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INVESTIGATING MENTAL AND PHYSICAL COMORBIDITY: Protocol for a survey in people with severe mental illness in South Asia (IMPACT SMI survey)

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3 1 **INVESTIGATING MENTAL AND PHYSICAL COMORBIDITY: Protocol for a survey in people with severe**
4 2 **mental illness in South Asia (IMPACT SMI survey)**

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2
3 31 **Abstract**
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5 32 **Introduction:** People with severe mental illness (SMI) die on average 10-20 years earlier than the
6 33 general population. Most of these deaths are due to physical health conditions. The aim of this cross-
7 34 sectional study is to determine the prevalence and determinants of physical disorders in people with
8 35 SMI attending specialist mental health facilities in South Asia.

9 36 **Methods:** We will conduct a survey of patients with SMI attending specialist mental health facilities in
10 37 Bangladesh, India and Pakistan (n=4,500). Diagnosis of SMI will be confirmed using the MINI V-6.0. We
11 38 will collect information about: physical health and related health-risk behaviours (WHO STEPs); severity
12 39 of common mental disorders (PHQ-9 and GAD-7); and health-related quality of life (EQ-5D-5L). We will
13 40 measure blood pressure, height, weight and waist-circumference according to WHO guidelines. We will
14 41 also measure glycated haemoglobin (HbA1c), lipid profile, thyroid function, liver function, creatinine
15 42 and haemoglobin.

16 43 **Analysis:** Prevalence rates of physical health conditions and health-risk behaviours will be presented
17 44 and compared with the WHO STEPs survey findings in the general population. Regression analyses will
18 45 explore the association between health-risk behaviours, mental and physical health conditions. The
19 46 IMPACT SMI survey will provide the prevalence of different physical health conditions and health-risk
20 47 behaviours in the SMI population, and the influence of each of these conditions in terms of health
21 48 related quality of life

22 49 **Ethics and dissemination:** The study has been approved by the ethics committees of the Department
23 50 of Health Sciences University of York (UK), Centre for Injury Prevention and Rehabilitation (Bangladesh),
24 51 Health Ministry Screening Committee and Indian Council of Medical Research (India) and National
25 52 Bioethics Committee (Pakistan). Findings will be disseminated in peer reviewed articles, in local and
26 53 international conferences and as reports for policy makers and stakeholders in the countries involved.

27 54 **Trial registration:** ISRCTN88485933; <https://doi.org/10.1186/ISRCTN88485933>, 3th of June 2019

28 55 **Key words:** Multimorbidity, Comorbidity, Lifestyle, Severe mental illness, South Asia, health risk
29 56 behaviours, schizophrenia, bipolar disorders, psychosis
30 57

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3 58 **Article summary**
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5 59 ***Strengths and limitations***
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- 7 60 • The IMPACT SMI survey will provide the prevalence of different physical health conditions and
8 61 health-risk behaviours in the SMI population in the South Asian region for the first time.
- 9 62 • The study is using standardized tools to measure patient outcomes that will allow us to
10 63 compare the findings with those of the general population.
- 11
12 64 • The survey is being conducted in specialist centres (with patients with capacity) and is
13 65 therefore a health care utilisation sample drawn largely from tertiary care.
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67 Background

68 A considerable body of research has shown that people with severe mental illness (SMI; i.e. psychotic
69 disorders, bipolar affective disorder and severe depression with psychosis) die on average 10-20 years
70 earlier than the general population^{1 2}. This excess mortality is a major global public health challenge
71 but efforts to address it have been limited. Recent studies suggest that despite an overall improvement
72 in life expectancy for both the general population and people with severe mental illness, the absolute
73 mortality gap between these two groups is actually widening³⁻⁵.

74 Around 80% of deaths in people with SMI are due to preventable physical illnesses, most commonly
75 cardio-metabolic diseases, respiratory disorders, and infectious diseases^{6 7}. Prevalence of most physical
76 health conditions is higher and outcomes are poorer in this population.⁸ Multimorbidity (the presence
77 of two or more conditions) is also more common⁹ in the presence of SMI, contributing to poorer
78 physical health and quality of life. The majority of evidence for these health inequalities has been
79 generated in high-income countries (HICs), but a small number of studies from low- and middle-income
80 countries (LMICs) also show a similar pattern of increased mortality for people with SMI, with an even
81 shorter life expectancy, and larger mortality gap^{7 10-12}. The few studies available suggest that physical
82 comorbidity in SMI is at least as prevalent as in developed countries¹.

83 In South Asia, rates of mental illness and non-communicable diseases have been increasing rapidly¹³
84¹⁴. This increase, coupled with the lack of access to even basic mental healthcare¹⁵, and neglect of the
85 physical health needs of people with SMI by policymakers and healthcare services¹⁶, means that the
86 burden of disease due to physical disorders in people with mental illness is set to rise further, with a
87 corresponding increase in within country and global health inequalities. Addressing mental and physical
88 health comorbidity in LMICs is a global priority, recognized in global policies to help achieve the
89 Sustainable Development Goals, including “ensuring healthy lives and promoting well-being for all”¹⁷⁻
90¹⁹. A detailed understanding of the determinants of physical ill health in SMI in LMICs is needed to
91 progress this agenda²⁰.

92 Objectives

93 In people with SMI attending specialist mental health facilities:

- 94 1. Determine the prevalence of physical disorders and health-risk behaviours and compare these
95 findings with those established in the general population.
- 96 2. Determine the association between physical disorders, health-risk behaviours, health-related
97 quality of life and various demographic, behavioural, cognitive, psychological and social
98 variables.
- 99 3. Identify lifestyle advice that has been offered for this SMI population.
- 100 4. Support clinical trial readiness by providing evidence-based findings regarding outcome
101 measures and procedures relevant for clinical trials design.

102 Methods and analysis

103 Design, settings & population

104 We will conduct a cross-sectional survey among patients with a clinical diagnosis of SMI recruited at
105 specialist mental health institutions in Bangladesh (National Institute of Mental Health (NIMH)), India
106 (National Institute of Mental Health and Neurosciences (NIMHANS)) and Pakistan (Institute of
107 Psychiatry (IoP)). All three are national institutes offering specialist mental health services. Adults (18
108 years and over) with a clinical diagnosis of SMI (i.e. schizophrenia, schizoaffective disorder, bipolar
109 affective disorder, severe depression with psychosis) that are able to provide informed consent as
110 assessed by the treating clinician will be recruited. Patients who lack capacity to provide consent or are
111 unable to complete study questionnaires will be excluded (figure 1). The data will be collected from
112 June 2019 until September 2020.

113

114

115 **Figure 1.** Flow diagram of the study



116
117 **Sample size**

118 We aim to build as large a sample as possible within the resources available over the study period
119 (n=4500). As an indicative example of survey precision to address some of the key research questions,
120 we provide a sample size estimate for investigating the prevalence of diabetes. Assuming a prevalence
121 estimate of 10% (based on results from previous studies²¹), we will need 857 participants per country
122 to achieve $\pm 2\%$ precision assuming a 95% confidence interval²².

123 **Recruitment and random selection of the participants**

124 Both in- and outpatients attending the specialist mental health institutions of the study will be
125 recruited. When resources or the volume of patients do not allow recruitment of all patients presenting
126 at the institution, we will use random selection of attending patients.

127 **Informed consent**

128 In the first instance, the researchers will give an information sheet to the patient, providing written and
129 verbal information on the potential benefits and risks of taking part in the study and clarifying the
130 assessments involved in the study. Only people who provided written informed consent will be included
131 in the study. Where there are problems with literacy, the researchers will provide this information
132 verbally to both the carer and the patient. Those unable to provide a signature will be requested to
133 indicate their consent with a thumbprint. The information sheet will meet all the requirements of the
134 relevant ethics committees. Maintenance of confidentiality and compliance with international, UK and
135 relevant local Data Protection Acts will be emphasised to all study participants. Moreover, all
136 participants will be informed that their participation in the study is voluntary, consent can be
137 withdrawn at any stage and the decision about participation will not affect their care.

138 Mental capacity is time- and decision-specific. For patients who are assessed to lack capacity by their
139 local physician, seeking informed consent will be delayed until capacity is regained, if feasible. No
140 assessments will be continued where the patient appears reluctant, even where patient consent has
141 been obtained.

142 Optional 'consent to contact' about future studies will be sought from survey participants. Permission
143 will be sought to retain participant details and to contact participants about future studies that may be
144 relevant for them. Again, it will be emphasised that this is voluntary, they can withdraw permission at
145 any time and this will not affect their care in any way. After consenting to participate, the participant
146 will be given a unique patient identifier (ID) by the researcher. The patient consent and contact
147 information will be entered into a database (participant log), which will be kept separate from the
148 survey results database. The survey results database will include only the unique patient ID, and no
149 patient identifiable data.

150 **Confirmation of eligibility**

151 SMI diagnosis will be confirmed by trained researchers using the relevant modules from the Mini-
152 international neuropsychiatric interview (MINI) version 6.0²³. The MINI is a short diagnostic structured
153 interview to explore mental disorders. It is designed to allow administration by non-specialist
154 interviewers²⁴. The inter-rater reliability for the MINI will be assessed at each site at the start of study.
155 Within each study site, at least 10 MINI questionnaires will be completed and compared between two
156 different researchers blinded from each other. Where needed, further training will be offered to
157 achieve acceptable inter-rater reliability before researchers are assigned to the study.

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60**158 Data collection**

159 We will conduct a face-to-face digital survey to collect information about physical health and health-
160 risk behaviours, severity of common mental disorders and health-related quality of life using validated
161 instruments as described below.

162 The WHO STEPwise approach to Surveillance (STEPS) instrument Version 3.2 will be used to collect
163 information about non-communicable diseases and related health-risk behaviours²⁵. STEPs is an
164 international standardized tool that will allow comparisons with the general population within the
165 country and between countries²⁶. The instrument has already been translated, used and validated in
166 the general population in Bangladesh, India and Pakistan ²⁷⁻²⁹.

