

1 **Cardiovascular disease treatment among severe mental illness patients: a data linkage study**

2 CHARLOTTE WOODHEAD¹, MARK ASHWORTH¹, MATTHEW BROADBENT², FELICITY CALLARD³, MATTHEW
3 HOTOPF¹, PETER SCHOFIELD¹, MURAT SONCUL², ROBERT STEWART¹, MAX HENDERSON¹

4 ¹King's College London, Institute of Psychiatry, Psychology & Neuroscience, London, UK

5 ²South London and Maudsley NHS Foundation Trust, London, UK

6 ³Durham University, Centre for Medical Humanities, Durham, UK

7 Correspondence to: Charlotte Woodhead NIHR CLAHRC North Thames, University College London, 1-19
8 Torrington Place, London, UK WC1E 7HB E-mail: c.woodhead@ucl.ac.uk

9

10 Keywords: primary health care, cardiovascular diseases, psychoses, health inequalities, data linkage

11

12 Word count (introduction, methods, results and discussion): 2564

13

14

15

16

17

18

19

20

21

22

23

24

25

26

27

28 **Abstract**

29 *Background.* Sub-optimal treatment of cardiovascular diseases (CVD) among severe mental illness (SMI)
30 patients may contribute to physical health disparities.

31 *Aims.* To identify SMI characteristics associated with meeting CVD treatment guidelines.

32 *Design & setting.* Population-based electronic health record database linkage between primary care and
33 the sole provider of secondary mental health care services in South East London, UK

34 *Methods.* Cardiovascular disease prevalence, risk factor recording and Quality and Outcomes
35 Framework (QOF) clinical target achievement was compared among 4,056 SMI primary care patients
36 whose records were linked to secondary health care records and 270,669 patients without SMI who
37 were not known to secondary care psychiatric services using multivariate logistic regression modelling.
38 Data available from secondary care records were then used to identify SMI characteristics associated
39 with QOF clinical target achievement.

40 *Results.* SMI patients with coronary heart disease and heart failure experienced reduced prescribing of
41 betablocker and Angiotensin-Converting Enzyme Inhibitor/Angiotensin Receptor Blockers (ACEI/ARB). A
42 diagnosis of schizophrenia, being identified with any indicator of risk or illness severity, and being
43 prescribed with depot injectable antipsychotic medication was associated with the lowest likelihood of
44 prescribing.

45
46 *Conclusions.* Linking primary and secondary care data allows the identification of SMI patients most at
47 risk of under treatment for physical health problems.

48
49 *How this fits in*

50 Patients with severe mental illness (SMI) experience lower life expectancy than the general population
51 and sub-optimal treatment of cardiovascular diseases has been identified as one potential contributory
52 factor. We find that SMI patients in South East London are under-prescribed betablockers and ACE
53 Inhibitors/Angiotensin Receptor Blockers as secondary prevention following coronary heart disease
54 (CHD) and heart failure (HF). Patients with schizophrenia, those prescribed depot injectable
55 antipsychotic medication, those with more severe illness and those identified with any indicator of 'risk'
56 are the least likely to be prescribed these medications following CHD and HF. This may help clinicians
57 identify patients at greatest risk of sub-optimal treatment.

58
59
60 **Introduction**

61 Patients with severe mental illness (SMI), including schizophrenia, bipolar affective disorder,
62 schizoaffective disorder or other non-organic psychoses, experience lower life expectancy than the
63 general population.^[1-4] This is largely attributed to common physical disorder, particularly cardiovascular
64 diseases (CVDs)^[2, 3, 5, 6] Excess mortality linked to CVDs is attributed to several factors, including elevated

65 risk factors such as smoking; side effects of pharmacological treatment; diagnostic overshadowing; and,
66 sub-optimal management of co-morbid physical conditions.^[7-14] Previous studies have been unable to
67 investigate associations for varying SMI-related characteristics since data on physical health and clinical
68 management sits mainly within primary care while mental health condition and management records
69 are mainly stored in secondary care.

70 We use London borough population-based data from a linkage of primary, and secondary mental health
71 care records to: compare CVD prevalence, risk factor recording and treatment for established CVD, and
72 primary care consultation frequency by SMI status; examine whether SMI illness characteristics are
73 differentially associated with CVD prevalence and treatment; and, assess the impact of adjustments for
74 consultation frequency.

75 **Methods**

76 *Setting & data sources*

77 Lambeth is a diverse borough in South East London, with a greater number of Black Caribbean and Black
78 African residents but fewer South Asian residents than other areas,^[15] and is more deprived than
79 England as a whole.^[16] Pseudonymised primary care data were extracted on 31st March 2013 from
80 computerised medical records of all except one GP practice (n=48) within Lambeth, as part of Lambeth
81 DataNet (LDN) covering a population of 366,317 registered patients. This was a cross-sectional extract of
82 LDN, but for some records (e.g., BP), information on all measures recorded during 31st January 2012 to
83 31st October 2013 were collected to determine whether Quality and Outcomes Framework (QOF) (an
84 annual reward and incentive programme detailing GP practice achievement results^[17]) clinical targets
85 had been met. Secondary care data came from the Case Register Interactive Search (CRIS),^[18] an
86 application allowing researchers access to pseudonymised electronic health record (EHR) data from the
87 South London and Maudsley NHS Foundation Trust (SLaM). CRIS provides searchable access to de-
88 identified text (unstructured data) from the clinical record.

89 *Data linkage*

90 Data were linked and stored by the Clinical Data Linkage Service (CDLS) which provides a safe haven
91 environment with strict governance arrangements. Data were linked using encrypted NHS numbers
92 which were subsequently removed and destroyed, fully anonymising the linked dataset.

