American Journal of
Preventive Medicine

RESEARCH ARTICLE

Type and Severity of Mental Illness and Participation in Colorectal Cancer Screening

Benedicte Kirkøen, PhD,[1,2] Paula Berstad, PhD,[1] Geir Hoff, PhD,[1,3,4] Tomm Bernklev, PhD,[4,5] Kristin R. Randel, PhD,[1] Øyvind Holme, PhD,[6,7] Thomas de Lange, PhD,[8,9,10] Kathryn A. Robb, PhD,[11] Edoardo Botteri, PhD[1,12]

Introduction: The effectiveness of colorectal cancer screening programs depends on the participation rate. This study examined the association between type and severity of mental illness and colorectal cancer screening participation.

Methods: Between 2012 and 2017, a total of 46,919 individuals were invited to sigmoidoscopy screening in Norway, and 70,019 were invited to fecal immunochemical testing. In 2022, logistic regression was used to evaluate the association between the use of antipsychotics, anxiolytics, hypnotics, and antidepressants in the year preceding the screening invitation and screening participation, adjusted for demographic and socioeconomic factors. Defined daily doses of individual drugs were used to assess dose–response relationships.

Results: Overall, 19.2% (24.8% of women, 13.4% of men) of all invitees used at least 1 psychotropic medication. Nonparticipation in the 2 arms combined was associated with the use of anxiolytics (60.7% in users vs 43.2% in nonusers; OR=1.53; 95% CI=1.45, 1.62) and antipsychotics (64.3% vs 43.8%; OR=1.41; 95% CI=1.30, 1.53) and increased with higher doses for both drugs. Hypnotics and antidepressants were only weakly associated with nonparticipation in higher doses. Participation rates were 57.3%, 52.3%, 42.9%, and 35.4% in those prescribed 0, 1, 2, and 3–4 classes of psychotropic medications, respectively. The associations between the use of psychotropic medications and nonparticipation were similar for the 2 screening tests.

Conclusions: These findings show significant disparities in colorectal cancer screening participation for individuals with mental illness, independent of the screening method. Moreover, screening participation varied depending on the type and severity of mental illness. Targeted interventions are warranted to ensure that people with mental illness are supported to access the benefits of colorectal cancer screening.

From the [1]From the Section for Colorectal Cancer Screening, Cancer Registry of Norway, Oslo, Norway; [2]Regional Center for Child and Adolescent Mental Health (RBUP), Oslo, Norway; [3]Department of Research and Development, Telemark Hospital Trust, Skien, Norway; [4]Institute of Clinical Medicine, University of Oslo Oslo, Norway; [5]Department of Research and Development, Vestfold Hospital Trust, Tønsberg, Norway; [6]Department of medicine, Sørlandet Hospital, Kristiansand, Norway; [7]Institute of Health & Society, University of Oslo, Oslo, Norway; [8]Department of Medicine, Sahlgrenska University Hospital-Mölndal, Region Västra Götaland, Sweden; [9]Department of Molecular and Clinical Medicine, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden; [10]Department of Medical Research, Bærum Hospital, Gjettum, Norway; [11]Institute of Health and Wellbeing, University of Glasgow, Glasgow, United Kingdom; and [12]and the Department of Research, Cancer Registry of Norway, Oslo, Norway

Address correspondence to: Benedicte Kirkøen, PhD, Section for Colorectal Cancer Screening, Cancer Registry of Norway, Ullernchausseen 64, 0379 Oslo, Norway. E-mail: benedictekirkoen@gmail.com.

0749-3797/$36.00
https://doi.org/10.1016/j.amepre.2022.08.011

INTRODUCTION

Colorectal cancer (CRC) is one of the most frequent causes of cancer-related deaths in high-income countries,[1] and organized screening programs for CRC are recommended by the European Union.[2] However, a high screening participation rate is essential to optimize the effectiveness of such programs.[3] Studies show that among people with mental illnesses, participation in cancer screening programs are lower,[4–7] and cancer mortality is higher.[8–10] Together, this indicates that people with a higher risk of cancer mortality may attend screening less often—a paradox long observed in health care.[11]

Some studies find an inverse association between mental illness and CRC screening participation,[7,12–16] whereas others find no association.[17,18] There may be several reasons for this inconsistency. First, different studies investigate different mental illnesses. Different mental illnesses may influence behavior differently, and the impact of mental illness may vary with disease severity.[6] Second, some studies rely on self-reports of mental illness,[7,13,17] whereas others use registry data of all invited individuals. Studies using self-reports rarely gain data on all individuals invited and may consequently rely on selected samples that might lead to biased results.[19,20] To avoid this limitation, 3 previous studies of mental illness and CRC screening participation used registry data. However, these samples consisted of veterans[12,15] or women only.[14]

Thus, there is a need to investigate whether there is an association between mental illness and CRC screening participation among all invitees in a general population. Third, different screening tests with different levels of invasiveness are available for CRC screening, and the participation rate in a screening program may vary widely, depending on the test offered.[21,22] It is possible that mental illnesses cause stronger barriers to participation in some tests than in others.

