecker, 2007 (38)	*	*	*	-	-	*	*	*	6
Thomas, 2018 (39)	*	-	*	*	-	*	*	*	6
Tuesley, 2018 (40)	*	*	*	*	**	*	*	*	9
Vigod, 2011(41)	*	*	*	*	**	*	*	*	9
Werneke, 2006 (42)	*	*	*	*	**	*	*	-	8
Weitlauf, 2013 (43)	*	*	*	*	**	*	-	-	7
Woodhead, 2016 (44)	*	*	*	*	**	*	*	-	8
Xiong, 2008 (45)	*	-	*	-	-	-	*	*	4
Yee, 2011 (46)	*	*	*	*	**	*	*	*	9
Yen, 2014 (47)	*	*	*	-	-	*	*	*	6

Supplementary table 3. Excluded studies after full text assessment, with reason.

Author, year	Reason for exclusion
Altman, 2016 (48)	no cancer screening
Andrykowski, 2014 (49)	no cancer screening
Bagur et al., 2015 (50)	no cancer screening
Bergerot 2016 (51)	no cancer screening
Bergerot, 2018 (52)	no cancer screening
Bhattacharya, 2016 (53)	no cancer screening
Dauchy, 2013 (54)	no cancer screening
De la Cruz, 2014 (55)	no cancer screening
De la Garza, 2015 (56)	no cancer screening
Del Fabbro, 2015 (57)	no cancer screening
Dixon, 2017 (58)	no cancer screening
El-Zorkany, 2016 (59)	no cancer screening
Esser, 2018 (60)	no cancer screening
Fatiregun, 2016 (61)	no cancer screening
Goel, 2003 (62)	no cancer screening
Grassi, 2018 (63)	no cancer screening
Hahn, 2017 (64)	no cancer screening
Hallet, 2018 (65)	no cancer screening
Hartung, 2017 (66)	no cancer screening
Hirata, 2016 (67)	no cancer screening
Husson, 2015 (68)	no cancer screening
Ito, 2013 (69)	no cancer screening
Jones, 2014 (70)	no cancer screening
Kang, 2014 (71)	no cancer screening
Kim, 2019 (72)	No cancer screening
Kimmel, (73)	no cancer screening
Kisely, 2016(74)	no cancer screening
Klein, 2017 (75)	no cancer screening
Ko, 2018 (76)	no cancer screening
Konstantakopoulos, 2013 (77)	no cancer screening
Lemogne, 2012 (78)	no cancer screening
Li, 2016 (79)	no cancer screening
Lotfi-Jam, 2013 (80)	no cancer screening
Ma, 2013 (81)	no cancer screening
Malalur, 2016 (82)	no cancer screening
Maske, 2016 (83)	no cancer screening
Meiser, 2016 (84)	no cancer screening
Mertz 2017 (85)	no cancer screening
Meyer, 2015 (86)	no cancer screening
Millman, 2018 (87)	no cancer screening
Osório, 2015 (88)	no cancer screening
Pan, 2013 (89)	no cancer screening
Panagiotou, 2014 (90)	no cancer screening
Park, 2017 (91)	no cancer screening

Author, year	Reason for exclusion
Parrino, 2017 (92)	no cancer screening
Randhawa, 2017 (93)	no cancer screening
Recklitis, 2017 (94)	no cancer screening
Rhondali, 2014 (95)	no cancer screening
Rhondali, 2015 (96)	no cancer screening
Riedl, 2018 (97)	no cancer screening
Saracino, 2017 (98)	no cancer screening
Schaeffeler, 2018 (99)	no cancer screening
Schellekens, 2016 (100)	no cancer screening
Scherber, 2016 (101)	no cancer screening
Shimizu, 2012 (102)	no cancer screening
Shippee, 2017 (103)	no cancer screening
Sitaram, 2014 (104)	no cancer screening
Song, 2013 (105)	no cancer screening
Stadelmaier, 2017 (106)	no cancer screening
Trosman, 2017 (107)	no cancer screening
Tsai, 2014 (108)	no cancer screening
Underwood, 2015 (109)	no cancer screening
Valdes-Stauber, 2013 (110)	no cancer screening
Wagner, 2017 (111)	no cancer screening
Walming, 2018 (112)	no cancer screening
Watkins, 2015 (113)	no cancer screening
Xu, 2013 (114)	no cancer screening
Zhao, 2014 (115)	no cancer screening
Agay, 2017 (116)	no data available
Aggarwal, 2010 (117)	no data available
Andreassen, 2019 (118)	no data available
Baughman, 2016 (119)	no data available
Bires, 2016 (120)	no data available
Burke, 2017(121)	no data available
Caruso, 2012 (122)	no data available
Chen 2018 (123)	no data available
Fields, 2017 (124)	no data available
Gross, 2018 (125)	no data available
Halbert, 2016 (126)	no data available
Irwin, 2016 (127)	no data available
Kelly, 2014 (128)	no data available
Kronman, 2012 (129)	no data available
Lin, 2010 (130)	no data available
McLay, 2017 (131)	no data available
Montagna, 2019 (132)	no data available
Rashid, 2015 (133)	no data available
Sabia, 2016 (134)	no data available
Uemura, 2014 (135)	no data available
Kobayashi, 2018 (136)	no mental illness
Leiferman, 2006 (137)	no mental illness