93 *Measures*

94 *Lambeth DataNet (LDN)*

95 Data were extracted on gender, year of birth, ethnicity, and 2011-defined lower super output area
96 (LSOA). LSOA data were used to estimate deprivation on the basis of patient area of residence using the
97 Index of Multiple Deprivation (IMD-2010) and a conversion to 2011 LSOA values. GP clinical register data
98 (lists established and maintained by practices of patients identified with particular clinical outcomes for

99 QOF purposes) were collected for heart failure (HF), coronary heart disease (CHD), hypertension (HYP)
100 and stroke/transient ischaemic attack (STIA). Data were also collected on CVD risk factor recording, e.g.,
101 blood pressure (BP); clinical values and dates; and, mean number of primary care consultations
102 (including GP, nurse, face-to-face, and telephone) between 2010 and 2013. A binary variable was
103 created to distinguish median or below and above median mean annual number of consultations.

104

105 *Case Register Interactive Search (CRIS)*

106 Diagnostic codes for any primary or secondary diagnosis of schizophrenia, bipolar affective disorder, and
107 schizoaffective disorder or other non-organic psychoses were extracted. An indicator of SMI severity
108 was created coding SMI patients as 1 if they ever had a record of an inpatient stay, being treated under
109 the Mental Health Act, difficulty managing their physical health, or contact with Assertive Outreach,
110 Crisis or A&E liaison team (or 0 if they had not been recorded with any of these). Similarly, an indicator
111 of risk coded SMI patients as 1/0 to indicate if they had ever been identified under the 'violence and
112 aggression' subscale of risk assessment with a history of violence, non-compliance, or forensic history.
113 Lastly, binary indicators of antipsychotic medication prescription were extracted - including binary
114 indicators of atypical, typical, and depot injectable medication.

115 *Statistical analyses*

116 Pearson's chi squared tests and logistic regression analyses were used to compare CVD prevalence, risk
117 factor recording, QOF target achievement, and primary care consultation frequency by SMI status. Using
118 linked data, comparisons by SMI status in CVD prevalence and prescribing were then examined by
119 individual SMI characteristics. Logistic regression analyses were used to assess whether any differences
120 in CVD prevalence or prescribing could be accounted for by adjustment for socio-demographic
121 characteristics and consultation frequency. P-values, unadjusted and adjusted odds ratios (OR) and 95%
122 confidence intervals (CI) are shown. Due to the large number of statistical tests conducted, we used an
123 alpha level of $p < 0.01$ to determine statistical significance. All analyses were conducted using STATA
124 v12.^[19]

125 **Results**

126 Data were obtained for LDN patients aged 16+ years (n=295,301); of these, 8.1% (n=23,919) were linked
127 to secondary mental health care records. Among those with linked records, n=4056 (16.9%) were
128 recorded with SMI by their GP in LDN. Analyses compared those with recorded SMI in primary care with
129 linked secondary care records (n=4056) to those not recorded with SMI in primary care or linked to
130 secondary care (n=270,669).

131 *Socio-demographics, CVD prevalence and consultation frequency among patients with and without SMI*

132 SMI status was associated with gender, age, ethnicity, deprivation, consultation frequency, and greater
133 prevalence of CVDs (Table 1). In patients with an established CVD (data not shown) there were no longer
134 associations between SMI status and gender, nor age among patients with CHD or STIA. SMI status was

135 only associated with ethnicity and GP consultation rate among HYP patients and SMI status was no
136 longer associated with deprivation among patients with any CVD condition.

137 *Socio-demographic characteristics of SMI sub-groups*

138 The SMI characteristics extracted from secondary care data are illustrated in Table 2. Adjusting for all
139 socio-demographic characteristics simultaneously (data not shown), being Black African, Black
140 Caribbean, other Black and younger age was associated with indicators of risk and severity, and with
141 receiving depot injectable antipsychotic medication; male gender was also associated with risk. Being
142 Black Caribbean and older was associated with receipt of typical antipsychotics, while younger age and
143 being Black African was associated with receipt of atypical antipsychotics. Relative to those with a
144 diagnosis of schizophrenia, those diagnosed with bipolar disorder were younger, more likely to be
145 identified as British/mixed British, female, and to consult primary care more frequently ($p=0.01$). Those
146 diagnosed with schizoaffective disorder/other non-organic psychoses were younger, more likely to be
147 female, and to consult primary care less frequently relative to schizophrenia patients (except where
148 indicated, all p -values <0.001).

149 *CVD risk factor recording and QOF target achievement*

150 CVD risk factor recording (e.g. BP) was in general high for patients with and without SMI (Table 3).
151 Among those with established CVDs, SMI patients were more likely to have a record of their alcohol
152 intake. Among HYP patients, SMI status was also associated with greater recording of BMI and HbA1c
153 levels. SMI patients with CHD were less likely to have a BP record, while those with STIA were less likely
154 to have a record of BP and smoking status. CVD risk assessment (e.g. Framingham risk score) was
155 significantly less common among SMI patients. Despite significantly higher prevalence of CVDs in the
156 SMI group overall, there was little or no difference in the prevalence of co-morbid CVDs or diabetes by
157 SMI status among those with established CVDs. Among HYP patients, diabetes was significantly more
158 common among SMI than non-SMI patients.

159 For most QOF targets, there was no significant difference between SMI and non-SMI patients. For SMI
160 patients with HF and CHD, a significant shortfall was observed in prescribing with ACE inhibitors or
161 angiotensin receptor blockers (ACEIs/ARBs) and beta-blockers.

162 *Regression analyses of QOF target achievement*

163 Regression analyses (Table 4) focussed on differences in CVD prescribing by SMI status as these
164 differences have previously been identified as a potential contributor to excess cardiovascular mortality
165 among SMI patients^[12] and were the key differences identified in Table 3. Associations between SMI
166 status and beta-blocker and ACEI/ARB medication among HF patients remained after accounting for
167 both socio-demographic characteristics and consultation rates. Among CHD patients, the association
168 between SMI status and betablocker prescription was accounted for by ethnicity but the shortfall in
169 ACEI/ARB prescribing among CHD patients with SMI remained following adjustments.