167 To allow patients to disclose information on sexually transmitted diseases, HIV diagnosis, alcohol and
168 tobacco consumption, in agreement with patient's wishes, the interviewer will ask the caregivers/
169 attendants to leave the room for this part of the interview

170 Demographic information

171 The STEPs demographic module will be used to collect information on age, sex, education, marital
172 status, employment and income ²⁵.

173 Health-risk behaviours

174 The STEPs tobacco modules will be used to assess tobacco-related behaviours ²⁵.

175 Alcohol consumption

176 The STEPs alcohol module will be used to determine lifetime abstainers, past 12 months abstainers and
177 current users of alcohol using the WHO cut-off scores ²⁵.

178 Diet

179 The STEPs diet module will be used to record the number of days that respondents consumed fruit and
180 vegetables in a typical week, and the number of servings of fruit and vegetables consumed on average
181 per day ³⁰.

182 Physical activity

183 The STEPs physical activity module will be used to record activity for transport purposes (e.g. walking,
184 cycling), vigorous and moderate activity at work, and vigorous, moderate activity in leisure time, and
185 time spent sitting. Show-cards with culturally relevant examples will be used to aid respondents in
186 classifying activities. Analysis and categorization will follow the WHO guidelines³¹.

187 Non-communicable diseases

188 Any medically-diagnosed history of raised blood pressure, heart disease, hypercholesterolemia, and
189 high blood glucose, and treatment advised by a health worker for these diseases (such as prescribed
190 medicines, a special diet, advice to reduce salt intake, lose weight, stop smoking, or do more exercise)
191 will be collected using the STEPs module for non-communicable diseases. Lung disease is not included
192 in the STEPs survey. However, it will be recorded asking the same set of questions as the non-
193 communicable diseases included in the STEPs survey.

194 Infectious diseases

195 Self-report of medically-diagnosed history of hepatitis B, C, syphilis, tuberculosis, HIV and intestinal
196 parasites will be recorded.

197 Risk behaviours related to sexually transmitted diseases

198 Risk behaviours related to sexually transmitted diseases will be assessed using three questions that
199 examine the presence of multiple sexual partners, unprotected sexual contact and use of injectable
200 drugs that have been adapted from the 10 item HIV risk Screening Instrument ³². This instrument has
201 been previously used in research involving persons with severe mental illness in India ³³.

202 *Depressive and anxiety symptoms*

203 The 9-item depression module (PHQ-9)³⁴ will be used to measure the severity of depressive symptoms
204 and the generalized anxiety disorder 7 item scale (GAD-7)³⁵ for the severity of anxiety symptoms.

205 *Health-Related Quality of life*

206 The EQ-5D-5L will be used to measure health-related quality of life^{36,37}. The EQ-5D-5L is a standardised
207 measure of health status, it provides a simple, generic measure of health for clinical and economic
208 appraisal. The impact of disease/disorder is characterised on five dimensions (mobility, self-care, ability
209 to undertake usual activities, pain, anxiety / depression). The EQ-5D-5L further assesses a patient's
210 subjective evaluation of their health state based on a visual analogue scale (EQ-5d-VAS) between "0 -
211 worst imaginable health state" and "100 - best imaginable health state".

212 *Blood pressure and heart rate*

213 Blood pressure (BP) and pulse rate will be taken three times using an automated blood pressure
214 measuring instrument (OMRON®). For BP measurement the participant must be comfortable and
215 rested. If he/she had been exerting themselves, then there will be a minimum of a 15 minute rest period
216 before the recording is taken. There should be at least a three minute gap between the BP recordings.
217 The procedure will follow the step wise instructions in the WHO STEPS surveillance manual³⁸.

218 *Height weight and waist circumference*

219 Height will be measured to a precision of 0.1 cm using a portable height measuring board without
220 footwear and headgear. Weight will be measured in kilograms using a portable weighing scale placed
221 on a firm flat surface with light clothing and without footwear and socks. Waist circumference will be
222 measured in to a precision of 0.1 cm, using a flexible fibre glass anthropometric tape at the end of
223 normal expiration, at the midpoint between the lower margin of the last palpable rib and the top of the
224 iliac crest (hip bone), with the arms relaxed at the sides. All measurements will be taken in duplicate
225 and the average of the two values will be recorded and the protocols of the WHO STEPS surveillance
226 manual will be followed³⁸.

227 *Biochemical analysis*

228 A blood sample (8 to 9 ml) will be taken from consenting participants for: glycated haemoglobin
229 (HbA1c), lipid profile (triglycerides, total cholesterol, HDL cholesterol, LDL cholesterol), thyroid function
230 tests (includes T3, T4, TSH), liver function tests (total Bilirubin, AST, ALT, ALP, total protein, albumin,
231 albumin to globulin ratio), creatinine and haemoglobin.

232 *Data management*

233 To ensure quality of collected data, validation, checking, proofing and cleaning procedures will be
234 carried out according to standard procedures³⁹. All consent forms will be stored separately from survey
235 data in locked cabinets in locked offices at study research offices at each study site. All coded data will
236 be transferred to, and stored as anonymous data at the University of York which will act as the data
237 curator. A secure password protected and encrypted electronic database will be set up to store the
238 data.

239 *Statistical analysis*

240 Quantitative data will be summarised using descriptive statistics. First, prevalence rates of infectious
241 diseases, long-term physical health conditions (e.g. diabetes, heart disease) and health-risk behaviours
242 for type II diabetes, cardiovascular and respiratory disorders (e.g. tobacco use, obesity, physical activity,
243 diet) will be estimated in the severe mental illness population. Second, these rates will be compared
244 with results from the WHO STEPs survey in the general population. Finally, we will examine the
245 associations between physical health conditions and health-risk behaviours, using regression models
246 with random intercepts for data collection site with the following potential covariates: demographic
247 variables (i.e. age, sex, and level of education), history of mental and physical conditions and
248 biomarkers (e.g. BMI, blood pressure). These regression models will also be used to calculate
249 prevalence rates of physical health conditions and health-risk behaviors adjusted for these covariates.

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250 Further regression analyses will explore the association between mental and physical health conditions
251 and health-related quality of life measured using EQ-5D-5L.

252 Regression models will take account of the nature and distribution of data (e.g. count versus continuous
253 data; skewed versus normally distributed data). Additional analyses using network models⁴⁰ and
254 psychometric approaches will investigate comorbidity patterns (within and across physical and mental
255 symptoms) as well as the structure of severe mental illness symptoms⁴¹⁻⁴³.

256

257 **Ethics and dissemination**

258 The study has been approved by the ethics committees of the Department of Health Sciences University
259 of York (UK), Centre for Injury Prevention and Rehabilitation (Bangladesh), Health Ministry Screening
260 Committee and Indian Council of Medical Research (India) and National Bioethics Committee
261 (Pakistan).

262 The study will adhere to the fundamental principles of human rights and dignity laid down in the
263 Declaration of Helsinki⁴⁴. Study procedures will comply with legislation and guidance for good practice
264 governing the participation in research of people lacking capacity as set out in the Mental Capacity Act
265 (UK) 2005⁴⁵. Participants will not receive any financial inducement to participate, but the results of the
266 physical measurements and blood tests will be shared with the participant and the treating clinician.

267 As a non-interventional study, there is minimal risk of adverse events associated with the study. Due to
268 the vulnerability of the severe mental illness population, however, there is a potential (albeit low) risk
269 that some questions or the burden of the assessments may cause distress for participants or the family
270 carers. If there is any indication of this, the survey or assessments will be stopped, the participant
271 offered reassurance and support, and if needed, referral to the clinical team. If a participant during the
272 interview reveals any suicidal ideation, the interviewer will refer them to the treating clinician for a
273 clinical risk assessment and further management. If a physical condition or blood test abnormality
274 (outside the normal range for age and sex) is detected as a part of the research assessments, the
275 research team will inform the clinician responsible for the patient, who will evaluate the result and give
276 the patient the option of referral to a specialist if this is required for their condition.

277 **Community, patient and public involvement**

278 A 'Community Panel' comprising stakeholders from these constituencies ensures community, patient
279 and public involvement. The Panel has reviewed the planned survey and advised on its feasibility. The
280 panel will continue to provide feedback on the conduct of the study and presentation of findings. To
281 support dissemination efforts, findings will be presented to the community panel, with advice sought
282 about the format and content of lay summaries and other outputs aimed at patients and the public.

283 **Dissemination**

284 Findings will be disseminated in peer-reviewed articles, in local and international conferences and as
285 reports for policy makers and stakeholders in the countries involved.

286 **Discussion**

287 People with SMI have a reduced life expectancy. Research in high income countries has shown that a
288 large proportion of this inequality is accounted for by chronic diseases^{1 2}. This has been consistently
289 observed in high income countries^{6 7}. However information is lacking in minority groups and LMICs,
290 which is surprising considering the increased risk of physical health conditions in these populations due
291 to poverty, education, poor diet, low access to healthcare, exposure to infectious diseases and other
292 environmental factors⁴⁶. The IMPACT SMI survey will address this gap in knowledge, demonstrating
293 the prevalence of different physical health conditions and health-risk behaviours in the SMI population,
294 and the influence of each of these conditions in terms of health related quality of life. It will support
295 SMI clinical trial readiness by providing evidence-based findings regarding outcome measures and
296 procedures relevant for clinical trials design.

297 **Strengths and limitations**

298 To the best of the authors' knowledge, this will be the first large scale study to investigate the physical
299 health and health-risk behaviours in the SMI population in LMICs. The main limitation is that the survey
300 is conducted in specialist centres (with patients with capacity) and is therefore a health care utilisation
301 sample drawn largely from tertiary care. The gaps in treatment and care utilisation and systematic
302 factors influencing these have been well documented (e.g.⁴⁷), therefore, the study population may not
303 be representative of the total severe mental illness population in each country. However, a community
304 survey would not be feasible, and primary and secondary care mental health services are not
305 sufficiently developed to be used to recruit participants for this survey (see for example work by PRIME
306¹⁵ and Emerald⁴⁸ programmes on strengthening these services as access points). However, unlike
307 services in high-income countries, tertiary care services in these South Asian countries accept self-
308 referral without the need for primary or secondary care referral and we include outpatient services
309 offered by the collaborating centres which often function as 'the first port of call' for people with mental
310 illness⁴⁹⁻⁵¹. Therefore, the selected centres are likely covering a broad range of the treatment-seeking
311 population.