This study examines the impact of different types and doses of psychotropic medications on CRC screening participation among all invitees in a screening program in Norway. The study comprises an unselected population who were invited to participate in a randomized trial comparing 2 screening methods—once-only sigmoidoscopy and fecal immunochemical testing (FIT)—an ideal setting for comparing disparities in participation between different screening tests.[23]

METHODS

Study Sample

This observational study utilized data from a large randomized trial[23] (NCT01538550 at clinicaltrials.gov). In 2012, a total of 140,000 individuals aged 50–74 years and living in 2 geographic areas in South-East Norway (municipalities in the catchment areas of Bærum and Moss hospitals) were identified through the population registry and randomized 1:1 to be invited for screening by once-only sigmoidoscopy or biennial FIT screening. Enrolment to FIT screening ended in January 2017. Enrolment in sigmoidoscopy was slower because of limited endoscopic capacity in the screening centers and was completed in December 2018. For this study, data extraction was conducted in October 2017 before the completion of the enrolment to the sigmoidoscopy arm and included 46,919 individuals invited to sigmoidoscopy screening and 70,019 invited to the first round of FIT.

Individuals were invited by mail, and those randomized to FIT received a kit for stool sampling. Reminders were sent once in case of no response after 6 weeks. Participants in the sigmoidoscopy group provided written informed consent on participation at the screening center, whereas *return of the fecal sample* was defined as consent in the FIT group.

Measures

Data on psychotropic medication prescriptions from 4 years before the date of the screening invitation were obtained from the Norwegian Prescription Database. Mental illness was operationalized by the prescription of the following psychotropic medication records according to the WHO's Anatomical Therapeutic Chemical classification system: antipsychotics (N05A), anxiolytics (N05B), hypnotics and sedatives (N05C), and antidepressants (N06A). These medications are often prescribed for the most common mental illnesses, such as anxiety and depression. An individual was defined as a user of a particular drug class if he/she received 2 prescriptions of that drug class during the 12 months before the screening invitation. To assess potential dose–response relationships between the use of psychotropic medications and nonparticipation, the *defined daily dose* (DDD) was used, which is a theoretical unit of measurement defined as the assumed average maintenance daily dose for a drug and may be used as a measure of treatment intensity.[24]

Data on marital status, immigration status, education, employment, and household income for all invited individuals were retrieved from Statistics Norway. *Immigrant status* was defined as being born outside Norway by 2 non-Norwegian parents. Data on psychotropic medication prescriptions were merged with demographic data and information on participation in sigmoidoscopy and FIT screening (yes/no) as well as acceptance of workup colonoscopy after a positive screening test (yes/no). The merging of these data was approved by the Regional Ethical Committee and The Norwegian Data Protection Authority. The Regional Committee for Medical Research Ethics in South-East Norway approved the use of registry-based data on all individuals invited, regardless of consent. The association between sociodemographic factors, use of other drugs, and nonparticipation are published elsewhere.[25]

Statistical Analysis

Multivariable logistic regression models were used to calculate AORs and 95% CIs for nonparticipation of users compared with no use of a specific class of psychotropic medications. Separate models were used to estimate the association between categories of DDDs and nonparticipation and to estimate the association

between the number of prescribed psychotropic drug classes and nonparticipation. Age, sex, education, marital status, and occupational status, household income, immigration status, screening arm, screening center, driving time to screening center and use of antidiabetics, antiasthmatics, antithrombotics, antihypertensives, cardiac therapy, and anti-Parkinson drugs were included as covariates in all models.[25] Participation by psychotropic drug use was analyzed for participation in CRC screening in total, separately for sigmoidoscopy and first-round FIT, and for follow-up colonoscopy after a positive FIT. Acceptance of follow-up colonoscopy after a positive sigmoidoscopy screening examination was not analyzed because the number of individuals not accepting colonoscopy was too small (only 2.2% declined). The overall CRC screening participation analysis was additionally stratified by sex and age group (≤60 years and >60 years). In users, for each class of psychotropic medication, the average DDD was calculated by summing all the DDDs prescribed in the 4 years before invitation and dividing the total amount of DDDs by the total length of exposure. The length of exposure was the difference in days between the last and the first prescription dates, plus the days covered by the last prescription (e.g., number of DDDs of the last prescription). To test for the interaction between psychotropic drug use and arm, sex, or age, interaction terms were added to the multivariable models. All tests were 2-sided, and p-values <0.05 were considered statistically significant. Statistical analyses were performed using SAS software, Version 9.4 (SAS Institute Inc., Cary, NC, U.S.).