170 For analyses examining SMI-subgroups associated with betablocker and ACEI/ARB prescribing, CHD and
171 HF were combined due to small numbers (Table 5). After adjustments, prescribing of betablocker and
172 ACEI/ARB medication among patients with CHD or HF combined was significantly lower for SMI patients
173 overall (OR 0.48 and 0.42, respectively); and, was particularly reduced for patients ever prescribed depot
174 injectable antipsychotic medication (OR 0.22 and 0.32, respectively), those with any indicator of risk (OR
175 0.25 and 0.22, respectively), those diagnosed with schizophrenia (OR 0.38 and 0.27, respectively) and
176 those with any indicator of SMI severity (OR 0.39 and 0.31, respectively).

177 **Discussion**

178 *Summary*

179 We found elevated rates of CVDs among SMI patients; however, there may be under-recording of CVD
180 co-morbidities among SMI patients with established CVDs. Risk factor recording was high, though
181 significant differences by SMI status were identified. Overall, QOF target achievement was not impaired
182 in SMI patients but we found significant consistent associations between SMI status and reduced
183 prescribing of ACEI/ARB and betablocker medication as secondary prevention of CHD and HF. SMI
184 patients with schizophrenia, those identified with any indicator of risk or illness severity, and those ever
185 prescribed depot injectable antipsychotics were least likely to be prescribed ACEI/ARBs and
186 betablockers.

187 *Strengths and limitations*

188 This study makes use of a population-based data linkage between primary and secondary care records.
189 We were able to identify patient and illness-related characteristics associated with recording and
190 treatment of CVDs and to highlight issues warranting further investigation that may best target
191 disparities and reduce inequalities in physical co-morbidity and mortality. The main limitation pertains
192 to the generalisability to other geographical areas; however, our findings are in line with evidence from
193 national and international research, and we believe that this study is proof of principle of the utility of
194 data linkage, which could be used elsewhere to corroborate the findings. While our analyses focus on
195 incentivised QOF targets; it is possible that discrepancies in non-QOF targets may differ.

196 *Comparison with existing literature*

197 While SMI patients were more likely to be recorded with CVDs overall, we found little evidence for
198 elevated rates of CVD co-morbid conditions among those with established CVDs. Previous research has
199 found no difference in the pattern of physical health co- and multi-morbidities by SMI status and lower
200 than expected rates of certain CVDs among SMI patients given higher CVD-related mortality.^[3, 21, 22] One
201 of several explanations suggested is that this may be linked to less frequent GP consultations^[21, 22];
202 however, we report elevated consultation rates among SMI patients overall, and among SMI patients
203 with established CVD, in line with previous findings.^[23] SMI patients were less likely to have a CVD risk
204 assessment, and while such tools may not be as accurate for the SMI population,^[24, 25] it is unclear
205 whether this concern - or other factors accounted for this observation.

206 Lower than expected CVD co-morbidities may also be linked to increased CVD-related mortality, since
207 we found that SMI patients with established CVDs were under-represented in older age groups. We also
208 found lower than expected differences in the proportion of Black SMI patients among those with CHD
209 and HYP. This suggests that for these patients, either SMI status does not confer an excess risk of these
210 outcomes; that unlike other ethnic groups, compared to those without SMI, CHD and HYP is not
211 elevated for Black SMI patients; or, that CHD and HYP is less frequently recorded among Black SMI
212 patients; for example, due to excess mortality.

213 *Treatment differences*

214 In line with previous findings,^[7, 14, 22, 26] we found evidence for reduced prescription of ACEI/ARB and
215 betablocker medications for CVD secondary prevention. Under-prescribing in CVDs has been previously
216 linked with excess mortality among SMI patients^[7, 12, 22, 26, 27] and therefore may contribute to disparities
217 in life expectancies. Reduced ACEI/ARB prescribing in CHD among SMI patients could partly reflect
218 differences in the effectiveness of these drugs as hypotensive agents among Black Caribbean and Black
219 African patients.^[28] National Institute for Health and Care Excellence (NICE) HYP guidelines^[29] indicate
220 prescribing of ARBs rather than ACEIs among Black patients; however, the associations remained after
221 adjustments for ethnicity and were robust when ACEIs and ARB prescriptions were analysed separately.
222 Reduced prescribing is also unlikely linked to reduced attendance at primary care since we found greater
223 consultation frequency among SMI patients and adjustments strengthened negative associations with
224 prescribing.

225 There may, however, be reluctance to prescribe certain CVD medications due to concerns about
226 adherence. Adherence may be lower for drugs where the dose has to be up-titrated to maximally
227 tolerated doses as for beta-blockers and ACEI/ARBs; these medications require monitoring, and thus
228 adherence to a monitoring regime to assess for side-effects. Monitoring also involves regular blood
229 tests; such a commitment may be perceived as too demanding for GPs assessing SMI patients, and/or
230 SMI patients may be less willing to commit themselves to such monitoring. However, a recent US study
231 assessing adherence in patients with and without schizophrenia found no evidence for reduced
232 adherence to ACEI/ARB medication.^[30] One reason previously suggested for reluctance to prescribe
233 certain cardiovascular medications is the potential for harm in overdose.^[14, 22] While research does not
234 support an association between cardiovascular medication and excess suicide,^[31, 32] practitioners could
235 conceivably have concerns around correct adherence among SMI patients, for example, leading to
236 accidental overdose.

237 Further quantitative and qualitative work may usefully further explore these explanations. Qualitative
238 evidence suggests that primary care physicians may view SMI patients as harder to manage^[32, 33] and be
239 less willing to intervene when cardiovascular risk factors are identified.^[34] Further, there may be
240 reluctance among SMI patients to accept prescriptions due to mistrust or lack of adequate
241 communication between physician and patient.^[35] For patients with greater illness severity, the role of
242 secondary care physicians may be more pertinent in managing physical health.

243 Lastly, QOF exception rates (e.g. due to informed dissent or treatment unsuitability) are higher in SMI
244 patients,^[36, 37] potentially inflating QOF achievement. However, our analyses did not exclude exception
245 reported patients, so our reported achievement rates were not influenced by exception reporting
246 among SMI patients.