312 **Conclusion**

313 Multimorbidity in people with SMI is not well documented particularly in low- and middle-income
314 countries. The IMPACT survey will be the first to study it using a standardised approach in South Asia
315 that can be compared to the general population.

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460 **Authors' contributions**

461 NS conceived the study, KP, FA, DB, RH, SM, PM, AN, SK and KS provided important contextual
462 information, KP, FP, DB, RH, SM, NS and JB developed the methodology and selected the outcomes,
463 GZ, AH, KH and JB developed the analysis plan, GZ, NS, KS and JB wrote the manuscript, and all authors
464 revised and approved the manuscript.

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470 preparation of the manuscript.

471 **Competing interests statement**

472 The authors declare that they have no competing interests

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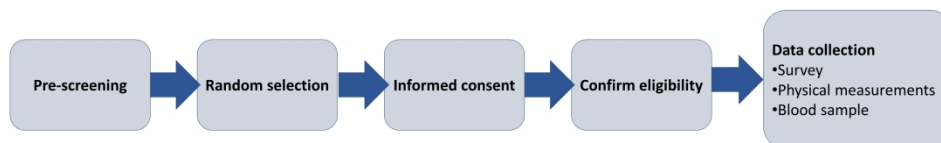


Figure 1. Flow diagram of the study

1399x600mm (96 x 96 DPI)

INVESTIGATING MENTAL AND PHYSICAL COMORBIDITY: Protocol for a survey in people with severe mental illness in South Asia (IMPACT SMI survey)

STROBE Statement—Checklist of items that should be included in reports of *cross-sectional studies*

| | Item No | Recommendation |
|------------------------------|---------|--|
| Title and abstract | 1 | (a) Indicate the study's design with a commonly used term in the title or the abstract Title and abstract lines 1 to 56 |
| | | (b) Provide in the abstract an informative and balanced summary of what was done and what was found Abstract lines 32 to 56 |
| Introduction | | |
| Background/rationale | 2 | Explain the scientific background and rationale for the investigation being reported Background paragraphs 1 to 3 |
| Objectives | 3 | State specific objectives, including any prespecified hypotheses Background, objectives section lines 93 to 101 |
| Methods | | |
| Study design | 4 | Present key elements of study design early in the paper Methods paragraph 1 design setting and population 103 to 115 |
| Setting | 5 | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection Methods paragraph 1 design setting and population lines 103 to 115 |
| Participants | 6 | (a) Give the eligibility criteria, and the sources and methods of selection of participants Methods paragraph 1 design setting and population lines 103 to 115 |
| Variables | 7 | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable Methods, data collection section lines 158 to 231 |
| Data sources/ measurement | 8* | For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group Methods, data collection section lines 158 to 231 |
| Bias | 9 | Describe any efforts to address potential sources of bias Discussion, strengths and limitation section lines 297 to 307 |
| Study size | 10 | Explain how the study size was arrived at Methods section Sample size lines 298 to 311 |
| Quantitative variables | 11 | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why NA |
| Statistical methods | 12 | (a) Describe all statistical methods, including those used to control for confounding Methods Statistical analysis section lines 240 to 255 |
| | | (b) Describe any methods used to examine subgroups and interactions Methods Statistical analysis section lines 240 to 255 |
| | | (c) Explain how missing data were addressed NA |
| | | (d) If applicable, describe analytical methods taking account of sampling strategy Methods, Recruitment and random selection of the participants lines 123 to 126 |
| | | (e) Describe any sensitivity analyses |

Methods Statistical analysis section lines 239 to 255

| Results | | |
|--------------------------|-----|---|
| Participants | 13* | (a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed NA (b) Give reasons for non-participation at each stage NA (c) Consider use of a flow diagram NA |
| Descriptive data | 14* | (a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (b) Indicate number of participants with missing data for each variable of interest NA |
| Outcome data | 15* | Report numbers of outcome events or summary measures NA |
| Main results | 16 | (a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (b) Report category boundaries when continuous variables were categorized (b) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period NA |
| Other analyses | 17 | Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses NA |
| Discussion | | |
| Key results | 18 | Summarise key results with reference to study objectives NA |
| Limitations | 19 | Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias NA |
| Interpretation | 20 | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence NA |
| Generalisability | 21 | Discuss the generalisability (external validity) of the study results NA |
| Other information | | |
| Funding | 22 | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based NA |

*Give information separately for exposed and unexposed groups.

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2 **Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and
3 published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely
4 available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at
5 <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is
6 available at www.strobe-statement.org.
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BMJ Open

Prevalence of physical health conditions and health risk behaviours in people with severe mental illness in South Asia: Protocol for a cross-sectional study (IMPACT SMI survey)

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3 **1 Prevalence of physical health conditions and health risk behaviours in people with severe mental**
4 **2 illness in South Asia: Protocol for a cross-sectional study (IMPACT SMI survey)**

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6 3 G.A. Zavala¹, K. Prasad-Muliyala², F. Aslam³, D. Barua⁴, A. Haidar⁴ C. Hewitt¹, R. Huque⁴, S. Mansoor³, P.
7 4 Murthy², A. T. Nizami³, N. Siddiqi^{1,5,6}, S. Sikander^{7,8}, K. Siddiqi^{1,5}, J.R. Boehnke^{1,9} and on behalf of the
8 5 IMPACT team.

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31 Abstract

32 **Introduction:** People with severe mental illness (SMI) die on average 10-20 years earlier than the
33 general population. Most of these deaths are due to physical health conditions. The aim of this cross-
34 sectional study is to determine the prevalence of physical health conditions and their associations with
35 health-risk behaviours, health-related quality of life and various demographic, behavioural, cognitive,
36 psychological and social variables in people with SMI attending specialist mental health facilities in
37 South Asia.

38 **Methods and analysis:** We will conduct a survey of patients with SMI attending specialist mental health
39 facilities in Bangladesh, India and Pakistan (n=4,500). Diagnosis of SMI will be confirmed using the MINI
40 V-6.0. We will collect information about: physical health and related health-risk behaviours (WHO
41 STEPs); severity of common mental disorders (PHQ-9 and GAD-7); and health-related quality of life (EQ-
42 5D-5L). We will measure blood pressure, height, weight and waist-circumference according to WHO
43 guidelines. We will also measure glycated haemoglobin (HbA1c), lipid profile, thyroid function, liver
44 function, creatinine and haemoglobin. Prevalence rates of physical health conditions and health-risk
45 behaviours will be presented and compared with the WHO STEPs survey findings in the general
46 population. Regression analyses will explore the association between health-risk behaviours, mental
47 and physical health conditions.

48 **Ethics and dissemination:** The study has been approved by the ethics committees of the Department
49 of Health Sciences University of York (UK), Centre for Injury Prevention and Rehabilitation (Bangladesh),
50 Health Ministry Screening Committee and Indian Council of Medical Research (India) and National
51 Bioethics Committee (Pakistan). Findings will be disseminated in peer reviewed articles, in local and
52 international conferences and as reports for policy makers and stakeholders in the countries involved.

53 **Trial registration:** ISRCTN88485933; <https://doi.org/10.1186/ISRCTN88485933>, 3rd of June 2019

54 **Key words:** Multimorbidity, Comorbidity, Lifestyle, Severe mental illness, South Asia, health risk
55 behaviours, schizophrenia, bipolar disorders, psychosis

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57 **Article summary**

58 ***Strengths and limitations***

- 59 • The study uses standardized tools to measure patient outcomes that will allow us to compare
60 the findings with those of the general population.
- 61 • The survey will be conducted face to face by trained researchers
- 62 • The questionnaire has been translated into the most common languages used in Bangladesh
63 India and Pakistan using validated translations of standardized measures where available.
- 64 • The survey is being conducted in specialist centres and is therefore a health care utilisation
65 sample drawn largely from tertiary care.
- 66 • The study population may not be representative of all the people with severe mental illness in
67 each country, as those not accessing specialist centres are not included in the survey.

69 Background

70 A considerable body of research has shown that people with severe mental illness (SMI; i.e. psychotic
71 disorders, bipolar affective disorder and severe depression with psychotic symptoms) die on average
72 10-20 years earlier than the general population^{1,2}. Around 80% of deaths in people with SMI are due
73 to preventable physical illnesses, most commonly cardio-metabolic diseases, respiratory disorders, and
74 infectious diseases^{3,4}. This excess mortality is a major global public health challenge but efforts to
75 address it have been limited. Recent studies suggest that despite an overall improvement in life
76 expectancy for both the general population and people with SMI, the absolute mortality gap between
77 these two groups is actually widening⁵⁻⁷.

78 Prevalence of most physical health conditions is higher and outcomes are poorer in this population⁸.
79 Multimorbidity (the presence of two or more conditions) is also more common⁹ in the presence of SMI,
80 contributing to poorer physical health and quality of life. The majority of evidence for these health
81 inequalities has been generated in high-income countries (HICs), but a small number of studies from
82 low- and middle-income countries (LMICs) also show a similar pattern of increased mortality for people
83 with SMI, with an even shorter life expectancy, and larger mortality gap^{4,10-12}. The few studies available
84 suggest that physical comorbidity in SMI is at least as prevalent as in developed countries¹.

85 In South Asia, rates of mental illness and physical non-communicable diseases have been increasing
86 rapidly^{13,14}. This increase, coupled with the lack of access to even basic mental healthcare¹⁵, and
87 neglect of the physical health needs of people with SMI by policymakers and healthcare services¹⁶,
88 means that the burden of disease due to physical disorders in people with mental illness is set to rise
89 further, with a corresponding increase within country and global health inequalities. This increase is
90 coupled with a recognized lack of information about the prevalence of physical conditions and health
91 risk behaviours in the SMI population in South Asia¹⁷. This gap in knowledge, particularly in relation to
92 health service planning in LMICs, has been pointed out repeatedly as a priority for research¹⁸.
93 Addressing mental and physical health comorbidity in LMICs is also a global priority, recognized in global
94 policies to help achieve the Sustainable Development Goals, including “ensuring healthy lives and
95 promoting well-being for all”¹⁹⁻²¹. A detailed understanding of the prevalence of physical health
96 conditions, health risk behaviours and health service utilization in SMI in LMICs is needed to progress
97 this agenda²².