RESULTS

Table 1 shows a description of the sample. The participation rate was 52.1% in sigmoidoscopy screening, 58.5% in FIT screening, and 55.7% in the 2 arms combined (Table 1). In the 12 months preceding screening invitation, 19.2% of the invitees (24.8% of women, 13.4% of men) were prescribed at least 1 class of psychotropic medication (1 class=13.0%, 2 classes=4.5%, and 3−4 classes=1.7%). Of the invitees, 10.1% used hypnotics or sedatives, 8.5% used antidepressants, 6.3% used anxiolytics, and 2.6% used antipsychotics. Women, older individuals; individuals with lower levels of education; lower income and individuals who were retired, not married, or not cohabiting; and non-immigrants were more often prescribed psychotropic medication. Moreover, users of a particular class of medications were more likely to use the other classes of psychotropic medications.

Table 2 shows the number of invitees and participants in the 2 screening arms combined who were prescribed different psychotropic drugs. Multivariable analyses show that the use of anxiolytics was associated with the greatest odds of nonparticipation in the 2 arms combined (OR=1.53; 95% CI=1.45, 1.62) (Table 2 and Figure 1), followed by the use of antipsychotics (OR=1.41; 95% CI=1.30, 1.53). There was no association with the use of hypnotics (OR=1.03; 95% CI=0.99, 1.08) or antidepressants (OR=1.02; 95% CI=0.99, 1.07) compared with not using these medications.

There was a higher probability of nonparticipation with an increasing dose of antipsychotics and anxiolytics, as identified by the average number of DDDs used (Table 2 and Figure 1). Only medium and high doses of hypnotics (DDD≥0.5) were associated with nonparticipation. For antidepressants, only high doses (DDD≥1) were associated with nonparticipation. Notably, a low dose of hypnotics and antidepressants (DDD<0.5) were associated with increased participation. The risk of nonparticipation increased with an increasing number of psychotropic medication classes. Participation rates in the 2 arms combined were 57.3%, 52.3%, 42.9%, and 35.4% in those who were prescribed 0, 1, 2, and 3−4 classes of psychotropic medications, respectively (p for trend<0.01).

The association between the use of psychotropic medication and nonparticipation did not differ between the sigmoidoscopy and the FIT arm (Appendix Table , available online, and Appendix Figure 1, available online). The association between the use of anxiolytics, compared with no use, and nonparticipation was stronger in women than in men (p for heterogeneity=0.02). This was particularly true in the sigmoidoscopy arm, where the use of anxiolytics had a stronger association with nonparticipation for women (OR=1.71; 95% CI=1.53, 1.91) than for men (OR=1.41; 95% CI=1.21, 1.6; p for heterogeneity 0.04). The difference was not significant among FIT invitees (p for heterogeneity 0.16).

Among the individuals who participated in FIT screening, 3,300 (8.1%) participants received a positive result and were invited to follow-up colonoscopy. In total, 3,100 (94%) accepted the colonoscopy (Table 3). Users of anxiolytics or hypnotics had a higher probability of not accepting colonoscopy than individuals without this prescription. There was no association between the use of antidepressives or antipsychotics and acceptance of colonoscopy. There was an increased probability of not accepting the colonoscopy with an increasing number of prescribed psychotropic medication classes (p for trend<0.001).

DISCUSSION

To the authors' knowledge, this study is the first to investigate the association between mental illness and CRC screening participation using registry data of all invited individuals in a general population. In this population eligible for CRC screening, almost 1 in 5 invitees used psychotropic medications in the year before the invitation. The use of psychotropic medications, in particular anxiolytics and antipsychotics, was inversely

Table 1. Characteristics of the Invited Population and Association With Nonparticipation and Psychotropic Drugs