247 *SMI subgroups*

248 Betablocker and ACEI/ARB prescription was reduced in SMI patients with CHD or HF overall, but the
249 reduction was greatest in SMI patients identified with any indicator of risk, prescription of depot
250 injectable antipsychotics, schizophrenia diagnosis, and any indicator of SMI severity. While these
251 associations have not been previously investigated to our knowledge, Laursen et al.^[25] reported that
252 rates of ‘unnatural’ deaths were elevated among patients with SMI who were not prescribed
253 cardiovascular medication, also indicating an association with illness severity. The sub-groups identified
254 as most at risk of under-prescribing may be those most likely to be seen as the ‘hardest to treat’ by GPs
255 and those least likely commit to the monitoring and follow-up as implied above. Further qualitative work
256 should explore these associations among clinicians and patients who have been identified as at risk of
257 under-prescribing.

258 *Implications*

259 Our findings deepen the understanding of disparities in morbidity and healthcare among individuals
260 with SMI and help to build possible explanations for these discrepancies by identifying characteristics of
261 SMI patients associated with the lowest likelihood of optimal treatment. Our findings underline the
262 value of closer working between primary and secondary care in improving outcomes for SMI patients.

263 **Ethics:** The linkage was a service evaluation and did not require ethical approval. Approvals for the
264 database linkage were obtained via a Section 251 application to the Health Research Authority
265 (reference: CAG 6-07(f)/2013) and from the Lambeth Clinical Commissioning Group (CCG) Information
266 Governance committee.

267 **Funding:** The data linkage was funded by the Medical Research Council (ref: MR/J013471/1)

268 **Competing interests:** All authors have completed the ICMJE uniform disclosure form
269 at www.icmje.org/coi_disclosure.pdf and declare: no support from any organisation for the submitted
270 work; no financial relationships with any organisations that might have an interest in the submitted
271 work in the previous three years; no other relationships or activities that could appear to have
272 influenced the submitted work.

273 **Acknowledgements:** MA is supported by the National Institute for Health Research (NIHR) Biomedical
274 Research Centre (BRC) based at Guy’s and St Thomas’ NHS Foundation Trust and King’s College London
275 (KCL). MH, MB, and RS are part-funded by the NIHR BRC and Dementia Biomedical Research Unit at
276 South London and Maudsley NHS Foundation Trust (SLAM) and KCL. FC is supported by The Wellcome
277 Trust (103817/Z/14/Z). The data linkage was supported by the Mental and Physical Health in Lambeth
278 Steering Group and the Clinical Data Linkage Service. CRIS is supported by the NIHR BRC for Mental

279 Health BRC Nucleus at SLAM and the Institute of Psychiatry, Psychology & Neuroscience, KCL - jointly
280 funded by the Guy's and St Thomas' Trustees and the SLAM Trustees. The views expressed are those of
281 the authors and not necessarily those of the NHS, the NIHR or the Department of Health.

282

283 **References**

- 284 1. Henderson M, Hotopf M, Shah I, Hayes RD, Kuh D. Psychiatric disorder in early adulthood and risk of
285 premature mortality in the 1946 British Birth Cohort. *BMC Psychiatry* 2011; 11(1): 37-44.
- 286 2. Laursen TM, Munk Olsen T, Vestergaard M. Life expectancy and cardiovascular mortality in persons
287 with schizophrenia. *Curr Opin Psychiatr* 2012; 25(2): 83-8.
- 288 3. Crump C, Winkleby M, Sundquist K, Sundquist J. Comorbidities and mortality in persons with
289 schizophrenia: A Swedish national cohort study. *Am J Psychiatry* 2013; 170 (3): 324-33.
- 290 4. Lawrence D, Hancock KJ, Kisely S. The gap in life expectancy from preventable physical illness in
291 psychiatric patients in Western Australia: retrospective analysis of population based registers.
292 *BMJ* 2013; 346(1): f2539-f2539.
- 293 5. Brown S, Kim M, Mitchell C, Inskip H. Twenty-five year mortality of a community cohort with
294 schizophrenia. *Br J Psychiatry* 2010; 196 (2):116-21.
- 295 6. Dutta R, Murray RM, Allardyce J, Jones PB, Boydell JE. Mortality in first-contact psychosis patients in
296 the UK: a cohort study. *Psychol Med* 2012; 42(8): 1649-61.
- 297 7. Druss B, Bradford W, Rosenheck R, Radford MJ, Krumholz HM. Quality of medical care and excess
298 mortality in older patients with mental disorders. *Arch Gen Psychiatry* 2001; 58(6): 565-72.
- 299 8. Kreyenbuhl J, Dickerson F, Medoff D, Brown CH, Goldberg RW, Fang LJ et al. Extent and management
300 of cardiovascular risk factors in patients with type 2 diabetes and serious mental illness. *J Nerv Ment*
301 *Dis* 2006; 194(6): 404-10.
- 302 9. Nash M. Diagnostic overshadowing: a potential barrier to physical health care for mental health
303 service users. *Mental Health Practice* 2013; 17(4): 22-26.
- 304 10. Goldberg R, Kreyenbuhl J, Medoff D, Dickerson FB, Wohlheiter K, Fang LJ et al. Quality of diabetes
305 care among adults with serious mental illness. *Psychiatr Serv* 2007; 58(4): 536-43.
- 306 11. Hippisley-Cox J, Parker C, Coupland C, Vinogradova Y. Inequalities in the primary care of patients with
307 coronary heart disease and serious mental health problems: a cross-sectional study. *Heart* 2007;
308 93(10): 1256-62.
- 309 12. Mitchell, AJ, Lord O. Review: Do deficits in cardiac care influence high mortality rates in
310 schizophrenia? A systematic review and pooled analysis. *J Psychopharmacol* 2010; 24(4 suppl): 69-80.
- 311 13. DeHert M, Correll CU, Bobes J, Cetkovich-Bakmas M, Cohen D, Asai. Physical illness in patients with
312 severe mental disorders. I. Prevalence, impact of medications and disparities in health care. *World*
313 *Psychiatry* 2011; 10 (1): 52-77.
- 314 14. Mitchell AJ, Lord O, Malone D. Differences in the prescribing of medication for physical disorders in
315 individuals with v. without mental illness: meta-analysis. *Br J Psychiatry* 2012; 201(6): 435-43.
- 316 15. Office of National Statistics. 2011 Census: KS201UK Ethnic group, local authorities in the United
317 Kingdom, 2011. [http://www.ons.gov.uk/ons/publications/re-reference-](http://www.ons.gov.uk/ons/publications/re-reference-tables.html?edition=tcm%3A77-327143)
318 [tables.html?edition=tcm%3A77-327143](http://www.ons.gov.uk/ons/publications/re-reference-tables.html?edition=tcm%3A77-327143) (accessed August 2015).