Author, year	Reason for exclusion
Schwarz, 2003 (138)	no mental illness
Sullivan, 2003 (139)	no mental illness
Thorpe, 2006 (140)	no mental illness
Xiang, 2015 (141)	no mental illness
Constantinou, 2016 (142)	no valid diagnosis (self-report)
Kearns. 2018 (143)	no valid diagnosis (self-report)
Massetti, 2017 (144)	no valid diagnosis (self-report)
Rockson, 2016 (145)	no valid diagnosis (self-report)

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Country/region and Mental illness	Cancer	Publications/samples	Prevalence	Heterogeneity	Subgroup comparison between schizophrenia and mood disorders
Schizophrenia spectrum disorders	Colorectal cancer	3/3	27.4% (17.3-40.4)	79.04%	
Prostate cancer					
Any mental illness	Prostate cancer	5/11	48.2% (31.3-65.5)	99.56%	
Asia	Prostate cancer	1 /1	20.8% (16.1-26.4)	NA	<0.001
Israel	Prostate cancer	1/1	26.2% (25.3-27.1)	NA	
USA	Prostate cancer	3/9	54.9% (42-67.2)	98.24%	
Mood disorders	Prostate cancer	1/2	49.4% (35.5-63.6)	NA	<0.001
Schizophrenia spectrum disorders	Prostate cancer	1/1	26.2% (25.3-27.1)	NA	

Country/region	Publications/samples	OR (95%CI)*	p value	I²	Subgroup difference across different regions p value
Cervical cancer					
USA	3/5	1.015(0.707-1.457)	0.935	97.66%	0.089
Canada	1 / 1	0.700(0.652-0.752)	<0.001	NA	
Europe	3/4	0.562(0.351-0.899)	0.016	99.08%	
Mood disorders					
Any cancer					
Europe	5/7	0.948(0.875-1.028)	0.195	88.47%	0.012
USA*	15/33	0.850(0.752-0.962)	0.010	99.13%	
Israel	1 / 1	0.767(0.691-0.851)	<0.001	NA	
Canada*	4/7	0.761(0.510-1.136)	0.181	85.70%	
Australia	1 / 1	0.630(0.419-0.947)	0.026	NA	
Breast cancer					
Canada*	3/3	1.205(0.594-2.447)	0.605	40.22%	0.215
Europe	3/3	0.862(0.766-0.969)	0.013	27.88%	
Israel	1 / 1	0.767(0.691-0.851)	<0.001	NA	
USA*	12/17	0.733(0.618-0.869)	<0.001	98.57%	
Cervical cancer					
Europe	3/3	0.964(0.904-1.028)	0.266	81.24%	0.079
USA*	8/11	0.943(0.794-1.120)	0.505	97.81%	
Australia	1 / 1	0.630(0.419-0.947)	0.026	NA	
Canada*	4/4	0.629(0.385-1.028)	0.065	92.06%	
Colorectal cancer					
Europe	1 / 1	1.300(1.095-1.543)	0.003	NA	0.354
USA	4/4	1.157(0.970-1.381)	0.106	97.50%	

#USA and Canada have been considered separately given the difference in health-care system

* Blackwell[1] provided data from both Canada and USA

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Cancer screening	Publications/samples	OR (95%CI)*	p value	I²	Egger's test p value / Fail safe N / Effect size after trim and fill (in case of publication bias)
Any	25/49	0.851 (0.783-0.926)	<0.001	98.84%	0.639 / 4224
Breast	18/24	0.770 (0.668-0.886)	<0.001	98.09%	0.198 / 3838
Cervical	16/19	0.93 (0.856-1.011)	0.094	96.84%	0.776 / NA
Colorectal	5/5	1.181 (1.011-1.381)	0.036	96.70%	0.820 / 148
DSM or ICD diagnosis					
Any	9/15	0.966 (0.866-1.077)	0.534	96.87%	0.935 / NA
Breast	4/6	0.658 (0.475-0.911)	0.012	96.11%	0.232 / 172
Cervical	7/8	1.138 (1.000-1.294)	0.05	97.068%	0.174 / NA
Adjusted studies*					
Any	20/39	0.87 (0.816-0.928)	<0.001	95.13%	0.126 / 1240
Breast	14/20	0.799 (0.732-0.873)	<0.001	88.90%	0.521 / 817
Cervical	13/16	0.911 (0.82-1.011)	0.08	96.25%	0.802 / NA
Colorectal	2/2	1.075 (0.751-1.539)	0.694	92.48%	NA

NA, not applicable; #Any psychiatric disorders include schizophrenia spectrum disorders, mood disorders, substance abuse, adjustment disorders, somatoform disorders, eating disorders, anxiety disorders, sexual disorders, sleep disorders, post-traumatic stress disorder.* studies adjusted for age, behavioral risk, body dissatisfaction, body mass index, comorbidity, country of origin, educational level, employment status, ethnicity, health-services use, insurance status, marital status, number of inpatient episodes, region, smoking status, social deprivation, socio-economic status, type of mental disorder, urbanicity.