Characteristics	All invited, frequency (column %)	Participated, frequency (row %)	Antipsychotics, frequency (row %)	Anxiolytics, frequency (row %)	Hypnotics and sedatives, frequency (row %)	Antidepressants, frequency (row %)
All invited	116,938 (100.0)	65,090 (55.7)	3,004 (2.6)	7,316 (6.3)	11,783 (10.1)	9,981 (8.5)
Arm						
FIT	70,019 (59.9)	40,931 (58.5)	1,814 (2.6)	4,383 (6.3)	7,016 (10.0)	5,925 (8.5)
Sigmoidoscopy	46,919 (40.1)	24,159 (51.5)	1,190 (2.5)	2,933 (6.3)	4,767 (10.2)	4,056 (8.6)
Sex						
Females	59,299 (50.7)	34,024 (57.4)	1,729 (2.9)	4,919 (8.3)	7,977 (13.5)	6,792 (11.5)
Males	57,639 (49.3)	31,066 (53.9)	1,275 (2.2)	2,397 (4.2)	3,806 (6.6)	3,189 (5.5)
Age, years						
50–55	22,207 (19.0)	11,187 (50.4)	566 (2.5)	982 (4.4)	1,463 (6.6)	1,648 (7.4)
56–60	27,209 (23.3)	14,630 (53.8)	717 (2.6)	1,426 (5.2)	2,176 (8.0)	2,239 (8.2)
61–65	24,347 (20.8)	14,156 (58.1)	623 (2.6)	1,587 (6.5)	2,395 (9.8)	2,213 (9.1)
66–70	23,878 (20.4)	14,520 (60.8)	621 (2.6)	1,705 (7.1)	2,817 (11.8)	2,086 (8.7)
>70	19,297 (16.5)	10,597 (54.9)	477 (2.5)	1,616 (8.4)	2,932 (15.2)	1,795 (9.3)
Education						
Primary school	25,540 (22.1)	10,746 (42.1)	1,073 (4.2)	2,895 (11.3)	3,456 (13.5)	3,174 (12.4)
High school	53,503 (46.3)	30,466 (56.9)	1,233 (2.3)	3,183 (5.9)	5,427 (10.1)	4,549 (8.5)
1–4 years of university	26,105 (22.6)	16,831 (64.5)	460 (1.8)	891 (3.4)	2,225 (8.5)	1,703 (6.5)
>4 years of university	10,337 (9.0)	6,714 (65.0)	133 (1.3)	255 (2.5)	560 (5.4)	438 (4.2)
Occupation						
Employed	70,163 (60.0)	41,627 (59.3)	2,265 (4.9)	2,115 (3.0)	4,637 (6.6)	3,770 (5.4)
Retired	45,954 (39.3)	23,159 (50.4)	719 (1.0)	5,166 (11.2)	7,084 (15.4)	6,149 (13.4)
Unemployed	773 (0.7)	298 (38.6)	15 (1.9)	29 (3.8)	51 (6.6)	55 (7.1)
Household income (NOK)						
≤484,000	29,215 (25)	11,805 (40.4)	1,691 (5.8)	3,598 (12.3)	4,483 (15.3)	3,928 (13.4)
484,001–755,000	29,211 (25)	16,429 (56.2)	662 (2.3)	1,857 (6.4)	3,306 (11.3)	2,781 (9.5)
755,001–1,130,000	29,240 (25)	17,829 (61.0)	397 (1.4)	1,186 (4.1)	2,295 (7.8)	2,025 (6.9)
>1,130,000	29,204 (25)	19,020 (65.1)	246 (0.8)	665 (2.3)	1,683 (5.8)	1,238 (4.2)
Marital status						
Cohabit/married	87,304 (74.7)	52,039 (59.6)	1,451 (1.7)	4,256 (4.9)	7,576 (8.7)	6,518 (7.5)
Single/widow	29,593 (25.3)	13,043 (44.1)	1,552 (5.2)	3,060 (10.3)	4,207 (14.2)	3,462 (11.7)
Immigration background						
Norwegian	106,695 (91.2)	60,924 (57.1)	2,759 (2.6)	6,944 (6.5)	11,121 (10.4)	9,174 (8.6)
Immigrant	10,242 (8.8)	4,165 (40.7)	245 (2.4)	372 (3.6)	662 (6.5)	807 (7.9)
Antipsychotics						
No	113,934 (97.4)	64,017 (56.2)	–	6,305 (5.5)	10,744 (9.4)	8,621 (7.6)
Yes	3,004 (2.6)	1,073 (35.7)	–	1,011 (33.7)	1,039 (34.6)	1,360 (45.3)
Anxiolytics						
No	109,622 (93.7)	62,215 (56.8)	1,993 (1.8)	–	8,761 (8.0)	7,224 (6.6)
Yes	7,316 (6.3)	2,875 (39.3)	1,011 (13.8)	–	3,022 (41.3)	2,757 (37.7)
Hypnotics and sedatives						
No	105,155 (89.9)	59,140 (56.2)	1,965 (1.9)	4,294 (4.1)	–	6,848 (6.5)
Yes	11,783 (10.1)	5,950 (50.5)	1,039 (8.8)	3,022 (25.6)	–	3,133 (26.6)
Antidepressants						
No	106,957 (91.5)	60,290 (56.4)	1,644 (1.5)	4,559 (4.3)	8,650 (8.1)	–
Yes	9,981 (8.5)	4,800 (48.1)	1,360 (13.6)	2,757 (27.6)	3,133 (31.4)	–

Note: Row percentages refer to all invited individuals.
FIT, fecal immunochemical testing; NOK, Norwegian Kroner.