- 319 16.English Indices of Deprivation 2010. <https://www.gov.uk/government/statistics/english-indices-of->
320 [deprivation-2010](https://www.gov.uk/government/statistics/english-indices-of-deprivation-2010) (accessed August 2015).
- 321 17.Health & Social Care Information Centre. Quality and Outcomes Framework-2012-132013.
322 <http://www.hscic.gov.uk/catalogue/PUB12262> (accessed October 2015).
- 323 18.Stewart R, Soremekun M, Perera G, Broadbent M, Callard F, Denis M, et al. The South London and
324 Maudsley NHS Foundation Trust Biomedical Research Centre (SLAM BRC) case register: development
325 and descriptive data. *BMC Psychiatry* 2009; 9(1): 51-63.
- 326 19.StataCorp. Stata Statistical Software: Release 12. College Station, TX: StataCorp LP, 2011.
- 327 20.Woodhead C, Ashworth A, Schofield P, Henderson M. Patterns of physical co-/multi-morbidity among
328 patients with serious mental illness: a London borough-based cross-sectional study. *BMC Family*
329 *Practice* 2014; 15(1): 117.
- 330 21.Smith DJ, Langan J, McLean G, Guthrie B, Mercer SW. Schizophrenia is associated with excess
331 multiple physical-health comorbidities but low levels of recorded cardiovascular disease in primary
332 care: cross-sectional study. *BMJ Open* 2013a; 3(4): e002808.
- 333 22.Smith DJ, Martin D, McLean G, Langan J, Guthrie B, Mercer SW. Multimorbidity in bipolar disorder
334 and undertreatment of cardiovascular disease: a cross sectional study. *BMC Med* 2013b; 11: 263.
- 335 23.Kontopantelis E, Olier I, Planner C, Reeves D, Ashcroft DM, Gask L, Doran T, Reilly S. Primary care
336 consultation rates among people with and without severe mental illness: a UK cohort study using the
337 Clinical Practice Research Datalink. *BMJ Open*. 2015; 1:5(12):e008650.
- 338 24.McLean G, Langan Martin J, Martin DJ, Guthrie B, Mercer SW, Smith DJ. Standard cardiovascular
339 disease risk algorithms underestimate the risk of cardiovascular disease in schizophrenia: evidence
340 from a national primary care database. *Schizophr Res* 2014; 159(1): 176-81.
- 341 25.Osborn DP, Hardoon S, Omar RZ, Holt RI, King M, Larsen J et al. Cardiovascular risk prediction models
342 for people with severe mental illness: results from the prediction and management of cardiovascular
343 risk in people with severe mental illnesses (PRIMROSE) research program. *JAMA Psychiatry* 2015;
344 72(2): 143-51.
- 345 26.Laursen TM, Mortensen PB, MacCabe JH, Cohen D, Gasse C. Cardiovascular drug use and mortality in
346 patients with schizophrenia or bipolar disorder: a Danish population-based study. *Psychol Med* 2014;
347 44(8): 1625-37.
- 348 27.Laursen T, Munk-Olsen T, Agerbo E, Gasse C, Mortensen PB. Somatic hospital contacts, invasive
349 cardiac procedures, and mortality from heart disease in patients with severe mental disorder. *Arch*
350 *Gen Psychiatry* 2009; 66(7): 713-20.
- 351 28.Gupta AK. Racial differences in response to antihypertensive therapy: does one size fits all? *Int J Prev*
352 *Med* 2010; 1(4):217-19.
- 353 29.National Institute for Health and Care Excellence (NICE). Hypertension: clinical management of
354 primary hypertension in adults 2011. <https://www.nice.org.uk/guidance/cg127> (accessed October
355 2015).
- 356 30.Owen-Smith A, Stewart C, Green C, Ahmedani BK, Waitzfelder BE, et al. Adherence to common
357 cardiovascular medications in patients with schizophrenia vs. patients without psychiatric illness. *Gen*
358 *Hosp Psychiatry* Published Online First 29 July 2015. doi:10.1016/j.genhosppsy.2015.07.010.
- 359 31.Callréus T, Andersen UA, Hallas J, Andersen M. Cardiovascular drugs and the risk of suicide: a nested
360 case-control study. *Eur J Clin Pharmacol* 2007; 63(6): 591-6.

- 361 32. Jepsen P, Johnsen SP, Sørensen HT. Risk of Suicide in Users of Cardiovascular Drugs: A Review of the
362 Epidemiological Evidence. *Am J Cardiovasc Drugs* 2003; 3(3): 163-67.
- 363 33. Lester H, Tritter JQ, Sorohan H. Patients' and health professionals' views on primary care for people
364 with serious mental illness: focus group study. *BMJ* 2005; 330(7500): 1122.
- 365 34. Oud MJT, Schuling J, Slooff CJ, Groenier KH, Dekker JH, Meyboom-de Jong B. Care for patients with
366 severe mental illness: the general practitioner's role perspective. *BMC Fam Pract* 2009; 10: 29.
- 367 35. Kendrick T. Cardiovascular and respiratory risk factors and symptoms among general practice
368 patients with long-term mental illness. *Br J Psychiatry* 1996; 169(6): 733-39.
- 369 36. O'Day B, Killeen MB, Sutton J, Lezzoni LI. Primary care experiences of people with psychiatric
370 disabilities: barriers to care and potential solutions. *Psychiatr Rehabil J* 2005; 28: 339-45.
- 371 37. Martin JL, Lowrie R, McConnachie A, McLean G, Mair F, Mercer SW, Smith DJ. Physical health
372 indicators in major mental illness: analysis of QOF data across UK general practice. *Br J Gen Pract*,
373 2014; 64(627): e649-56.
- 374 38. Mitchell AJ, Hardy SA. Screening for metabolic risk among patients with severe mental illness and
375 diabetes: a national comparison. *Psychiatr Serv* 2013; 64(10):1060-63.

