Cardiovascular risk screening of patients with serious mental illness or using antipsychotics in family practice.

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Abstract

Background

Patients with a serious mental illness (SMI) and those using antipsychotics (AP) have an elevated risk for cardiovascular disease (CVD). In the Netherlands, the mental healthcare for these patients is increasingly provided by family practitioners (FPs), following a shift from secondary to primary care. It is therefore essential to better understand the characteristics of this patient group and the (somatic) care provided by their FPs. The aim of this study was to examine the rate of cardiovascular risk (CVR) screening in patients with SMI or those using APs in family practice.

Methods

We performed a retrospective cohort study of 151,238 patients registered with 24 family practices in the Netherlands. From electronic medical records, we extracted data concerning diagnoses, the measurement of CVR factors, medication, and the frequency of visits over a two-year year period. The primary outcome was the proportion of patients who were screened for CVR factors. We compared three groups: patients with SMI or using AP without diabetes or CVD (SMI/AP only), patients with SMI or using AP and diabetes mellitus (SMI/AP+DM), and patients with SMI or using AP and a history of CVD (SMI/AP+CVD). We explored the factors associated with adequate screening using a multilevel logistic regression.

Results

We identified 1705 patients with SMI or using AP, 834 of whom had a SMI diagnosis and 1150 of whom used AP. CVR was adequately screened in 8.5% of the SMI/AP-only group (117 of 1383 patients). Screening was much more commonly performed in the SMI/AP+DM (n=206, 68.4% adequate) and SMI/AP+CVD (n=116, 26.7% adequate) groups. (ORs for moderate and adequate screening 21.8 (95%CI, 15.4-30.8) and 4.3 (95%CI, 2.8-6.6) respectively). A high frequency of FP visits, age, the use of AP, and a diagnosis of chronic obstructive pulmonary disease were associated with a higher screening rate. In addition, we examined the differences between patients with SMI and patients using AP in the absence of a SMI.

Conclusions

CVR screening in patients with SMI or using AP is often inadequate or lacking in Dutch family practices. Acceptable screening rates were found only among SMI/AP patients with diabetes mellitus as a comorbidity.

Background

Both a diagnosis of serious mental illness (SMI) and the use of antipsychotics (AP) are associated with an elevated cardiovascular risk (CVR)(1–16). People with SMI, including schizophrenia, bipolar disorder, and other psychotic disorders (8), have an 8–20-year reduction in life expectancy compared with the

general population (2, 5), which is mainly caused by cardiovascular disease (CVD) (3, 4, 15). The etiology of the increased risk for CVD in patients with SMI is multifactorial, involving high levels of smoking and other substance misuse, poor dietary intake, inadequate amounts of exercise, less access to medical care, obesity, diabetes, and the adverse effects of AP (6, 7, 9–17). The use of AP increases the risk of CVD via metabolic pathways involving weight gain, glucose intolerance, and dyslipidemia, and can cause cardiac toxicity (3, 18–20). AP are typically prescribed for SMI, but a growing group receives AP prescriptions for unlicensed uses (off-label prescriptions), including the treatment of mood disorders, anxiety disorders, insomnia, and agitation (21).

Health guidelines (22–25) and medicine agencies (26, 27) recommend annual screening for CVR factors in patients with SMI and all patients using AP. Unfortunately, this assessment of, and treatment for, CVR is often inadequate or lacking (7, 28–35) due to both patient- (7, 17, 33–35) and physician-related (7, 17) factors and a lack of collaboration between family physicians (FPs) and psychiatrists (4, 33, 36). In addition, some psychiatrists lack the knowledge and competence required to diagnose and treat CVR factors (17, 33).