98 Objectives

99 In people with SMI attending specialist mental health facilities:

- 100 1. Determine the prevalence of physical health conditions (i.e. type 2 diabetes, hypertension,
101 heart disease, obesity and infectious diseases) and health-risk behaviours (i.e. diet, physical
102 activity, alcohol and tobacco use) and compare these findings with those reported in the
103 general population.
- 104 2. Determine the association between physical health conditions, health-risk behaviours, health-
105 related quality of life and various demographic, behavioural, cognitive, psychological and
106 social variables.
- 107 3. Identify health-service utilization and the type of lifestyle advice that has been offered for this
108 SMI population.
- 109 4. Support clinical trial readiness by providing evidence-based findings regarding outcome
110 measures and procedures relevant for clinical trials design.

111 Methods and analysis

112 Design, settings & population

113 We will conduct a cross-sectional survey among patients with a clinical diagnosis of SMI recruited at
114 national specialist mental health institutions. In Bangladesh the study will be conducted at the National
115 Institute of Mental Health and Hospital (NIMH) in Dhaka. NIMH offers 200 beds for in-patient care
116 and on average 400 out-patients attend every day. In India the study will be conducted at the National
117 Institute of Mental Health and Neurosciences (NIMHANS) in Bengaluru, with 650 beds for in-patient
118 care; on average at NIMHANS 400 out-patients attend every day. In Pakistan, the study will be

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3 119 conducted at the Institute of Psychiatry (IOP) Rawalpindi Medical University, a WHO collaborating
4 120 centre for the Eastern Mediterranean (EMRO). IOP offers 60 beds for inpatients and on average 400
5 121 out-patients attend every day. All three national institutes serve patients from all over the country.
6 122 Adults (18 years and over) with a clinical diagnosis of SMI (defined by the International Classification of
7 123 Disease 10th revision (ICD-10²³) as schizophrenia, schizotypal and delusional disorders (F20-F29); bipolar
8 124 affective disorder (F30, F31); and severe depression with psychotic symptoms (F32.3, F33.3)²³, who
9 125 are able to provide informed consent as assessed by the treating clinician will be recruited. Patients
10 126 who lack capacity to provide consent or are unable to complete study questionnaires will be excluded
11 127 (figure 1). The data will be collected from June 2019 until September 2020.

128 **Sample size**

129 We aim to build as large a sample as possible within the resources available over the study period
130 (n=1500 per country). As an indicative example of survey precision to address some of the key research
131 questions, we provide a sample size estimate for investigating the prevalence of diabetes. Assuming a
132 prevalence estimate of 10% (based on results from previous studies ²⁴), we will need 857 participants
133 per country to achieve $\pm 2\%$ precision assuming a 95% confidence interval²⁵.

134 **Recruitment and random selection of the participants**

135 Both in- and outpatients attending one of the three specialist mental health institutions collaborating
136 in this study will be recruited. At NIMHH and NIMHANS patients will be selected randomly using random
137 number tables generated centrally to determine for outpatients, which patient to approach on a given
138 day, and for inpatients by randomly selecting beds. Recruitment is separated by in- vs outpatients,
139 resulting in a proportion of 80% outpatients and 20% inpatients (which has been reported as the
140 "usual" proportion of in- and outpatients). Due to the lower volume of patients and outpatients
141 reaching the centre outside working hours at the IOP, all patients attending the IOP during the study
142 duration will be invited to participate in the survey.

143 **Informed consent**

144 In the first instance, the researchers will give an information sheet to the patient, providing written and
145 verbal information on the potential benefits and risks of taking part in the study and clarifying the
146 assessments involved in the study. Only people who provided written informed consent will be included
147 in the study. Where there are problems with literacy, the researchers will provide this information
148 verbally to both the carer and the patient. Those unable to provide a signature will be requested to
149 indicate their consent with a thumbprint. The information sheet will meet all the requirements of the
150 relevant ethics committees. Maintenance of confidentiality and compliance with international, UK and
151 relevant local Data Protection Acts will be emphasised to all study participants. Moreover, all
152 participants will be informed that their participation in the study is voluntary, consent can be
153 withdrawn at any stage and the decision about participation will not affect their care.

154 Mental capacity is time- and decision-specific. For patients who are assessed to lack capacity by their
155 local physician, seeking informed consent will be delayed until capacity is regained, if feasible. No
156 assessments will be continued where the patient appears reluctant, even where patient consent has
157 been obtained.

158 Optional 'consent to contact' about future studies will be sought from survey participants. Permission
159 will be sought to retain participant details and to contact participants about future studies that may be
160 relevant for them. Again, it will be emphasised that this is voluntary, they can withdraw permission at
161 any time, and this will not affect their care in any way. After consenting to participate, the participant
162 will be given a unique patient identifier (ID) by the researcher. The patient consent and contact
163 information will be entered into a database (participant log), which will be kept separate from the
164 survey results database. The survey results database will include only the unique patient ID, and no
165 patient identifiable data.

166 **Confirmation of eligibility**

167 SMI diagnosis will be confirmed by trained researchers using the relevant modules from the Mini-
168 international neuropsychiatric interview (MINI) version 6.0 ²⁶. The MINI is a short diagnostic structured
169 interview to explore mental disorders. It is designed to allow administration by non-specialist

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170 interviewers²⁷. The inter-rater reliability for the MINI will be assessed at each site at the start of study.
171 Within each study site, at least 10 MINI questionnaires will be completed and compared between two
172 different researchers blinded from each other. Where needed, further training will be offered to
173 achieve acceptable inter-rater reliability before researchers are assigned to the study.

174 **Data collection**

175 We will conduct a face-to-face digital survey to collect information about physical health and health-
176 risk behaviours, severity of common mental disorders and health-related quality of life using validated
177 instruments as described below. The survey has been translated into the most common languages in
178 the countries (Urdu in Pakistan, Bangla in Bangladesh and Hindi, Kannada, Tamil and Telugu for India).
179 The team of interviewers in each county will include males and females and will include researchers
180 that speak regional dialects, which is consistent with usual clinical practice in these settings²⁸.

181 The WHO STEPwise approach to Surveillance (STEPS) instrument Version 3.2 will be used to collect
182 information about non-communicable diseases and related health-risk behaviours²⁹. STEPs is an
183 international standardized tool that will allow comparisons with the general population within the
184 country and between countries³⁰. The instrument has already been translated, used and validated in
185 the general population in Bangladesh, India and Pakistan³¹⁻³³.

186 To allow patients to disclose information on sexually transmitted diseases, HIV diagnosis, alcohol and
187 tobacco consumption, in agreement with patient's wishes, the interviewer will ask the caregivers/
188 attendants to leave the room for this part of the interview.

189 *Demographic information*

190 The STEPs demographic module will be used to collect information on age, sex, education, marital
191 status, employment, household assets and income²⁹.

192 *Mental health*

193 We will collect information relevant to the SMI diagnosis of each participant, including duration of the
194 mental illness, any treatment or medication and duration of the treatment and/or medication. The 9-
195 item depression module (PHQ-9)³⁴ will be used to measure the severity of depressive symptoms and
196 the generalized anxiety disorder 7 item scale (GAD-7)³⁵ for the severity of anxiety symptoms.

197 *Health risk behaviours*

198 The STEPs tobacco modules will be used to assess tobacco-related behaviours²⁹.

199 *Alcohol consumption*

200 The STEPs alcohol module will be used to determine lifetime abstainers, past 12 months abstainers and
201 current users of alcohol using the WHO cut-off scores²⁹.

202 *Diet*

203 The STEPs diet module will be used to record the number of days that respondents consumed fruit and
204 vegetables in a typical week, and the number of servings of fruit and vegetables consumed on average
205 per day³⁶.

206 *Physical activity*

207 The STEPs physical activity module will be used to record activity for transport purposes (e.g. walking,
208 cycling), vigorous and moderate activity at work, and vigorous, moderate activity in leisure time, and
209 time spent sitting. Show-cards with culturally relevant examples will be used to aid respondents in
210 classifying activities. Analysis and categorization will follow the WHO guidelines³⁷.

211 *Non-communicable diseases*

212 Any medically-diagnosed history of raised blood pressure, heart disease, hypercholesterolemia, and
213 high blood glucose, and treatment advised by a health worker for these diseases (such as prescribed
214 medicines, a special diet, advice to reduce salt intake, lose weight, stop smoking, or do more exercise)
215 will be collected using the STEPs module for non-communicable diseases. Lung disease is not included

216 in the STEPSs survey. However, it will be recorded asking the same set of questions as the non-
217 communicable diseases included in the STEPs survey.

218 *Infectious diseases*

219 Self-report of medically diagnosed history of hepatitis B, C, syphilis, tuberculosis, HIV and intestinal
220 parasites will be recorded.

221 *Risk behaviours related to sexually transmitted diseases*

222 Risk behaviours related to sexually transmitted diseases will be assessed using three questions that
223 examine the presence of multiple sexual partners, unprotected sexual contact and use of injectable
224 drugs that have been adapted from the 10 item HIV risk Screening Instrument³⁸. This instrument has
225 been previously used in research involving persons with severe mental illness in India³⁹.

226 *Health-Related Quality of life*

227 The EQ-5D-5L will be used to measure health-related quality of life^{40,41}. The EQ-5D-5L is a standardised
228 measure of health status, it provides a simple, generic measure of health for clinical and economic
229 appraisal. The impact of disease/disorder is characterised on five dimensions (mobility, self-care, ability
230 to undertake usual activities, pain, anxiety / depression). The EQ-5D-5L further assesses a patient's
231 subjective evaluation of their health state based on a visual analogue scale (EQ-5d-VAS) between "0 -
232 worst imaginable health state" and "100 - best imaginable health state". We will use validated
233 translations provided by EUROQOL.