Table 2. ORs for Nonparticipation in Colorectal Cancer Screening From Multivariable Logistic Regression Models

Characteristics	Invited, frequency (column %)	Participated, frequency (row %)	OR (95% CI)	*p*-value[a]
Antipsychotics				
No	113,934 (97.4)	64,017 (56.2)	Ref	**<0.01**
Yes	3,004 (2.6)	1,073 (35.7)	1.41 (1.30, 1.53)	
<0.5 DDD	1,804 (1.5)	733 (40.6)	1.17 (1.05, 1.29)	**<0.01**
≥0.5 and <1 DDD	533 (0.5)	177 (33.2)	1.47 (1.21, 1.78)	
≥1 DDD	667 (0.6)	163 (24.4)	1.96 (1.62, 2.36)	
Anxiolytics				
No	109,622 (93.7)	62,215 (56.8)	ref	**<0.01**
Yes	7,316 (6.3)	2,875 (39.3)	1.53 (1.45, 1.62)	
<0.5 DDD	4,848 (4.1)	2,108 (43.5)	1.38 (1.29, 1.47)	**<0.01**
≥0.5 and <1 DDD	1,445 (1.2)	494 (34.2)	1.61 (1.43, 1.81)	
≥1 DDD	1,023 (0.9)	273 (26.7)	2.16 (1.86, 2.50)	
Hypnotics and sedatives				
No	105,155 (89.9)	59,140 (56.2)	ref	0.17
Yes	11,783 (10.1)	5,950 (50.5)	1.03 (0.99, 1.08)	
<0.5 DDD	4,770 (4.1)	2,780 (58.3)	0.87 (0.82, 0.93)	**<0.01**
≥0.5 and <1 DDD	3,870 (3.3)	1,913 (49.4)	1.10 (1.02, 1.18)	
≥1 DDD	3,143 (2.7)	1,257 (40)	1.28 (1.18, 1.39)	
Antidepressants				
No	106,957 (91.5)	60,290 (56.4)	ref	0.36
Yes	9,981 (8.5)	4,800 (48.1)	1.02 (0.99, 1.07)	
<0.5 DDD	2,138 (1.8)	1,172 (54.8)	0.87 (0.79, 0.95)	0.09
≥0.5 and <1 DDD	2,997 (2.6)	1,509 (50.4)	0.99 (0.91, 1.07)	
≥1 DDD	4,842 (4.1)	2,117 (43.7)	1.09 (1.02, 1.17)	
Number of psychotropic drug classes				
0	94,477 (80.8)	54,171 (57.3)	ref	**<0.01**
1	15,207 (13.0)	7,959 (52.3)	1.08 (1.04, 1.12)	
2	5,215 (4.5)	2,239 (42.9)	1.42 (1.34, 1.51)	
≥3	2,039 (1.7)	721 (35.4)	1.84 (1.67, 2.03)	

Note: Boldface indicates statistical significance ($p<0.05$).
Participation rates are shown for sigmoidoscopy and FIT combined. *Row percentages* refer to invited individuals. No use of a particular class of drugs is set as the ref category for the yes/no and DDD analyses. ORs were adjusted for sex; age; screening arm; occupation; education; household income; marital status; immigration income; screening center; driving time; and the use of antidiabetics, antiasthmatics, antithrombotics, antihypertensives, cardiac therapy, anti-Parkinson drugs.
a*p*-Value for trend.
DDD, defined daily dose; FIT, fecal immunochemical testing.

associated with screening participation, independent of the screening method. Interestingly, increasing dose of anxiolytics and antipsychotics was associated with decreased participation. Only higher doses of hypnotics and antidepressants showed weak but significant associations with nonparticipation. With increasing number of classes of psychotropic medications used, the odds of participation in CRC screening decreased. The study is the first to show a dose–response association between psychotropic drugs and nonparticipation in CRC screening. Together, these findings show significant disparities in CRC screening participation for people with mental illness, differing according to type and dose of psychotropic medication.

This study shows that the association between mental illness and CRC screening participation depends on the type of psychotropic drugs investigated. The use of anxiolytics was associated with the lowest odds of participation, consistent with the findings of previous studies on anxiety and nonparticipation in CRC screening.[12,15] Anxious individuals have a greater fear of cancer,[26] have a higher perceived risk of developing CRC,[27] and tend to underestimate personal resources for coping with threats.[28] Therefore, screening for cancer may be