In the UK, a SMI register has been established(37); however, the monitoring of CVR in patients receiving AP in the absence of SMI remains unaccounted for. The mental healthcare for patients with SMI or those receiving AP (SMI/AP) in the Netherlands, as in the UK, is increasingly provided by FPs following a shift from secondary to primary care (38–40). This creates an opportunity for the uptake of CVR screening in the customary chronic care programs for these patients, with a financial incentive for the FP. FPs play an important role in CVR screening because their daily tasks include the prevention of CVD in high-risk patients. The care of patients with SMI or those using AP by FPs also introduces the question of who is responsible for CVR screening in relation to AP medication use: The initiator (usually the psychiatrist) or the doctor who prescribes the continuation (usually the FP). It is therefore essential to better understand the (somatic) care provided by FPs for these patients.

The primary aim of our study is to examine the CVR screening practice in patients with SMI or those using AP in family practice, and to identify the patient characteristics associated with the rate of screening. We will describe a) the screening rate in patients with SMI or those using AP without additional comorbidities, and compare this to b) the screening rate in a group of patients with SMI or those using AP who have an additional reason for CVR screening, such as diabetes and/or a known cardiovascular morbidity. The latter shows what can be achieved in primary care in this patient category, despite the above-mentioned barriers, while the former shows what is typically achieved for patients with SMI or those using AP alone.

Methods

Study design

This study is a retrospective cohort study of patients with SMI or those using AP in Dutch family practice.

Study population and procedure

We followed the 'STrengthening the Reporting of OBservational studies in Epidemiology' (STROBE) guidelines for reporting observational studies (41). Our data were derived from a de-identified database, the Radboud university medical center (Radboudumc) Technology Center Health Data. This database contains electronic medical records (EMRs) from Dutch family practices, with information on patient demographics, symptoms and diagnoses, laboratory test results, drug prescriptions, and number of visits to the practice, along with characteristics of the family practices themselves, such as the number of registered patients and the geographical location. Drug prescriptions are coded according to the WHO Anatomical Therapeutic Chemical (ATC) Classification system (42). Diagnoses and symptoms are coded according to the International Classification of Primary Care (ICPC) (43). The database contains reliable data because nearly everyone in the Netherlands is registered in a family practice, and because FPs classify each visit using the ICPC system. The FP operates as a "gatekeeper" for secondary care, with medical specialists subsequently informing the FP about the diagnosis and treatment of referred patients (44). The electronic records for outpatient psychiatric visits in the Netherlands are separate from the FP system; therefore, visits to a psychiatrist and data concerning CVR collected there were not included in this study.

We collected data for patients who require a yearly assessment of their CVR based on their psychiatric disorder or their use of AP medication or lithium(22). A total of 151,238 people were included in this study, all of whom were registered at one of the 24 involved family practices, which were selected by region and for the availability of data in the FP database between January 2013 and December 2014. We selected patients with (I) schizophrenia, affective psychosis, bipolar disorder, or psychosis not otherwise specified (NOS) with a diagnosis date prior to January 1st, 2013; or (II) at least two prescriptions of AP or (III) a prescription of lithium prescribed for the first time before July 1st, 2013. This date was chosen because we only had access to the prescription records in this defined study period. Patients were excluded if they were (I) younger than 18 years old; (II) diagnosed with dementia; (III) diagnosed with delirium without the presence of a psychotic disorder; (IV) not registered in the selected family practice for more than 12 months in our study period, since FPs usually assess a patient's CVR profile once a year (45); or (V) diagnosed with rheumatoid arthritis, since CVR assessment in this patient category was introduced just before our study period and could possibly have confounded our results (45, 46).

Data collection

Patients with SMI or those using AP were divided into three groups: (I) patients without another indication for a yearly assessment of CVR, according to the current FP guidelines (45) (SMI/AP-only group); (II) patients with SMI or those using AP and diabetes mellitus (DM), and thus an extra indication for CVR assessment (SMI/AP + DM group); or (III) patients with SMI or those using AP and a history of a CVD (i.e., stroke, angina pectoris, acute myocardial infarction, transient ischemic attack, intermittent claudication, and aortic aneurysm), and therefore an extra indication for CVR assessment (SMI/AP + CVD group).

Patients with both DM and CVD at the baseline were included in the SMI/AP + DM group because patients with DM are routinely part of a chronic care program that pro-actively invites patients for monitoring.