234 *Blood pressure and heart rate*

235 Blood pressure (BP) and pulse rate will be taken three times using an automated blood pressure
236 measuring instrument (OMRON®). For BP measurement the participant must be comfortable and
237 rested. If he/she had been exerting themselves, then there will be a minimum of a 15 minute rest period
238 before the recording is taken. There should be at least a three minute gap between the BP recordings.
239 The procedure will follow the step wise instructions in the WHO STEPS surveillance manual⁴².

240 *Height weight and waist circumference*

241 Height will be measured to a precision of 0.1 cm using a portable height measuring board without
242 footwear and headgear. Weight will be measured in kilograms using a portable weighing scale placed
243 on a firm flat surface with light clothing and without footwear and socks. Waist circumference will be
244 measured in to a precision of 0.1 cm, using a flexible fiberglass anthropometric tape at the end of
245 normal expiration, at the midpoint between the lower margin of the last palpable rib and the top of the
246 iliac crest (hip bone), with the arms relaxed at the sides. All measurements will be taken in duplicate
247 and the average of the two values will be recorded and the protocols of the WHO STEPS surveillance
248 manual will be followed⁴².

249 *Biochemical analysis*

250 A blood sample (8 to 9 ml) will be taken from consenting participants for: glycated haemoglobin
251 (HbA1c), lipid profile (triglycerides, total cholesterol, HDL cholesterol, LDL cholesterol), thyroid function
252 tests (includes T3, T4, TSH), liver function tests (total Bilirubin, AST, ALT, ALP, total protein, albumin,
253 albumin to globulin ratio), creatinine and haemoglobin.

254 *Data management*

255 To ensure quality of collected data, validation, checking, proofing and cleaning procedures will be
256 carried out according to standard procedures⁴³. All consent forms will be stored separately from survey
257 data in locked cabinets in locked offices at study research offices at each study site. All coded data will
258 be transferred to, and stored as anonymous data at the University of York which will act as the data
259 curator. A secure password protected and encrypted electronic database will be set up to store the
260 data.

261 **Statistical analysis**

262 Quantitative data will be summarised using descriptive statistics. First, prevalence rates of infectious
263 diseases, long-term physical health conditions (e.g. diabetes, heart disease) and health-risk behaviours
264 for type II diabetes, cardiovascular and respiratory disorders (e.g. tobacco use, obesity, physical activity,
265 diet) will be estimated in the severe mental illness population. Second, we will examine the associations
266 between physical health conditions and health-risk behaviours, using regression models with random
267 intercepts for data collection site with the following potential covariates: demographic variables (i.e.
268 age, sex, and level of education), history of mental and physical conditions and biomarkers (e.g. BMI,
269 blood pressure). These regression models will also be used to calculate prevalence rates of physical
270 health conditions and health-risk behaviours adjusted for these covariates (e.g., for comparison with
271 external general population data) Further regression analyses will explore the association between
272 mental and physical health conditions and health-related quality of life measured using EQ-5D-5L.
273 Regression models will take account of the nature and distribution of data (e.g. count versus continuous
274 data; skewed versus normally distributed data). To investigate the prevalence of physical health
275 conditions and health risk behaviours in the general population, we will extract aggregated data on the
276 prevalence of physical health conditions, health risk behaviours and lifestyle advice from the last
277 available WHO STEPs survey from Bangladesh⁴⁴, India⁴⁵ and Pakistan⁴⁶.

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279 **Ethics and dissemination**

280 The study has been approved by the ethics committees of the Department of Health Sciences University
281 of York (UK), Centre for Injury Prevention and Research (Bangladesh), Health Ministry Screening
282 Committee and Indian Council of Medical Research (India) and National Bioethics Committee
283 (Pakistan).

284 The study will adhere to the fundamental principles of human rights and dignity laid down in the
285 Declaration of Helsinki⁴⁷. Study procedures will comply with legislation and guidance for good practice
286 governing the participation in research of people lacking capacity as set out in the Mental Capacity Act
287 (UK) 2005⁴⁸. Participants will not receive any financial inducement to participate, but the results of the
288 physical measurements and blood tests will be shared with the participant and the treating clinician.

289 As a non-interventional study, there is minimal risk of adverse events associated with the study. Due to
290 the vulnerability of the severe mental illness population, however, there is a potential (albeit low) risk
291 that some questions or the burden of the assessments may cause distress for participants or the family
292 carers. If there is any indication of this, the survey or assessments will be stopped, the participant
293 offered reassurance and support, and if needed, referral to the clinical team. If a participant during the
294 interview reveals any suicidal ideation, the interviewer will refer them to the treating clinician for a
295 clinical risk assessment and further management. If a physical condition or blood test abnormality
296 (outside the normal range for age and sex) is detected as a part of the research assessments, the
297 research team will inform the clinician responsible for the patient, who will evaluate the result and give
298 the patient the option of referral to a specialist if this is required for their condition.

299 **Community, patient and public involvement**

300 A 'Community Panel' comprising stakeholders from these constituencies ensures community, patient
301 and public involvement. The Panel has reviewed the planned survey and advised on its feasibility. The
302 panel will continue to provide feedback on the conduct of the study and presentation of findings. To
303 support dissemination efforts, findings will be presented to the community panel, with advice sought
304 about the format and content of lay summaries and other outputs aimed at patients and the public.

305 **Dissemination**

306 Findings will be disseminated in peer-reviewed articles, in local and international conferences and as
307 reports for policy makers and stakeholders in the countries involved. An open access repository of all
308 materials will be built that covers the survey materials as well as statistical syntax used by the team
309 publications.

310 **Discussion**

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3 311 People with SMI have a reduced life expectancy. Research in high income countries has shown that a
4 312 large proportion of this inequality is accounted for by chronic diseases^{1,2}. This has been consistently
5 313 observed in high income countries^{3,4}. However information is lacking in minority groups and LMICs,
6 314 which is surprising considering the increased risk of physical health conditions in these populations due
7 315 to poverty, education, poor diet, low access to healthcare, exposure to infectious diseases and other
8 316 environmental factors⁴⁹. The IMPACT SMI survey will address this gap in knowledge, demonstrating
9 317 the prevalence of different physical health conditions and health-risk behaviours in the SMI population,
10 318 and the association of each of these conditions in terms of health related quality of life. It will support
11 319 SMI clinical trial readiness by providing evidence-based findings regarding outcome measures and
12 320 procedures relevant for clinical trials design.

14 321 **Strengths and limitations**

15 322 To the best of the authors' knowledge, this will be the first large scale study to investigate the physical
16 323 health and health-risk behaviours in the SMI population in LMICs. The main limitation is that the survey
17 324 is conducted in specialist centres (with patients with capacity) and is therefore a health care utilisation
18 325 sample drawn largely from tertiary care. The gaps in treatment and care utilisation and systematic
19 326 factors influencing these have been well documented⁵⁰, therefore, the study population may not be
20 327 representative of the total severe mental illness population in each country. However, a community
21 328 survey would not be feasible, and primary and secondary care mental health services are not
22 329 sufficiently developed to be used to recruit participants for this survey (see for example work by PRIME
23 330¹⁵ and Emerald⁵¹ programmes on strengthening these services as access points). However, unlike
24 331 services in high-income countries, tertiary care services in these South Asian countries accept self-
25 332 referral without the need for primary or secondary care referral and we include outpatient services
26 333 offered by the collaborating centres which often function as 'the first port of call' for people with mental
27 334 illness⁵²⁻⁵⁴. Therefore, the selected centres are likely covering a broad range of the treatment-seeking
28 335 population. We will not have a control group since the study is only conducted in people with SMI,
29 336 however we are using the same questions and measurements as the WHO STEPs survey. This will allow
30 337 us to compare the prevalence of physical health conditions and health risk behaviours with that of a
31 338 survey representative for the population in each country.

33 339 **Conclusion**

34 340 Multimorbidity in people with SMI is not well documented particularly in low- and middle-income
35 341 countries. The IMPACT survey will be the first to study it using a standardised approach in South Asia
36 342 that can be compared to the general population.

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45 349 taking the time to complete the survey.

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499 **Authors' contributions**

500 NS conceived the study, KP, FA, DB, RH, SM, PM, AN, SK and KS provided important contextual
501 information, KP, FP, DB, RH, SM, NS and JB developed the methodology and selected the outcomes,
502 GZ, AH, KH and JB developed the analysis plan, GZ, NS, KS and JB wrote the manuscript, and all authors
503 revised and approved the manuscript.

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510 **Competing interests statement**

511 The authors declare that they have no competing interests

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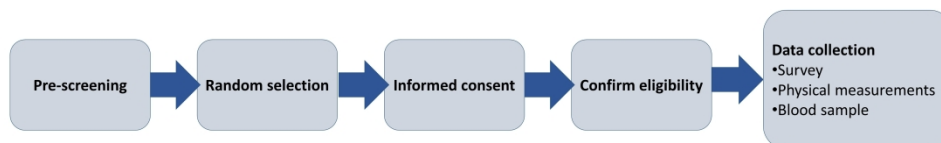


Figure 1. Flow diagram of the study

1399x600mm (96 x 96 DPI)

INVESTIGATING MENTAL AND PHYSICAL COMORBIDITY: Protocol for a survey in people with severe mental illness in South Asia (IMPACT SMI survey)