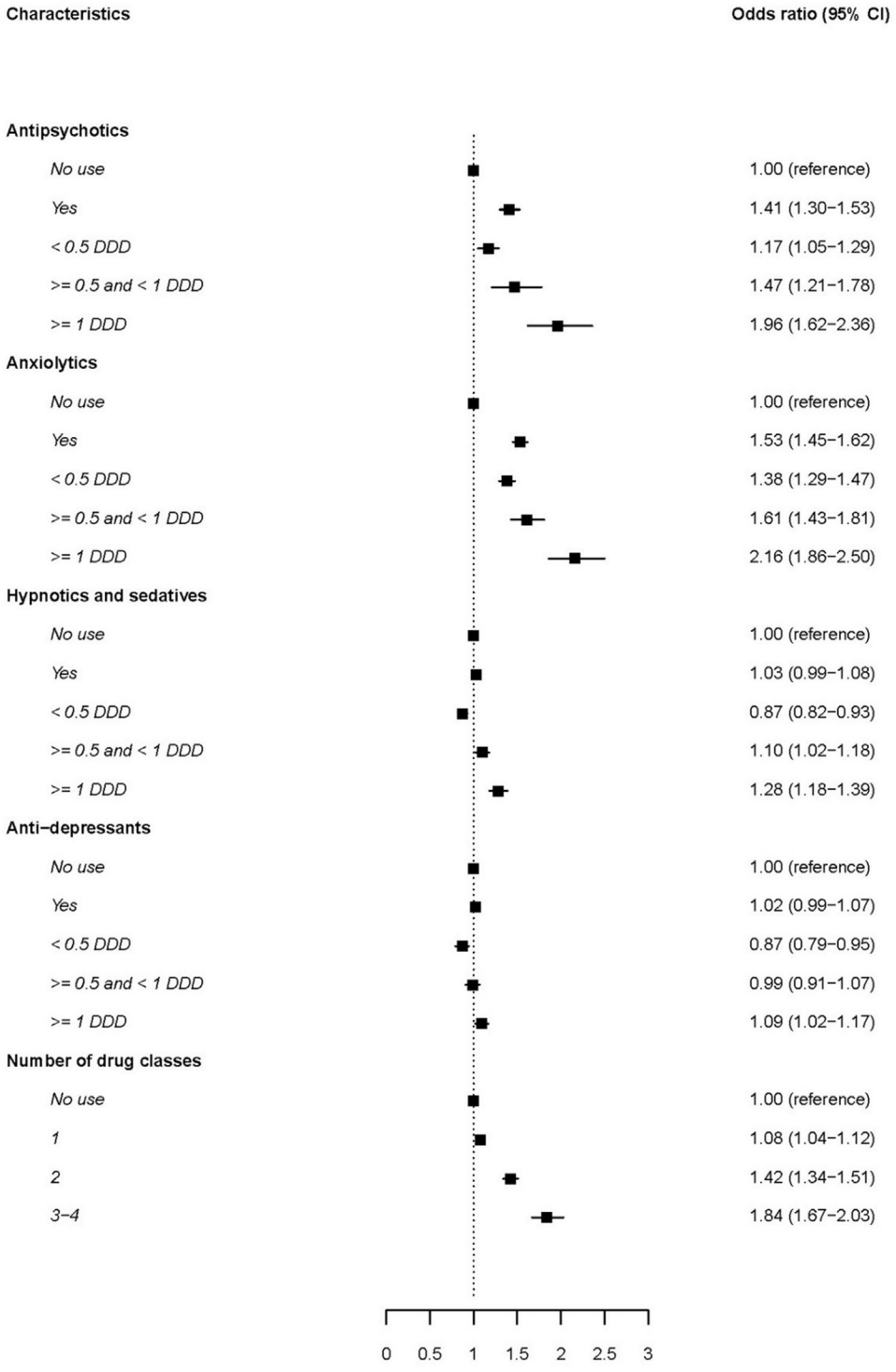

Figure 1. The association between the use of antipsychotics, anxiolytics, hypnotics and sedatives, and antidepressants and the number of psychotropic drug classes used and nonparticipation in colorectal cancer screening.

perceived as especially anxiety provoking, and anxiety may trigger avoidance of anxiety-provoking situations.

In congruence with the literature,[12,15] nonparticipation was associated with using antipsychotics. Individuals who use antipsychotics are likely to have symptoms that are limiting and severe and are associated with severe barriers to screening participation, such as hospitalization.[5]