Our primary outcome measure was the screening rate of CVR, defined as the proportion of patients in each subgroup who received screening for CVR factors in the defined study period. The CVR factors selected were those recommended by the Dutch FP guidelines; body mass index (BMI), blood pressure, estimated Glomerular Filtration Rate (eGFR), smoking status, fasting glucose, a lipid spectrum, use of alcohol, and a family history of CVD (45). Considering the observational nature of this study and the screening criteria described in previous studies (30, 31), we also included a broader range of assessments (Appendix A1).

Based on current Dutch FP guidelines, we divided the observed screening rate into three levels: adequate, moderate, and insufficient (45). The screening rate was considered 'adequate' when the BMI, smoking status, blood pressure, glucose, and cholesterol/HDL ratio were all recorded at least once during the observation period, since these are the assessments needed to quantify the 10-year CVR of a patient and identify the need for CVR-lowering medication. The screening rate was considered 'moderate' when the assessment included BMI, smoking status, and blood pressure, all of which can be measured without a blood test, while the screening rate was considered 'insufficient' if it did not meet these requirements. A two-year window was chosen to gain insight into the role and awareness of the FP in this matter. FPs usually invite their high-risk patients for screening once a year, so the two-year window ensured that patients who were screened at intervals just over one year because of a delay in their response would be included in the screened cohort.

Moreover, we wanted to identify factors associated with any CVR screening (adequate or moderate). The following factors were studied: age, sex, type of psychiatric disease, use of AP, use of antidepressants, CVR medication (i.e., statins, blood pressure drugs, and aspirin), chronic obstructive pulmonary disease (COPD), abuse of alcohol or drugs, any records of social issues, and the frequency of FP visits. We selected ICPC-codes concerning diseases and social problems (see Appendix A2) and obtained prescription records of antidepressants for this purpose. The ATC codes of AP, lithium, and antidepressants are listed in Appendix A3.

Statistical analyses

Descriptive analyses were used to describe the patient characteristics and provide insights into the screening rates in the three different patient groups. The hierarchical structure of the study (patients nested within practices) required us to perform multilevel analyses (random intercept model) taking into account the variability associated with each level of clustering. A multilevel logistic regression analysis was performed to test the differences in screening rates between the three groups.

In addition, for the SMI/AP-only group, we investigated the patient characteristics (Table 1) associated with an adequate or moderate screening rate. First, we included characteristics for the multivariate model that were univariately associated with screening ($p < 0.20$), after which a backward regression analysis

was performed for these characteristics. A p-value < 0.05 was considered to be statistically significant, based on two-sided tests. A further analysis was performed to determine whether the results differed between the patients who were included based on their diagnosis (SMI) and the patients who use AP without a SMI diagnosis (see Addendum 1). All analyses were performed using IBM SPSS statistics 22.0.

Table 1

Comparison of patient characteristics

	SMI/AP-only group n = 1383	SMI/AP + DM group n = 206	SMI/AP + CVD group n = 116	Total sample n = 1705
Sex, female	720 (52.1)	110 (53.4)	51 (44.0)	881 (51.7)
Mean age, years (SD)	44.9 (14.8)	58.5 (14.0)	61.8 (12.3)	47.7 (15.7)
SMI diagnosis, total	629 (45.5)	97 (47.1)	48 (41.4)	834 (48.9)
Schizophrenia	197 (14.2)	38 (18.4)	15 (12.9)	250 (14.7)
Affective psychosis/bipolar disorder	217 (15.7)	34 (16.5)	24 (20.7)	275 (16.1)
Psychosis not otherwise specified	307 (22.2)	28 (13.6)	11 (9.5)	346 (20.3)
SMI/AP				
SMI with AP	290 (21.0)	55 (26.7)	20 (17.2)	365 (21.4)
SMI without AP	399 (28.9)	42 (20.4)	28 (24.1)	469 (27.5)
AP without SMI	630 (45.6)	95 (46.1)	60 (51.7)	785 (46.0)
OLithium without AP	64 (4.6)	14 (6.8)	8 (6.9)	86 (5.1)
Medication use				
AP	920 (66.5)	150 (72.8)	80 (69.0)	1150 (67.4)
Lithium	160 (11.6)	31 (15.0)	22 (19.0)	213 (12.5)
Antidepressants	558 (40.3)	91 (44.2)	58 (50)	707 (41.5)
CVR-lowering medication	295 (21.3)	186 (90.3)	103 (88.8)	584 (34.3)
Comorbidity				
COPD	65 (4.7)	25 (12.1)	23 (19.8)	113 (6.6)
Alcohol abuse	68 (4.9)	19 (9.2)	12 (10.3)	99 (5.8)
Smoker	233 (16.8)	83 (40.3)	42 (36.2)	358 (21.0)