STROBE Statement—Checklist of items that should be included in reports of *cross-sectional studies*

| | Item No | Recommendation |
|------------------------------|---------|--|
| Title and abstract | 1 | (a) Indicate the study's design with a commonly used term in the title or the abstract Title and abstract lines 1 to 56 |
| | | (b) Provide in the abstract an informative and balanced summary of what was done and what was found Abstract lines 32 to 56 |
| Introduction | | |
| Background/rationale | 2 | Explain the scientific background and rationale for the investigation being reported Background paragraphs 1 to 3 |
| Objectives | 3 | State specific objectives, including any prespecified hypotheses Background, objectives section lines 93 to 101 |
| Methods | | |
| Study design | 4 | Present key elements of study design early in the paper Methods paragraph 1 design setting and population 103 to 115 |
| Setting | 5 | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection Methods paragraph 1 design setting and population lines 103 to 115 |
| Participants | 6 | (a) Give the eligibility criteria, and the sources and methods of selection of participants Methods paragraph 1 design setting and population lines 103 to 115 |
| Variables | 7 | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable Methods, data collection section lines 158 to 231 |
| Data sources/ measurement | 8* | For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group Methods, data collection section lines 158 to 231 |
| Bias | 9 | Describe any efforts to address potential sources of bias Discussion, strengths and limitation section lines 297 to 307 |
| Study size | 10 | Explain how the study size was arrived at Methods section Sample size lines 298 to 311 |
| Quantitative variables | 11 | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why NA |
| Statistical methods | 12 | (a) Describe all statistical methods, including those used to control for confounding Methods Statistical analysis section lines 240 to 255 |
| | | (b) Describe any methods used to examine subgroups and interactions Methods Statistical analysis section lines 240 to 255 |
| | | (c) Explain how missing data were addressed NA |
| | | (d) If applicable, describe analytical methods taking account of sampling strategy Methods, Recruitment and random selection of the participants lines 123 to 126 |
| | | (e) Describe any sensitivity analyses |

Methods Statistical analysis section lines 239 to 255

| Results | | |
|--------------------------|-----|---|
| Participants | 13* | (a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed NA (b) Give reasons for non-participation at each stage NA (c) Consider use of a flow diagram NA |
| Descriptive data | 14* | (a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (b) Indicate number of participants with missing data for each variable of interest NA |
| Outcome data | 15* | Report numbers of outcome events or summary measures NA |
| Main results | 16 | (a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (b) Report category boundaries when continuous variables were categorized (b) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period NA |
| Other analyses | 17 | Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses NA |
| Discussion | | |
| Key results | 18 | Summarise key results with reference to study objectives NA |
| Limitations | 19 | Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias NA |
| Interpretation | 20 | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence NA |
| Generalisability | 21 | Discuss the generalisability (external validity) of the study results NA |
| Other information | | |
| Funding | 22 | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based NA |

*Give information separately for exposed and unexposed groups.

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2 **Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and
3 published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely
4 available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at
5 <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is
6 available at www.strobe-statement.org.
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BMJ Open

Prevalence of physical health conditions and health risk behaviours in people with severe mental illness in South Asia: Protocol for a cross-sectional study (IMPACT SMI survey)

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3 1 **Prevalence of physical health conditions and health risk behaviours in people with severe mental**
4 2 **illness in South Asia: Protocol for a cross-sectional study (IMPACT SMI survey)**

5
6 3 G.A. Zavala¹, K. Prasad-Muliyala², F. Aslam³, D. Barua⁴, A. Haidar⁴, C. Hewitt¹, R. Huque⁴, S. Mansoor³, P.
7 4 Murthy², A. T. Nizami³, N. Siddiqi^{1,5,6}, S. Sikander^{7,8}, K. Siddiqi^{1,5}, J.R. Boehnke^{1,9} and on behalf of the
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31 Abstract

32 **Introduction:** People with severe mental illness (SMI) die on average 10-20 years earlier than the
33 general population. Most of these deaths are due to physical health conditions. The aim of this cross-
34 sectional study is to determine the prevalence of physical health conditions and their associations with
35 health-risk behaviours, health-related quality of life and various demographic, behavioural, cognitive,
36 psychological and social variables in people with SMI attending specialist mental health facilities in
37 South Asia.

38 **Methods and analysis:** We will conduct a survey of patients with SMI attending specialist mental health
39 facilities in Bangladesh, India and Pakistan (n=4,500). Diagnosis of SMI will be confirmed using the MINI
40 V-6.0. We will collect information about: physical health and related health-risk behaviours (WHO
41 STEPs); severity of common mental disorders (PHQ-9 and GAD-7); and health-related quality of life (EQ-
42 5D-5L). We will measure blood pressure, height, weight and waist-circumference according to WHO
43 guidelines. We will also measure glycated haemoglobin (HbA1c), lipid profile, thyroid function, liver
44 function, creatinine and haemoglobin. Prevalence rates of physical health conditions and health-risk
45 behaviours will be presented and compared with the WHO STEPs survey findings in the general
46 population. Regression analyses will explore the association between health-risk behaviours, mental
47 and physical health conditions.

48 **Ethics and dissemination:** The study has been approved by the ethics committees of the Department
49 of Health Sciences University of York (UK), Centre for Injury Prevention and Rehabilitation (Bangladesh),
50 Health Ministry Screening Committee and Indian Council of Medical Research (India) and National
51 Bioethics Committee (Pakistan). Findings will be disseminated in peer reviewed articles, in local and
52 international conferences and as reports for policy makers and stakeholders in the countries involved.

53 **Trial registration:** ISRCTN88485933; <https://doi.org/10.1186/ISRCTN88485933>, 3rd of June 2019

54 **Key words:** Multimorbidity, Comorbidity, Lifestyle, Severe mental illness, South Asia, health risk
55 behaviours, schizophrenia, bipolar disorders, psychosis

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57 **Article summary**

58 ***Strengths and limitations***

- 59 • The study uses standardized tools to measure patient outcomes that will allow us to compare
60 the findings with those of the general population.
- 61 • The survey will be conducted face to face by trained researchers
- 62 • The questionnaire has been translated into the most common languages used in Bangladesh
63 India and Pakistan using validated translations of standardized measures where available.
- 64 • The survey is being conducted in specialist centres and is therefore a health care utilisation
65 sample drawn largely from tertiary care.
- 66 • The study population may not be representative of all the people with severe mental illness in
67 each country, as those not accessing specialist centres are not included in the survey.

69 Background

70 A considerable body of research has shown that people with severe mental illness (SMI; i.e. psychotic
71 disorders, bipolar affective disorder and severe depression with psychotic symptoms) die on average
72 10-20 years earlier than the general population^{1,2}. Around 80% of deaths in people with SMI are due
73 to preventable physical illnesses, most commonly cardio-metabolic diseases, respiratory disorders, and
74 infectious diseases^{3,4}. This excess mortality is a major global public health challenge but efforts to
75 address it have been limited. Recent studies suggest that despite an overall improvement in life
76 expectancy for both the general population and people with SMI, the absolute mortality gap between
77 these two groups is actually widening⁵⁻⁷.

78 Prevalence of most physical health conditions is higher and outcomes are poorer in this population⁸.
79 Multimorbidity (the presence of two or more conditions) is also more common⁹ in the presence of SMI,
80 contributing to poorer physical health and quality of life. The majority of evidence for these health
81 inequalities has been generated in high-income countries (HICs), but a small number of studies from
82 low- and middle-income countries (LMICs) also show a similar pattern of increased mortality for people
83 with SMI, with an even shorter life expectancy, and larger mortality gap^{4,10-12}. The few studies available
84 suggest that physical comorbidity in SMI is at least as prevalent as in developed countries¹.

85 In South Asia, rates of mental illness and physical non-communicable diseases have been increasing
86 rapidly^{13,14}. This increase, coupled with the lack of access to even basic mental healthcare¹⁵, and
87 neglect of the physical health needs of people with SMI by policymakers and healthcare services¹⁶,
88 means that the burden of disease due to physical disorders in people with mental illness is set to rise
89 further, with a corresponding increase within country and global health inequalities. This increase is
90 coupled with a recognized lack of information about the prevalence of physical conditions and health
91 risk behaviours in the SMI population in South Asia¹⁷. This gap in knowledge, particularly in relation to
92 health service planning in LMICs, has been pointed out repeatedly as a priority for research¹⁸.
93 Addressing mental and physical health comorbidity in LMICs is also a global priority, recognized in global
94 policies to help achieve the Sustainable Development Goals, including “ensuring healthy lives and
95 promoting well-being for all”¹⁹⁻²¹. A detailed understanding of the prevalence of physical health
96 conditions, health risk behaviours and health service utilization in SMI in LMICs is needed to progress
97 this agenda²².

98 Objectives

99 In people with SMI attending specialist mental health facilities:

- 100 1. Determine the prevalence of physical health conditions (i.e. type 2 diabetes, hypertension,
101 heart disease, obesity and infectious diseases) and health-risk behaviours (i.e. diet, physical
102 activity, alcohol and tobacco use) and compare these findings with those reported in the
103 general population.
- 104 2. Determine the association between physical health conditions, health-risk behaviours, health-
105 related quality of life and various demographic, behavioural, cognitive, psychological and
106 social variables.
- 107 3. Identify health-service utilization and the type of lifestyle advice that has been offered for this
108 SMI population.
- 109 4. Support clinical trial readiness by providing evidence-based findings regarding outcome
110 measures and procedures relevant for clinical trials design.

111 Methods and analysis

112 Design, settings & population

113 We will conduct a cross-sectional survey among patients with a clinical diagnosis of SMI recruited at
114 national specialist mental health institutions. In Bangladesh the study will be conducted at the National
115 Institute of Mental Health and Hospital (NIMH) in Dhaka. NIMH offers 200 beds for in-patient care
116 and on average 400 out-patients attend every day. In India the study will be conducted at the National
117 Institute of Mental Health and Neurosciences (NIMHANS) in Bengaluru, with 650 beds for in-patient
118 care; on average at NIMHANS 400 out-patients attend every day. In Pakistan, the study will be

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3 119 conducted at the Institute of Psychiatry (IOP) Rawalpindi Medical University, a WHO collaborating
4 120 centre for the Eastern Mediterranean (EMRO). IOP offers 60 beds for inpatients and on average 400
5 121 out-patients attend every day. All three national institutes serve patients from all over the country.
6 122 Adults (18 years and over) with a clinical diagnosis of SMI (defined by the International Classification of
7 123 Disease 10th revision (ICD-10²³) as schizophrenia, schizotypal and delusional disorders (F20-F29); bipolar
8 124 affective disorder (F30, F31); and severe depression with psychotic symptoms (F32.3, F33.3)²³, who
9 125 are able to provide informed consent as assessed by the treating clinician will be recruited. Patients
10 126 who lack capacity to provide consent or are unable to complete study questionnaires will be excluded
11 127 (figure 1). The data will be collected from June 2019 until September 2020.