Table 1 Socio-demographic characteristics and CVD prevalence by severe mental illness (SMI) status

	Non-SMI (N=270,669)	SMI (N=4,056)	p
	n (%)	n (%)	
Sex [†]			<0.001 ***
Female	137353 (50.8)	1797 (44.3)	
Male	133315 (49.3)	2259 (55.7)	
Age group			<0.001 ***
16-24	32776 (12.1)	162 (4.0)	
25-34	88062 (32.5)	678 (32.5)	
35-44	59279 (21.9)	907 (22.4)	
45-54	42839 (15.8)	1095 (27.0)	
55-64	23734 (8.8)	624 (15.4)	
65-74	14035 (5.2)	347 (8.6)	
75+	9944 (3.7)	243 (6.0)	
Ethnicity			<0.001 ***
British/mixed	78332 (35.0)	1124 (31.6)	
Irish	5253 (2.4)	104 (2.9)	
Indian/Pakistani/Bangladeshi/mixed	16042 (7.2)	219 (6.2)	
Caribbean/mixed	21401 (9.6)	840 (23.7)	
African/mixed	27286 (12.2)	545 (15.3)	
Chinese/other	10871 (4.9)	90 (2.5)	
Other white	54080 (24.2)	373 (10.5)	
Other black	6262 (2.8)	188 (5.3)	
Other mixed	4254 (1.9)	69 (1.9)	
Deprivation quintile			<0.001 ***
Most deprived	47162 (18.1)	1004 (25.0)	
2	54656 (21.0)	918 (22.9)	
3	54342 (20.9)	836 (20.8)	
4	57149 (22.0)	713 (17.8)	
Least deprived	47054 (18.1)	543 (13.5)	
Consultations			
Mean (SD)	4.7 (4.3)	9.4 (8.0)	
Median/below	123501 (53.1)	813 (20.9)	<0.001 ***
Above median	109286 (47.0)	3074 (79.1)	
Cardiovascular diseases			
Hypertension	28010 (10.4)	762 (18.8)	<0.001 ***
Coronary heart disease	4109 (1.5)	97 (2.4)	<0.001 ***
Heart Failure	1259 (0.5)	45 (1.1)	<0.001 ***
Stroke/transient ischaemic attack	2544 (0.9)	100 (2.5)	<0.001 ***

*** $p < 0.001$

[†] One patient recorded as sex “unknown”. SMI patients are those known to both primary and secondary care, non-SMI patients are those known only to primary care and not registered with SMI. ‘Consultations’ refers to mean number of GP and nurse telephone, face-to-face and home primary care consultations per calendar year between 2010 and 2013.

Table 2 Indicators of severity and risk identified from secondary care data among patients with severe mental illness (SMI)

	SMI (N=4056) <i>n</i> (%)
Diagnosis	
Schizophrenia	1721 (53.6)
Bipolar affective disorder	716 (22.3)
Other non-organic psychoses	773 (24.1)
Indicator of severity, ever:	2147 (53.0)
Treated under Mental Health Act	1416 (34.9)
Inpatient	1927 (47.5)
Seen by crisis team	23 (0.6)
Seen by assertive outreach	11 (0.3)
A & E outpatient episode	445 (11.0)
Difficulty managing physical health	676 (16.7)
Indicator of risk, ever:	1751 (43.0)
History of non-compliance	1296 (32.0)
History of violence	1171 (28.9)
Forensic history	620 (15.3)
Antipsychotics, ever:	
Depot injectable	1112 (32.3)
Atypical	3255 (94.5)
Typical	1506 (43.7)

Table 3 CVD risk factor recording and QOF CVD target achievement by serious mental illness (SMI) status and among patients with CVD conditions.