Values are shown as n (%) unless otherwise noted.

SMI: serious mental illness; AP: antipsychotics; DM: diabetes mellitus; CVD: cardiovascular disease; CVR: cardiovascular risk; FP: family practice; COPD: chronic obstructive pulmonary disease.

	SMI/AP-only group n = 1383	SMI/AP + DM group n = 206	SMI/AP + CVD group n = 116	Total sample n = 1705
Drug abuse	101 (7.3)	3 (1.5)	2 (1.7)	106 (6.2)
Number of FP visits/year				
0	393 (28.4)	46 (22.3)	25 (21.6)	464 (27.2)
1–5	565 (40.9)	60 (29.1)	27 (23.3)	652 (38.2)
6–10	234 (16.9)	41 (19.9)	27 (23.3)	302 (17.7)
> 10	191 (13.8)	59 (28.6)	37 (31.09)	287 (16.8)
Values are shown as n (%) unless otherwise noted.				
SMI: serious mental illness; AP: antipsychotics; DM: diabetes mellitus; CVD: cardiovascular disease; CVR: cardiovascular risk; FP: family practice; COPD: chronic obstructive pulmonary disease.				

Results

Of the 2247 patients with SMI or those using AP (prevalence in the 24 FP practices = 1.5%), 542 were excluded. Figure 1 shows the flow chart of in- and exclusion of these patients.

Table 1 shows the demographics and clinical characteristics of the patients included in this study. Of these, 14.7% patients were diagnosed with schizophrenia, 16.1% were diagnosed with an affective psychosis or bipolar disorder, and 20.3% had a diagnosis of psychosis NOS. Of all the 1150 patients using AP, 68.3% did not have any diagnoses concerning SMI in their medical records (n = 785). Quetiapine was the most commonly prescribed AP agent (20.1%). Of the included patients, 27.2% had fewer than one FP visit per year, while 16.8% had over 10 visits per year. The subgroup analysis (see Addendum 1) showed that patients with SMI more commonly had fewer than one visit per year, while patients using AP without SMI more frequently had over 10 visits a year.

CVR factor assessment

Table 2 presents the screening rate of the CVR assessment for the three SMI groups. These risk factors were adequately assessed in 8.5% of the SMI/AP-only group. A logistic regression analysis resulted in odds ratios (ORs) for moderate or adequate screening in the SMI/AP + DM and SMI/AP + CVD groups when compared to the SMI/AP-only group of 21.8 (95% CI 15.4–30.8) and 4.3 (95% CI 2.8–6.6), respectively.

Table 2

Completeness of CVR screening for patients with SMI/AP and for subgroups with comorbid DM or CVD.

Indication for CVR assessment	Insufficient	Moderate^	Adequate#	Odds ratio (95% CI)*
SMI/AP-only group (n = 1383)	90.2 (1247)	1.4 (19)	8.5 (117)	Reference group
SMI/AP + DM group (n = 206)	29.6 (61)	1.9 (4)	68.4 (141)	21.8 (15.4–30.8)
SMI/AP + CVD group (n = 116)	68.1 (79)	5.2 (6)	26.7 (31)	4.3 (2.8–6.6)
Values are shown in % (n) unless otherwise noted.				
^ BMI, smoking status, and blood pressure were all recorded (CVR screening without the need of a blood sample).				
# BMI, smoking status, blood pressure, glucose, and cholesterol/HDL ratio were all recorded.				
* OR for an adequate and moderate screening rate.				
CVR: cardiovascular risk; CI: confidence interval; SMI: serious mental illness; AP: antipsychotics; DM: diabetes mellitus; CVD: cardiovascular disease.				