128 **Sample size**

129 We aim to build as large a sample as possible within the resources available over the study period
130 (n=1500 per country). As an indicative example of survey precision to address some of the key research
131 questions, we provide a sample size estimate for investigating the prevalence of diabetes. Assuming a
132 prevalence estimate of 10% (based on results from previous studies ²⁴), we will need 857 participants
133 per country to achieve $\pm 2\%$ precision assuming a 95% confidence interval²⁵.

134 **Recruitment and random selection of the participants**

135 Both in- and outpatients attending one of the three specialist mental health institutions collaborating
136 in this study will be recruited. At NIMHH and NIMHANS patients will be selected randomly using random
137 number tables generated centrally to determine for outpatients, which patient to approach on a given
138 day, and for inpatients by randomly selecting beds. Recruitment is separated by in- vs outpatients,
139 resulting in a proportion of 80% outpatients and 20% inpatients (which has been reported as the
140 "usual" proportion of in- and outpatients). Due to the lower volume of patients and outpatients
141 reaching the centre outside working hours at the IOP, all patients attending the IOP during the study
142 duration will be invited to participate in the survey.

143 **Informed consent**

144 In the first instance, the researchers will give an information sheet to the patient, providing written and
145 verbal information on the potential benefits and risks of taking part in the study and clarifying the
146 assessments involved in the study. Only people who provided written informed consent will be included
147 in the study. Where there are problems with literacy, the researchers will provide this information
148 verbally to both the carer and the patient. Those unable to provide a signature will be requested to
149 indicate their consent with a thumbprint. The information sheet will meet all the requirements of the
150 relevant ethics committees. Maintenance of confidentiality and compliance with international, UK and
151 relevant local Data Protection Acts will be emphasised to all study participants. Moreover, all
152 participants will be informed that their participation in the study is voluntary, consent can be
153 withdrawn at any stage and the decision about participation will not affect their care.

154 Mental capacity is time- and decision-specific. For patients who are assessed to lack capacity by their
155 local physician, seeking informed consent will be delayed until capacity is regained, if feasible. No
156 assessments will be continued where the patient appears reluctant, even where patient consent has
157 been obtained.

158 Optional 'consent to contact' about future studies will be sought from survey participants. Permission
159 will be sought to retain participant details and to contact participants about future studies that may be
160 relevant for them. Again, it will be emphasised that this is voluntary, they can withdraw permission at
161 any time, and this will not affect their care in any way. After consenting to participate, the participant
162 will be given a unique patient identifier (ID) by the researcher. The patient consent and contact
163 information will be entered into a database (participant log), which will be kept separate from the
164 survey results database. The survey results database will include only the unique patient ID, and no
165 patient identifiable data.

166 **Confirmation of eligibility**

167 SMI diagnosis will be confirmed by trained researchers using the relevant modules from the Mini-
168 international neuropsychiatric interview (MINI) version 6.0 ²⁶. The MINI is a short diagnostic structured
169 interview to explore mental disorders. It is designed to allow administration by non-specialist

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170 interviewers²⁷. The inter-rater reliability for the MINI will be assessed at each site at the start of study.
171 Within each study site, at least 10 MINI questionnaires will be completed and compared between two
172 different researchers blinded from each other. Where needed, further training will be offered to
173 achieve acceptable inter-rater reliability before researchers are assigned to the study.

174 **Data collection**

175 We will conduct a face-to-face digital survey to collect information about physical health and health-
176 risk behaviours, severity of common mental disorders and health-related quality of life using validated
177 instruments as described below. The survey has been translated into the most common languages in
178 the countries (Urdu in Pakistan, Bangla in Bangladesh and Hindi, Kannada, Tamil and Telugu for India).
179 The team of interviewers in each county will include males and females and will include researchers
180 that speak regional dialects, which is consistent with usual clinical practice in these settings ²⁸.
181 Participants will be able to express a preference to be interviewed by a researcher of the same gender,
182 to reduce response bias that might arise due to the gender of the interviewer.

183 The WHO STEPwise approach to Surveillance (STEPS) instrument Version 3.2 will be used to collect
184 information about non-communicable diseases and related health-risk behaviours²⁹. STEPs is an
185 international standardized tool that will allow comparisons with the general population within the
186 country and between countries³⁰. The instrument has already been translated, used and validated in
187 the general population in Bangladesh, India and Pakistan ³¹⁻³³.

188 To allow patients to disclose information on sexually transmitted diseases, HIV diagnosis, alcohol and
189 tobacco consumption, in agreement with patient's wishes, the interviewer will ask the caregivers/
190 attendants to leave the room for this part of the interview.

191 *Demographic information*

192 The STEPs demographic module will be used to collect information on age, sex, education, marital
193 status, employment, household assets and income ²⁹.

194 *Mental health*

195 We will collect information relevant to the SMI diagnosis of each participant, including duration of the
196 mental illness, any treatment or medication and duration of the treatment and/or medication. The 9-
197 item depression module (PHQ-9)³⁴ will be used to measure the severity of depressive symptoms and
198 the generalized anxiety disorder 7 item scale (GAD-7)³⁵ for the severity of anxiety symptoms.

199 *Health risk behaviours*

200 The STEPs tobacco modules will be used to assess tobacco-related behaviours ²⁹.

201 *Alcohol consumption*

202 The STEPs alcohol module will be used to determine lifetime abstainers, past 12 months abstainers and
203 current users of alcohol using the WHO cut-off scores ²⁹.

204 *Diet*

205 The STEPs diet module will be used to record the number of days that respondents consumed fruit and
206 vegetables in a typical week, and the number of servings of fruit and vegetables consumed on average
207 per day ³⁶.

208 *Physical activity*

209 The STEPs physical activity module will be used to record activity for transport purposes (e.g. walking,
210 cycling), vigorous and moderate activity at work, and vigorous, moderate activity in leisure time, and
211 time spent sitting. Show-cards with culturally relevant examples will be used to aid respondents in
212 classifying activities. Analysis and categorization will follow the WHO guidelines³⁷.

213 *Non-communicable diseases*

214 Any medically-diagnosed history of raised blood pressure, heart disease, hypercholesterolemia, and
215 high blood glucose, and treatment advised by a health worker for these diseases (such as prescribed
216 medicines, a special diet, advice to reduce salt intake, lose weight, stop smoking, or do more exercise)

217 will be collected using the STEPs module for non-communicable diseases. Lung disease is not included
218 in the STEPs survey. However, it will be recorded asking the same set of questions as the non-
219 communicable diseases included in the STEPs survey.

220 *Infectious diseases*

221 Self-report of medically diagnosed history of hepatitis B, C, syphilis, tuberculosis, HIV and intestinal
222 parasites will be recorded.

223 *Risk behaviours related to sexually transmitted diseases*

224 Risk behaviours related to sexually transmitted diseases will be assessed using three questions that
225 examine the presence of multiple sexual partners, unprotected sexual contact and use of injectable
226 drugs that have been adapted from the 10 item HIV risk Screening Instrument³⁸. This instrument has
227 been previously used in research involving persons with severe mental illness in India³⁹.

228 *Health-Related Quality of life*

229 The EQ-5D-5L will be used to measure health-related quality of life^{40,41}. The EQ-5D-5L is a standardised
230 measure of health status, it provides a simple, generic measure of health for clinical and economic
231 appraisal. The impact of disease/disorder is characterised on five dimensions (mobility, self-care, ability
232 to undertake usual activities, pain, anxiety / depression). The EQ-5D-5L further assesses a patient's
233 subjective evaluation of their health state based on a visual analogue scale (EQ-5d-VAS) between "0 -
234 worst imaginable health state" and "100 - best imaginable health state". We will use validated
235 translations provided by EUROQOL.

236 *Blood pressure and heart rate*

237 Blood pressure (BP) and pulse rate will be taken three times using an automated blood pressure
238 measuring instrument (OMRON®). For BP measurement the participant must be comfortable and
239 rested. If he/she had been exerting themselves, then there will be a minimum of a 15 minute rest period
240 before the recording is taken. There should be at least a three minute gap between the BP recordings.
241 The procedure will follow the step wise instructions in the WHO STEPS surveillance manual⁴².

242 *Height weight and waist circumference*

243 Height will be measured to a precision of 0.1 cm using a portable height measuring board without
244 footwear and headgear. Weight will be measured in kilograms using a portable weighing scale placed
245 on a firm flat surface with light clothing and without footwear and socks. Waist circumference will be
246 measured in to a precision of 0.1 cm, using a flexible fiberglass anthropometric tape at the end of
247 normal expiration, at the midpoint between the lower margin of the last palpable rib and the top of the
248 iliac crest (hip bone), with the arms relaxed at the sides. All measurements will be taken in duplicate
249 and the average of the two values will be recorded and the protocols of the WHO STEPS surveillance
250 manual will be followed⁴².

251 *Biochemical analysis*

252 A blood sample (8 to 9 ml) will be taken from consenting participants for: glycated haemoglobin
253 (HbA1c), lipid profile (triglycerides, total cholesterol, HDL cholesterol, LDL cholesterol), thyroid function
254 tests (includes T3, T4, TSH), liver function tests (total Bilirubin, AST, ALT, ALP, total protein, albumin,
255 albumin to globulin ratio), creatinine and haemoglobin.

256 *Data management*

257 To ensure quality of collected data, validation, checking, proofing and cleaning procedures will be
258 carried out according to standard procedures⁴³. All consent forms will be stored separately from survey
259 data in locked cabinets in locked offices at study research offices at each study site. All coded data will
260 be transferred to, and stored as anonymous data at the University of York which will act as the data
261 curator. A secure password protected and encrypted electronic database will be set up to store the
262 data.