Table 3. ORs for Nonacceptance of Colonoscopy After a Positive FIT

Characteristics	Invited to colonoscopy, frequency (col %)	Accepted (row %)	OR (95% CI)	*p*-value[a]
Antipsychotics				
No	3,210 (97.3)	3,019 (94.0)	ref	0.92
Yes	90 (2.7)	81 (90.0)	0.96 (0.44, 2.10)	
<0.5 DDD	53 (1.6)	47 (88.7)	0.99 (0.38, 2.59)	0.93
≥0.5 and <1 DDD	15 (0.5)	15 (100.0)	–	
≥1 DDD	22 (0.7)	19 (86.4)	1.96 (0.52, 7.41)	
Anxiolytics				
No	3,067 (92.9)	2,902 (94.6)	ref	**<0.01**
Yes	233 (7.1)	198 (85.0)	2.05 (1.30, 3.24)	
<0.5 DDD	151 (4.6)	132 (87.4)	1.84 (1.05, 3.22)	**<0.01**
≥0.5 and <1 DDD	47 (1.4)	39 (83.0)	1.81 (0.73, 4.48)	
≥1 DDD	35 (1.1)	27 (77.1)	3.35 (1.33, 8.43)	
Hypnotics and sedatives				
No	2,933 (88.9)	2,778 (94.7)	ref	**0.02**
Yes	367 (11.1)	322 (87.7)	1.64 (1.09, 2.44)	
<0.5 DDD	139 (4.2)	127 (91.4)	1.22 (0.63, 2.36)	**<0.01**
≥0.5 and <1 DDD	130 (3.9)	114 (87.7)	1.62 (0.88, 2.98)	
≥1 DDD	98 (3.0)	81 (82.7)	2.21 (1.18, 4.15)	
Antidepressants				
No	2,979 (90.3)	2,805 (94.2)	ref	0.47
Yes	321 (9.7)	295 (91.9)	0.84 (0.52, 1.36)	
<0.5 DDD	64 (1.9)	59 (92.2)	0.83 (0.31, 2.18)	0.15
≥0.5 and <1 DDD	96 (2.9)	85 (88.5)	1.35 (0.66, 2.76)	
≥1 DDD	159 (4.8)	150 (94.3)	0.50 (0.23, 1.06)	
Number of psychotropic drug classes				
0	2,589 (78.5)	2,464 (95.2)	ref	**<0.01**
1	482 (14.6)	436 (90.5)	1.65 (1.13, 2.41)	
2	165 (5.0)	146 (88.5)	1.77 (1.02, 3.09)	
≥3	64 (1.9)	54 (84.4)	2.47 (1.16, 5.22)	

Note: Boldface indicates statistical significance ($p<0.05$).
No use of a particular class of drugs is set as the ref category for the yes/no and DDD analyses. ORs were adjusted for sex; age; screening arm; occupation; education; household income; marital status; immigration income; screening center; driving time; and the use of antidiabetics, antiasthmatics, antithrombotics, antihypertensives, cardiac therapy, and anti-Parkinson drugs.
a*p*-value for trend.
col, column; DDD, defined daily dose.

The use of antidepressants compared with no use was not associated with nonparticipation, but higher doses of antidepressants were associated with nonparticipation. This is consistent with the findings of previous studies showing no association between nonparticipation and lower, self-reported depression[17] but associations with more severe, diagnosed depression or prescriptions of antidepressants.[12,14,15] A recent study of breast cancer screening[5] found that the use of antidepressants was associated with the smallest reduction in screening participation compared to the use of other psychotropic drugs. This might be owing to good treatment effects that lessened inequalities.

This study found that the higher the doses of anxiolytics and antipsychotics or a higher number of classes of psychotropic medication an invitee used, the lower the odds of screening participation. To the best of the authors' knowledge, this study is the first to show a dose–response association between psychotropic drugs and nonparticipation in CRC screening. These results are novel for CRC and are consistent with research on breast and cervical cancer screening.[6]

A recent review showed no association between mental illness and nonparticipation in CRC screening.[18] In that review, CRC screening had a low participation rate (37.1%), and the authors argue that disparities for the mentally ill may not be evident in populations with low screening coverage because of a ceiling effect. This paper shows that in a population-based screening program with a participation rate of 55.7%, there was an

association between psychotropic medications prescribed and nonparticipation.

The association between the use of anxiolytics and nonparticipation was stronger in women than in men, particularly in the sigmoidoscopy arm. Because women use anxiolytics more frequently than men, this finding is important. Sigmoidoscopy is an invasive test that is more likely to be perceived as threatening than FIT. Although anxiety may trigger avoidance behavior in individuals with anxiety in general, there are gender differences in coping behavior. Men are socialized to approach threatening situations and use problem-solving strategies, whereas women are socialized to avoid threatening situations.[29] Consequently, it is possible that anxiety may cause more avoidance behavior in women than in men.

There may also be factors outside of the individual that explain the observed associations. It has been argued that general practitioners may prioritize other healthcare issues than cancer screening with individuals with mental disorders. However, the general practitioner is not involved in invitations to CRC screening in Norway. It is still possible that experiences with stigma in the healthcare system influence screening participation for individuals with mental illness.

Different CRC screening tests are differently associated with anxiety,[30] pain, and willingness to repeat screening.[31] However, this study showed that mental illness was not differentially associated with nonparticipation in sigmoidoscopy or FIT screening, providing important knowledge for the design of future screening programs. Among people with mental illness, cancer is detected later,[32] and a greater proportion of the cancers have metastases at diagnosis.[9] This paper showing that mental illness is associated with reduced CRC screening participation can provide a partial explanation for this observation.