Factors contributing to screening rate

Multivariate multilevel logistic analysis showed that a high frequency of visits, age, AP use, and a diagnosis of COPD were positively associated with an adequate screening rate in the SMI-only group (Table 3). SMI and AP are correlated, and therefore could not be simultaneously included as part of the model. We chose to include the variable with the most significant p-level, which was AP use.

Table 3
Factors most associated with CVR screening for patients with SMI/AP who have no comorbid diagnosis of diabetes or CVD (n = 1383).

Factor	OR	95% CI
Age	1.05	1.036–1.055
AP use	1.62	1.20–2.18
COPD	2.8	1.87–4.31
Number of FP visits/year*		
>10	2.24	1.65–3.03
Cardiovascular risk screening was considered to have been performed if the assessment included at least BMI, smoking status, and blood pressure.		
All significant variables identified using a logistic regression analysis ($p < 0.05$) were included in this backwards stepwise regression procedure. *Reference is ≤ 10 visits FP/year.		
OR: odds ratio; CI: confidence interval; AP: antipsychotics; COPD: chronic obstructive pulmonary disease; FP: family practice.		

Discussion

Summary

The rate of adequate CVR screening by FPs in patients with SMI or those using AP is very low (8.5%). In patients with an additional comorbidity that requires CVR screening, this rate was considerably higher, especially in patients with type 2 diabetes (68.4%). The screening rate increased with age and the number of visits, with AP use and the presence of COPD also being associated with a higher CVR screening rate. Furthermore, it was striking that, in the majority of patients using AP, a diagnosis of SMI was not recorded in their EMR.

Strengths and limitations

The main strength of our study is the size of the study sample and the broad inclusion of patients, based on diagnoses or on prescriptions of AP, which resulted in a realistic overview of the number of psychiatric patients with an increased CVR in primary care. We therefore think the diversity of our study group is representative of primary care patients in the Netherlands, which contributes to the validity and reliability of our findings.

Several limitations should also be mentioned. First, we studied whether FPs screened patients with SMI or those using AP for their CVR; however, the retrospective design used offers limited insight into their motives. Second, we did not have access to patient records in mental health institutions, since we only used the EMRs from FPs. About half of patients with SMI receive (additional) care from such institutions

(47); consequently, it is possible that CVR was assessed in mental healthcare institutions, meaning our results underestimate the level of CVR screening received by these patients. (47)Third, it is important to keep in mind that the exclusion of patients who were listed for less than 12 months in a family practice (n = 225, 10% of all patients) could result in a potential selection bias. Patients who switch FPs regularly might be homeless, uninsured, or move frequently, and consequently might not be screened at all. Their absence in our study could have resulted in an overestimation of CVR screening. Fourth, we think the relatively small number of patients reported to abuse of alcohol (5.9%) and drugs (6.2%) is due to a lack of capturing these data in the FP EMRs. A study in the US found the prevalence of substance use to be uniformly high in individuals with SMI (marihuana 43–52% and alcohol 26–30%)(48) The expected inverse relationship between alcohol/drug abuse and adequate CVR screening could therefore neither be proven nor rejected. Lastly, the large group of AP users without a SMI diagnosis may indicate an off-label use of AP; however, some of these patients could be those who did have SMI but whose FP lacked information about the precise psychiatric disease or did not use the correct code. In addition, there are a few on-label indications for non-psychotic diseases, such as the use of Quetiapine for unipolar therapy-resistant depression. Other studies endorse the possibility of a high prevalence of off-label AP use (21, 49–51).