263 **Statistical analysis**

264 Quantitative data will be summarised using descriptive statistics. First, prevalence rates of infectious
265 diseases, long-term physical health conditions (e.g. diabetes, heart disease) and health-risk behaviours
266 for type II diabetes, cardiovascular and respiratory disorders (e.g. tobacco use, obesity, physical activity,
267 diet) will be estimated in the severe mental illness population. Second, we will examine the associations
268 between physical health conditions and health-risk behaviours, using regression models with random
269 intercepts for data collection site with the following potential covariates: demographic variables (i.e.
270 age, sex, and level of education), history of mental and physical conditions and biomarkers (e.g. BMI,
271 blood pressure). These regression models will also be used to calculate prevalence rates of physical
272 health conditions and health-risk behaviours adjusted for these covariates (e.g., for comparison with
273 external general population data) Further regression analyses will explore the association between
274 mental and physical health conditions and health-related quality of life measured using EQ-5D-5L.
275 Regression models will take account of the nature and distribution of data (e.g. count versus continuous
276 data; skewed versus normally distributed data). To investigate the prevalence of physical health
277 conditions and health risk behaviours in the general population, we will extract aggregated data on the
278 prevalence of physical health conditions, health risk behaviours and lifestyle advice from the last
279 available WHO STEPs survey from Bangladesh⁴⁴, India⁴⁵ and Pakistan⁴⁶.

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281 **Ethics and dissemination**

282 The study has been approved by the ethics committees of the Department of Health Sciences University
283 of York (UK), Centre for Injury Prevention and Research (Bangladesh), Health Ministry Screening
284 Committee and Indian Council of Medical Research (India) and National Bioethics Committee
285 (Pakistan).

286 The study will adhere to the fundamental principles of human rights and dignity laid down in the
287 Declaration of Helsinki⁴⁷. Study procedures will comply with legislation and guidance for good practice
288 governing the participation in research of people lacking capacity as set out in the Mental Capacity Act
289 (UK) 2005⁴⁸. Participants will not receive any financial inducement to participate, but the results of the
290 physical measurements and blood tests will be shared with the participant and the treating clinician.

291 As a non-interventional study, there is minimal risk of adverse events associated with the study. Due to
292 the vulnerability of the severe mental illness population, however, there is a potential (albeit low) risk
293 that some questions or the burden of the assessments may cause distress for participants or the family
294 carers. If there is any indication of this, the survey or assessments will be stopped, the participant
295 offered reassurance and support, and if needed, referral to the clinical team. If a participant during the
296 interview reveals any suicidal ideation, the interviewer will refer them to the treating clinician for a
297 clinical risk assessment and further management. If a physical condition or blood test abnormality
298 (outside the normal range for age and sex) is detected as a part of the research assessments, the
299 research team will inform the clinician responsible for the patient, who will evaluate the result and give
300 the patient the option of referral to a specialist if this is required for their condition.

301 **Community, patient and public involvement**

302 A 'Community Panel' comprising stakeholders from these constituencies ensures community, patient
303 and public involvement. The Panel has reviewed the planned survey and advised on its feasibility. The
304 panel will continue to provide feedback on the conduct of the study and presentation of findings. To
305 support dissemination efforts, findings will be presented to the community panel, with advice sought
306 about the format and content of lay summaries and other outputs aimed at patients and the public.

307 **Dissemination**

308 Findings will be disseminated in peer-reviewed articles, in local and international conferences and as
309 reports for policy makers and stakeholders in the countries involved. An open access repository of all
310 materials will be built that covers the survey materials as well as statistical syntax used by the team
311 publications.

312 **Discussion**

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3 313 People with SMI have a reduced life expectancy. Research in high income countries has shown that a
4 314 large proportion of this inequality is accounted for by chronic diseases^{1,2}. This has been consistently
5 315 observed in high income countries^{3,4}. However information is lacking in minority groups and LMICs,
6 316 which is surprising considering the increased risk of physical health conditions in these populations due
7 317 to poverty, education, poor diet, low access to healthcare, exposure to infectious diseases and other
8 318 environmental factors⁴⁹. The IMPACT SMI survey will address this gap in knowledge, demonstrating
9 319 the prevalence of different physical health conditions and health-risk behaviours in the SMI population,
10 320 and the association of each of these conditions in terms of health related quality of life. It will support
11 321 SMI clinical trial readiness by providing evidence-based findings regarding outcome measures and
12 322 procedures relevant for clinical trials design.

14 323 **Strengths and limitations**

15 324 To the best of the authors' knowledge, this will be the first large scale study to investigate the physical
16 325 health and health-risk behaviours in the SMI population in LMICs. The main limitation is that the survey
17 326 is conducted in specialist centres (with patients with capacity) and is therefore a health care utilisation
18 327 sample drawn largely from tertiary care. The gaps in treatment and care utilisation and systematic
19 328 factors influencing these have been well documented⁵⁰, therefore, the study population may not be
20 329 representative of the total severe mental illness population in each country. However, a community
21 330 survey would not be feasible, and primary and secondary care mental health services are not
22 331 sufficiently developed to be used to recruit participants for this survey (see for example work by PRIME
23 332¹⁵ and Emerald⁵¹ programmes on strengthening these services as access points). However, unlike
24 333 services in high-income countries, tertiary care services in these South Asian countries accept self-
25 334 referral without the need for primary or secondary care referral and we include outpatient services
26 335 offered by the collaborating centres which often function as 'the first port of call' for people with mental
27 336 illness⁵²⁻⁵⁴. Therefore, the selected centres are likely covering a broad range of the treatment-seeking
28 337 population. We will not have a control group since the study is only conducted in people with SMI,
29 338 however we are using the same questions and measurements as the WHO STEPs survey. This will allow
30 339 us to compare the prevalence of physical health conditions and health risk behaviours with that of a
31 340 survey representative for the population in each country.

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40 347 taking the time to complete the survey.

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23 497 **Authors' contributions**

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25
26 498 NS conceived the study, KP, FA, DB, RH, SM, PM, AN, SS and KS provided important contextual
27 499 information, KP, FA, DB, AH, SM, NS, KS and JB developed the methodology and selected the outcomes,
28 500 GZ, AH, CH and JB developed the analysis plan, GZ, NS, KS and JB wrote the manuscript, and all authors
29 501 revised and approved the manuscript.

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31
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36 507 preparation of the manuscript.

37 508 **Competing interests statement**

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39 509 The authors declare that they have no competing interests

40 510

41 511 **Word count**

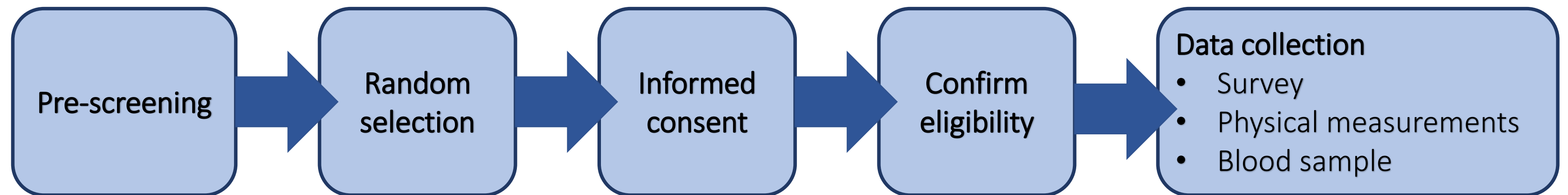
42 512 3159 words

43 513 **Figure legend**

44 514 Figure 1. Study flow chart

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INVESTIGATING MENTAL AND PHYSICAL COMORBIDITY: Protocol for a survey in people with severe mental illness in South Asia (IMPACT SMI survey)

STROBE Statement—Checklist of items that should be included in reports of *cross-sectional studies*

| | Item No | Recommendation |
|------------------------------|---------|--|
| Title and abstract | 1 | (a) Indicate the study's design with a commonly used term in the title or the abstract Title and abstract lines 1 to 56 |
| | | (b) Provide in the abstract an informative and balanced summary of what was done and what was found Abstract lines 32 to 56 |
| Introduction | | |
| Background/rationale | 2 | Explain the scientific background and rationale for the investigation being reported Background paragraphs 1 to 3 |
| Objectives | 3 | State specific objectives, including any prespecified hypotheses Background, objectives section lines 93 to 101 |
| Methods | | |
| Study design | 4 | Present key elements of study design early in the paper Methods paragraph 1 design setting and population 103 to 115 |
| Setting | 5 | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection Methods paragraph 1 design setting and population lines 103 to 115 |
| Participants | 6 | (a) Give the eligibility criteria, and the sources and methods of selection of participants Methods paragraph 1 design setting and population lines 103 to 115 |
| Variables | 7 | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable Methods, data collection section lines 158 to 231 |
| Data sources/ measurement | 8* | For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group Methods, data collection section lines 158 to 231 |
| Bias | 9 | Describe any efforts to address potential sources of bias Discussion, strengths and limitation section lines 297 to 307 |
| Study size | 10 | Explain how the study size was arrived at Methods section Sample size lines 298 to 311 |
| Quantitative variables | 11 | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why NA |
| Statistical methods | 12 | (a) Describe all statistical methods, including those used to control for confounding Methods Statistical analysis section lines 240 to 255 |
| | | (b) Describe any methods used to examine subgroups and interactions Methods Statistical analysis section lines 240 to 255 |
| | | (c) Explain how missing data were addressed NA |
| | | (d) If applicable, describe analytical methods taking account of sampling strategy Methods, Recruitment and random selection of the participants lines 123 to 126 |
| | | (e) Describe any sensitivity analyses |

Methods Statistical analysis section lines 239 to 255

| Results | | |
|--------------------------|-----|---|
| Participants | 13* | (a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed NA (b) Give reasons for non-participation at each stage NA (c) Consider use of a flow diagram NA |
| Descriptive data | 14* | (a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (b) Indicate number of participants with missing data for each variable of interest NA |
| Outcome data | 15* | Report numbers of outcome events or summary measures NA |
| Main results | 16 | (a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (b) Report category boundaries when continuous variables were categorized (b) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period NA |
| Other analyses | 17 | Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses NA |
| Discussion | | |
| Key results | 18 | Summarise key results with reference to study objectives NA |
| Limitations | 19 | Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias NA |
| Interpretation | 20 | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence NA |
| Generalisability | 21 | Discuss the generalisability (external validity) of the study results NA |
| Other information | | |
| Funding | 22 | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based NA |

*Give information separately for exposed and unexposed groups.

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2 **Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and
3 published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely
4 available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at
5 <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is
6 available at www.strobe-statement.org.
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