The results call for efforts to provide equity in screening opportunities. Providing information on potential discomfort of medical procedures and how to reduce it can decrease state anxiety.[33] Leaflets combined with video information before examination have been found to reduce anxiety levels in women undergoing colposcopy.[34] Moreover, trust and social support may be especially important for individuals with mental illness. For instance, studies indicate that patient navigation programs can increase screening participation among people with mental illness.[35,36] Moreover, increased healthcare visits have been associated with increased CRC screening participation among people with mental illness,[12] which may illustrate the importance of provider recommendation in populations with mental illness. Future research could investigate whether such efforts may reduce state anxiety and thereby decrease avoidance behavior.

Limitations

An important strength of this study is the investigation of different types and severity of mental illness. The mentally ill population is more heterogenic than many studies imply, and some illnesses may be associated with nonparticipation in CRC screening, whereas others may not. Whereas previous studies have focused on the presence or absence of mental illness in general, this study investigated different mental illnesses and their severity.

Second, previous research has relied on self-reports of mental illness,[7,13,17] causing potential selection bias. Other studies have handled this using registry data, with information on all invitees. However, the samples in those studies consist of veterans[12,15] or women only.[14] Thus, this study is the first to investigate the association between mental illness and CRC screening participation among all invitees in a general population, not limited by military attendance or sex, which allows for the generalizability of the findings.

Third, whereas most previous studies have investigated mental illness and nonparticipation in 1 type of screening test, this study is the first to show this association among individuals randomized to 2 different screening tests. This comparison has high validity because it is derived from a randomized trial.

This study did not measure diagnoses of mental illness, which is a limitation of this study. The identification of individuals on the basis of prescription of psychotropic medications may select for those with more severe mental illnesses. Furthermore, those who are undiagnosed or untreated and those undergoing standalone psychological therapies are not identified as mentally ill. Moreover, there is a large number of people who do not seek help for mental illnesses. Although severe mental illnesses (e.g., illnesses that require antipsychotics) are more often treated, there is more uncertainty regarding the findings for drugs often used to treat less severe illnesses. It is also important to note that medication data were based on prescriptions and not on compliance with medication regimens, which have been known to vary.[37] However, *a user* was defined as the recipient of 2 or more prescriptions preceding the invitation, which the authors believe limits this problem. One question that arises is whether there is a general association between drug use for health problems and nonparticipation, not restricted to mental health problems. There was an association between prescriptions for antidiabetics and nonparticipation. However, there was no association with other drugs (Appendix Table 2,

available online). Finally, because the study is observational, the possibility of confounding cannot be excluded.

CONCLUSIONS

These findings show significant disparities in CRC screening participation for individuals with mental illness, in particular those using anxiolytics or antipsychotics, independent of the screening method. Importantly, the disparities differ according to the type and dose of psychotropic medication. Lower participation was observed in those using anxiolytics and antipsychotics, and increasing doses of anxiolytics and antipsychotics were associated with decreased participation. Only higher doses of hypnotics and antidepressants showed weak but significant associations with nonparticipation. With increasing number of classes of psychotropic medications used, the odds of participation in CRC screening decreased. Targeted interventions are warranted to facilitate CRC screening participation in these patient groups.

CREDIT AUTHOR STATEMENT

Benedicte Kirkøen: Conceptualization, Investigation, Methodology, Writing – original draft; Paula Berstad: Conceptualization, Investigation, Methodology, Writing – original draft; Geir Hoff: Conceptualization, Investigation, Methodology, Writing – review & editing; Tomm Bernklev: Conceptualization, Investigation, Methodology, Writing – review & editing; Kristin R. Randel: Investigation, Writing – review & editing; Øyvind Holme: Conceptualization, Investigation, Methodology, Writing – review & editing; Thomas de Lange: Conceptualization, Investigation, Methodology, Writing – review & editing; Kathryn A. Robb: Writing – review & editing; Edoardo Botteri: Conceptualization, Formal analysis, Investigation, Methodology, Visualization, Writing – original draft.

ACKNOWLEDGMENTS

All authors made critical revisions to the article for important intellectual content and gave final approval of the version to be submitted. All the work reported in the study has been performed by the authors unless clearly specified in the text.

The trial study is funded by the Norwegian Parliament (Norwegian national budget from 2011) in preparation for a future nationwide colorectal cancer screening program. The bowel preparation used for colonoscopy was provided free of charge by Ferring Pharmaceuticals. The registry data extraction was funded by the fund of Cancer Registry of Norway.

No financial disclosures were reported by the authors of this paper.

SUPPLEMENTAL MATERIAL

Supplemental materials associated with this article can be found in the online version at https://doi.org/10.1016/j.amepre.2022.08.011.

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