Comparison with existing literature

The screening rate for CVR in patients with SMI and/or those using AP has been evaluated in several studies in different countries, resulting in a wide range of screening rates (28, 30, 32, 35, 52, 53). This variation can be explained by differences in the study population and methods, providing insights into the most important factors to take into account when considering an intervention. A study among patients with newly prescribed AP use in a US Medicaid program found that 79.6% of those without DM were tested for their glucose levels (non-fasting tests included) and 41.2% were tested for their blood lipids (35). The failure to receive metabolic testing was most strongly associated with younger age, fewer chronic conditions, and the frequency of healthcare utilization, regardless of the care setting (mental healthcare or primary care) (35). Mangurian et al. found that 73% of patients with both SMI and DM were adequately tested within a two-year timeframe in California(52), which was consistent with our results (68.4%) despite our broad inclusion of patients with SMI and those taking AP without SMI(52). A Canadian study among patients from a community health center specializing in patients with barriers to the healthcare system also found adequate screening rates in over 70% of patients with SMI (n = 106 of whom 28% with DM)(53).

Previous intervention studies to improve the CVR screening rate in patients with SMI focused on financial compensation or organizational changes. A primary care study in the UK showed that, without organizational embedding, financial compensation for the task alone is not enough (32). During the period explored in this study, every primary care center in the UK received payment to provide care for patients with chronic conditions, including SMI, but only just over a fifth of patients with SMI received a full CVD screen, compared with 96% of patients with diabetes (OR = 90.4; 95% CI = 64.5–126.6, $p < 0.01$) (32). Organizational changes are more promising; a large systematic review concluded that the presence

and implementation of standard screening protocols, triggered by a diagnosis of SMI, may be promising avenues to ensure the adequate diagnosis and screening of CVR in patients with SMI (28).

The patients in our SMI/AP + DM group took part in a guideline-based integrated chronic care program due to having diabetes, resulting in almost 70% adequate screening. Although relatively high, this is much lower than the CVR screening rate for all patients with type 2 diabetes as a whole, which exceeded 95% in the Netherlands (54). The National Diabetes Association (UK) reported that the proportion of people receiving the eight recommended care processes was not significantly different between people with type 2 diabetes and SMI and those with type 2 diabetes alone (2016–2017) (55).

Conclusions

The CVR screening of patients with SMI or those using AP poses a challenge. FPs hold a key position in the screening for CVR, as well as an increasing role in the care for patients with SMI. Standardized protocols to increase the involvement of FPs create an opportunity for improving cardiovascular screening and re-evaluating AP use in patients without a SMI diagnosis. Future studies should provide elucidate the most important elements of FP chronic care programs for patients with SMI or those using AP to extend their life expectancy.

Abbreviations

SMI:serious mental illness; AP:antipsychotics; SMI/AP:SMI and/or AP; CVR:cardiovascular risk; DM:type 2 diabetes mellitus; CVD:cardiovascular disease; OR:odds ratio; CI:confidence interval; EMR:electronic medical records; FP:family practitioner; ICPC:International Classification of Primary Care; ATC:Anatomical Therapeutic Chemical classification; COPD:chronic obstructive pulmonary disease.

Declarations

Ethics approval and consent to participate: All practices gave permission for us to extract data from the EMRs for research purposes and informed their patients, who could object to the use of their data. The written informed consent of patients was not required for this observational study because the de-identified data was extracted from the EMRs of a large number of patients. This study was performed according to the Code of Conduct for Health Research (2004), which was approved by the Data Protection Authorities for conformity with the applicable Dutch privacy legislation. Ethical approval for this study was requested and waived by the local Medical Research Ethics Committee Arnhem/Nijmegen (file number 2019-5515).

Consent for publication: Not applicable

Availability of data and materials: The datasets used and/or analyzed during the current study is available from the corresponding author on reasonable request.