	Heart failure (HF)			Coronary heart disease (CHD)			Hypertension (HYP)			Stroke/transient ischaemic attack (STIA)		
	Non-SMI (n=1259)	SMI (n=45)	<i>p</i>	Non-SMI (n=4109)	SMI (n=97)	<i>p</i>	Non-SMI (n=28010)	SMI (n=762)	<i>p</i>	Non-SMI (n=2544)	SMI (n=100)	<i>p</i>
	<i>n</i> (%)	<i>n</i> (%)		<i>n</i> (%)	<i>n</i> (%)		<i>n</i> (%)	<i>n</i> (%)		<i>n</i> (%)	<i>n</i> (%)	
Risk Factor recording												
BP record	1251 (99.4)	44 (97.8)	0.206	4079 (99.3)	94 (96.9)	0.009**	27859 (99.5)	754 (99.0)	0.061	2519 (99.0)	96 (96.0)	0.004**
Smoking status record	1257 (99.8)	45 (100.0)	0.789	4099 (99.8)	96 (99.0)	0.133	27977 (99.9)	759 (99.6)	0.034*	2537 (99.7)	97 (97.0)	<.001***
HbA1c record	805 (63.9)	26 (57.8)	0.398	2728 (66.4)	67 (69.1)	0.580	16468 (58.8)	531 (69.7)	<.001***	1544 (60.7)	69 (69.0)	0.095
Cholesterol record	1206 (95.8)	45 (100.0)	0.160	4017 (97.8)	94 (96.9)	0.576	26880 (96.0)	734 (96.3)	0.618	2441 (96.0)	94 (94.0)	0.336
BMI record	1187 (94.3)	45 (100.0)	0.099	3849 (93.7)	94 (96.9)	0.193	26386 (94.2)	743 (97.5)	<.001***	2317 (91.1)	95 (95.0)	0.174
Alcohol record	992 (78.8)	45 (100.0)	0.001***	3325 (80.9)	88 (90.7)	0.015*	22637 (80.8)	716 (94.0)	<.001***	1966 (77.3)	92 (92.0)	0.001***
eGFR record	1229 (97.6)	44 (97.8)	0.945	3987 (97.0)	94 (96.9)	0.943	26854 (95.9)	731 (95.9)	0.936	2415 (94.9)	96 (96.0)	0.631
CVD risk factor assessment	236 (18.8)	10 (22.2)	0.558	727 (17.7)	11 (11.3)	0.104	9995 (35.6)	230 (30.2)	0.002**	460 (18.1)	14 (14.0)	0.297
TSH record	1140 (90.6)	40 (88.9)	0.709	3619 (88.1)	85 (87.6)	0.893	23884 (85.3)	677 (88.9)	0.006**	2142 (84.2)	86 (86.0)	0.627
CHD co-morbidity	569 (45.2)	13 (28.9)	0.031*	-	-	-	2590 (9.3)	57 (7.5)	0.096	454 (17.9)	19 (19.0)	0.768
DM co-morbidity	428 (34.0)	17 (37.8)	0.599	1294 (31.5)	31 (32.0)	0.922	6837 (24.4)	276 (36.2)	<.001***	647 (25.4)	36 (36.0)	0.018*
HYP co-morbidity	886 (70.4)	27 (60.0)	0.136	2590 (63.0)	57 (58.8)	0.389	-	-	-	1680 (66.0)	66 (66.0)	0.994
QOF target achievement [†]												
Last BP record within 9 months	-	-	-	-	-	-	18286 (65.3)	500 (65.6)	0.849	-	-	-
Normal BP (150/90) in last 9 months	-	-	-	-	-	-	20829 (74.4)	557 (73.1)	0.430	1907 (75.0)	67 (67.0)	0.073
Normal BP (150/90) in last 15 months	-	-	-	3451 (84.0)	80 (82.5)	0.688	-	-	-	-	-	-
Cholesterol record in last 15 months	-	-	-	-	-	-	-	-	-	1786 (70.2)	69 (69.0)	0.796
Cholesterol <5mmol/l in last 15 months	-	-	-	2816 (68.5)	58 (59.8)	0.067	-	-	-	1477 (56.9)	52 (52.0)	0.334
Anticoagulant/antiplatelet last 15 months	-	-	-	3002 (73.1)	69 (71.1)	0.667	-	-	-	1460 (61.7)	59 (62.8)	0.840 ¹
Quadruple therapy ²	-	-	-	1530 (51.9)	28 (41.2)	0.082	-	-	-	-	-	-
Betablocker	879 (69.8)	18 (40.0)	<.001***	2710 (66.0)	53 (54.6)	0.020**	-	-	-	-	-	-
ACEI/ARB	1051 (83.5)	28 (62.2)	<.001***	-	-	-	-	-	-	-	-	-

p*<0.05, *p*<0.01, ****p*<0.001.

[†]Refers to QOF guidelines 2012/13^[17]

¹If non-haemorrhagic (non-SMI n=2366& SMI n=94).² If registered with MI (non-SMI n=2951 & SMI n=68). All QOF management guidelines refer to records since registration with outcomes. CHD= coronary heart disease, MI=myocardial infarction, HYP=hypertension, DM=diabetes mellitus, BP=blood pressure, ACEI/ARB=angiotensin-converting enzyme inhibitor/angiotensin receptor blocker, TSH=thyroid stimulating hormone, EGFR=estimated glomerular filtration rate, BMI=body mass index, HbA1c=glycated haemoglobin test.

²MI drugs - "quadruple therapy" including statin, antiplatelet/anticoagulant, betablocker and ACEI/ARB prescription.

Table 4 Differences in Quality and Outcomes Framework (QOF) CVD prescribing targets[†] by serious mental illness (SMI) status adjusted for socio-demographic characteristics and primary care consultation frequency.

	Reference (non-SMI)	Unadjusted OR (95% CI)	Adjusted for socio-demographics OR ^a (95% CI)	Additionally adjusted for consultation rate OR ^b (95% CI)
Betablocker				
After CHD	1.00	0.62 (0.41 - 0.93)*	0.68 (0.44 - 1.05)	0.66 (0.42 - 1.01)
After HF	1.00	0.29 (0.16 - 0.53)***	0.29 (0.15 - 0.55)***	0.27 (0.14 - 0.52)***
ACEI/ARB				
After CHD	1.00	0.59 (0.36 - 0.97)*	0.55 (0.33 - 0.94)*	0.47 (0.27 - 0.80)**
After HF	1.00	0.33 (0.18 - 0.61)***	0.34 (0.18 - 0.66)***	0.31 (0.16 - 0.60)***
Antiplatelet/anticoagulant				
After CHD	1.00	0.95 (0.54 - 1.65)	1.04 (0.57 - 1.89)	0.94 (0.51 - 1.73)
After STIA	1.00	1.04 (0.68 - 1.60)	0.99 (0.62 - 1.59)	1.04 (0.64 - 1.69)
Statin				
After CHD	1.00	0.76 (0.45 - 1.28)	0.78 (0.45 - 1.36)	0.70 (0.40 - 1.23)
Quadruple therapy ¹				
After CHD	1.00	0.65 (0.40 - 1.06)	0.62 (0.37 - 1.04)	0.28 (0.34 - 0.98)*

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

[†]Refers to QOF guidelines 2012/13^[17]

ACEI/ARB=angiotensin-converting enzyme inhibitor/angiotensin receptor blocker; CHD=coronary heart disease; HF=heart failure; ¹Quadruple therapy indicated in patients with history of myocardial infarction and includes statin, antiplatelet/anticoagulant, betablocker and ACEI/ARB medication.

^aAdjusted for age (continuous), gender, ethnicity, and borough-level deprivation; ^b additionally adjusted for mean annual number of primary consultations.

Table 5 Serious mental illness (SMI) characteristics associated with Betablocker and ACEI/ARB prescribing among CHD/HF patients

	Betablockers if recorded with CHD or HF (n=3347)				ACEI/ARB if recorded with CHD or HF (n=3760)			
	n (%)	Unadjusted OR (95% CI)	Adjusted for socio-demographics OR ^a (95% CI)	Additionally adjusted for consultation rate OR ^b (95% CI)	n (%)	Unadjusted OR (95% CI)	Adjusted for socio-demographics OR ^a (95% CI)	Additionally adjusted for consultation rate OR ^b (95% CI)
Non-SMI	3279 (68.3)	1.00	1.00	1.00	3677 (76.6)	1.00	1.00	1.00
SMI overall	68 (52.7)	0.52 (0.36 – 0.73)***	0.50 (0.35 – 0.73)***	0.48 (0.33 – 0.69)***	83 (64.3)	0.55 (0.38 – 0.79)***	0.49 (0.34 – 0.73)***	0.42 (0.28 – 0.62)***
SMI by diagnosis								
Schizophrenia	30 (50.0)	0.46 (0.28 - 0.77)**	0.42 (0.24 - 0.73)**	0.38 (0.22 - 0.67)***	36 (60.0)	0.46 (0.27 - 0.77)**	0.35 (0.20 - 0.60)***	0.27 (0.15 - 0.48)***
Bipolar affective disorder	8 (40.0)	0.31 (0.13 - 0.76)*	0.37 (0.15 - 0.94)*	0.35 (0.14 - 0.90)*	11 (55.0)	0.37 (0.15 - 0.90)*	0.49 (0.18 - 1.26)	0.41 (0.16 - 1.09)
Other non-organic psychoses	8 (61.5)	0.74 (0.24 - 2.27)	0.78 (0.25 - 2.42)	0.75 (0.24 - 2.33)	12 (92.3)	3.66 (0.48 - 28.2)	3.81 (0.49 - 29.4)	3.44 (0.44 - 26.7)
Depot injectable								
No	42 (56.8)	0.61 (0.38 - 0.97)*	0.58 (0.36 - 0.96)*	0.56 (0.34 - 0.92)*	48 (64.9)	0.56 (0.35 - 0.91)*	0.49 (0.29 - 0.81)**	0.43 (0.26 - 0.72)***
Yes	11 (36.7)	0.27 (0.13 - 0.57)***	0.26 (0.12 - 0.60)**	0.22 (0.09 - 0.52)***	18 (60.0)	0.46 (0.22 - 0.95)*	0.41 (0.18 - 0.91)*	0.32 (0.14 - 0.72)**
Typical antipsychotic								
No	28 (50.9)	0.48 (0.28 - 0.82)**	0.50 (0.28 - 0.89)*	0.49 (0.27 - 0.86)*	34 (61.8)	0.49 (0.29 - 0.85)*	0.42 (0.23 - 0.75)**	0.37 (0.21 - 0.67)***
Yes	25 (51.0)	0.48 (0.27 - 0.85)*	0.44 (0.24 - 0.81)**	0.39 (0.21 - 0.73)**	32 (65.3)	0.57 (0.32 - 1.03)	0.52 (0.28 - 0.97)*	0.42 (0.22 - 0.80)**
Atypical antipsychotic								
No	8 (87.1)	0.62 (0.21 - 1.78)	0.59 (0.20 - 1.71)	0.54 (0.18 - 1.58)	8 (57.1)	0.41 (0.14 - 1.18)	0.41 (0.14 - 1.20)	0.32 (0.10 - 0.96)*
Yes	45 (50.0)	0.46 (0.31 - 0.70)***	0.45 (0.29 - 0.71)***	0.43 (0.27 - 0.67)***	58 (64.4)	0.55 (0.36 - 0.86)**	0.47 (0.30 - 0.76)**	0.41 (0.26 - 0.66)***
Any indicator of severity ¹								
No	45 (57.0)	0.61 (0.39 - 0.96)*	0.56 (0.35 - 0.91)*	0.54 (0.33 - 0.87)*	56 (70.9)	0.74 (0.46 - 1.21)	0.61 (0.37 - 1.01)	0.52 (0.31 - 0.87)*
Yes	23 (46.0)	0.39 (0.23 - 0.69)***	0.43 (0.24 - 0.77)**	0.39 (0.21 - 0.71)**	27 (54.0)	0.36 (0.20 - 0.63)***	0.37 (0.20 - 0.66)***	0.31 (0.17 - 0.56)***
Any indicator of risk ²								
No	54 (59.3)	0.68 (0.44 - 1.03)	0.64 (0.41 - 1.00)	0.61 (0.39 - 0.96)*	64 (70.3)	0.72 (0.46 - 1.14)	0.65 (0.40 - 1.04)	0.56 (0.35 - 0.91)*
Yes	14 (36.8)	0.27 (0.14 - 0.52)***	0.28 (0.14 - 0.57)***	0.25 (0.12 - 0.51)***	19 (50.0)	0.31 (0.16 - 0.58)***	0.27 (0.14 - 0.54)***	0.22 (0.11 - 0.44)***

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

ACEI/ARB=angiotensin-converter enzyme inhibitor/angiotensin receptor blocker.¹ Includes any of: ever had an inpatient stay, any record of being treated under the Mental Health Act, any record of difficulty managing their physical health, or any record of an Assertive Outreach/Crisis/A&E episode. ²Includes any of: recorded history of violence, recorded history of non-compliance, and any record of a forensic history.

^aAdjusted for age (continuous), gender, ethnicity, borough-level deprivation and recorded coronary heart disease/heart failure; ^b additionally adjusted for mean annual number of primary consultations.