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Figures

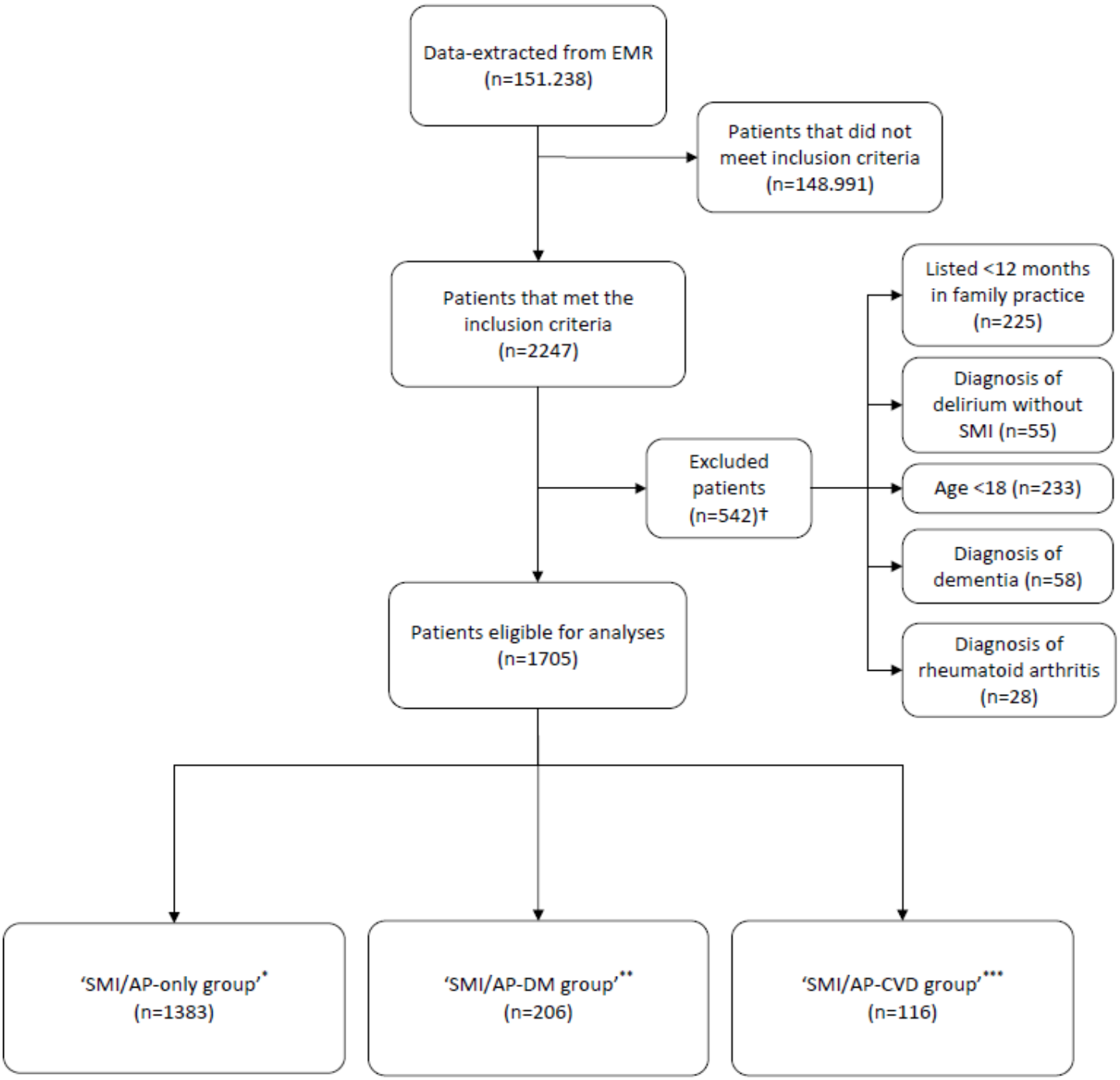

Figure 1

Flow chart of the in- and exclusion of patients. * Patients with SMI/AP without another indication for the yearly assessment of CVR. ** Patients with SMI/AP who also have diabetes. *** Patients with SMI/AP with additional cardiovascular morbidity without known diabetes. † Some excluded patients fitted more

than one exclusion criterion. EMR: electronic medical records; SMI: serious mental illness; DM: diabetes mellitus; CVD: cardiovascular disease.

Supplementary Files

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- Appendices.docx
- Addendum1.docx