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Protocol for the Evaluation of a Pilot Implementation of Essential Interventions for the Prevention of Cardiovascular Diseases in Primary Health Care in the Republic of Moldova

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3 **1 Protocol for the Evaluation of a Pilot Implementation of Essential Interventions for the**
4 **2 Prevention of Cardiovascular Diseases in Primary Health Care in the Republic of Moldova**
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ABSTRACT

Introduction

Nearly 90% of all deaths in Republic of Moldova are caused by NCDs, the majority of which (55%) are caused by CVD. In addition to reducing premature mortality from CVD, it is estimated that strengthening primary health care could cut the number hypertension-related hospital admissions and diabetes-related hospitalizations in half. The aim of this evaluation is to determine the feasibility of implementing and evaluating essential interventions for the prevention of CVD in primary health care in Republic of Moldova, with a view toward national scale-up.

Methods and Analysis

A national steering group including international experts will be convened to adapt WHO PEN protocols one and two to the health system of Republic of Moldova, develop and conduct training of primary health care workers, and test a core set of indicators to monitor the quality of care and change in clinical practice. To evaluate the impact of this pilot implementation, a pragmatic, sequential mixed methods explanatory design, composed of quantitative and qualitative strands of equal weight, will be used. Twenty primary health care centres will be selected and randomized to the training and implementation arm (n=10) and the usual care arm (n=10). At baseline and 12 months follow-up, a standardized data collection form will be piloted to extract data directly from patient paper records in order to estimate the change in clinical practice. Semi-structured interviews and inter-clinic peer workshops will be conducted at 12 months follow-up, and qualitative data collected from these formats will be analysed thematically for explanatory themes that relate to the quantitative findings.

Ethics and Dissemination

Ethical review and approval has been obtained. Findings of the evaluation will be shared in a project report to key stakeholders, presented back to participants, and written into a manuscript for an open access peer-reviewed scientific journal.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- To our knowledge, this is the first description of adapting and piloting WHO essential NCD interventions in primary health care in a low- or middle-income country and provides a methodological example to other jurisdictions
- A mixed methods design allows for a greater understanding of the potential barriers and facilitators to implementation and can inform future health systems development
- Primary health care facilities will be selected from different regions of Republic of Moldova in order to pilot implementation in a variety of contexts throughout the country
- Since this is an evaluation of a pilot implementation, the sample size is based on pragmatism and not statistical power
- We are unable to include patient perspectives and experience in the evaluation, which is an important aspect of health care quality

68 INTRODUCTION

69
70 Globally, non-communicable diseases (NCDs) account for more than one-half of the global
71 burden of disease.(1) In 2016, an estimated 41 million deaths were due to NCDs, of which nearly
72 half were due to cardiovascular diseases (CVD).(2) Primary health care systems play an
73 important role in the prevention, early detection, and appropriate management of these diseases,
74 but many nations lack primary health care capacity.(3,4)

75
76 To support national governments to realize their commitments in reducing the burden of NCDs,
77 as agreed in the United Nations Political Declaration on NCDs, the World Health Assembly
78 endorsed the WHO Global Action Plan for the Prevention and Control of NCDs 2013-2020. To
79 support implementation of this Action Plan, WHO has identified a set of cost-effective policy
80 options (“best buys”) for the prevention and control of NCDs within countries.(5)

81
82 The Republic of Moldova (henceforth “MDA”) is located in Eastern Europe, between Ukraine
83 and Romania; the Capital and largest city is Chisinau. By gross domestic product per capita,
84 MDA is one of the poorest countries in the WHO European Region and it is estimated that
85 21.9% of citizens live below the absolute poverty line of 1 US Dollar per day.(6)

86 87 **Non-communicable diseases are a leading cause of death in MDA**

88 While NCDs are a global epidemic, MDA ranks amongst the countries most affected. Nearly
89 90% of all deaths in MDA are caused by NCDs, the majority of which (55%) are caused by
90 CVD.(7) In 2016, the probability of dying prematurely from any of the four major NCDs (CVDs,
91 cancer, diabetes, chronic respiratory disease) was 24.9%,; almost twice as high for men (33.7%)
92 as women (17.3%).(8) Men and people residing in rural areas are disproportionately impacted by
93 CVD and represent key populations for public health intervention.(7)

94
95 This burden is driven by some of the highest rates of NCD risk factors, including tobacco and
96 alcohol use, in the WHO European region indicated by a 2013 STEPS survey.(9) One-in-four
97 (25.3%) Moldovans smoke tobacco and this rate nearly doubles in men.(9) Among adults aged
98 18 to 69, 61.9% currently consume alcohol and one in five people have engaged in heavy
99 episodic drinking (six or more drinks on any one occasion in the past 30 days).(9)

100
101 The overall prevalence of obesity amongst adults is 22.9%, being higher among women (28.5%)
102 as compared with men (17.8%).(7) The prevalence of raised blood pressure (defined as SBP \geq
103 140 mmHg and/or DBP \geq 90 mmHg or currently taking medication for raised blood pressure)
104 among MDA’s adult population is 39.8%, and 76.2% of these patients are not on blood pressure
105 lowering medication.(7) A total of 12.3% of the population have a blood glucose level of \geq 6.1
106 mmol/L, and 29.4% of the population has a total blood cholesterol level of \geq 5 mmol/L.(7) It is
107 estimated that one in five (23.0%) people aged 40–69 years have a 10-year fatal or non-fatal
108 CVD risk of over 30% (including those with an existing CVD).(7)

109 110 **Primary health care in MDA and commitment to NCDs**

111 According to the Constitution of Republic of Moldova of 1994, citizens are entitled to a free of
112 charge minimum package of essential health services, including primary health care. However,
113 resource constraints have made it difficult to offer these services and significant gaps in care

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3 114 exist.(10) According to the most recent data (2010), there were 5.3 family doctors per 10,000
4 115 inhabitants and 25.9 specialist doctors per 10,000 inhabitants. In rural areas these rates are
5 116 halved, leading to human resource shortages in primary care.(10) Approximately 17% of
6 117 practicing physicians in MDA work in primary health care, and 92% of them rely on paper
7 118 clinical records.(6) The most recent estimate (2009) states that there are approximately 630
8 119 primary health care centres throughout the country, or 21.2 centres per 100,000 people.(6)

9 120
10 121 Despite these health system challenges, the Government of Republic of Moldova is committed to
11 122 improving primary health care capacity for NCDs. It is estimated that 60% of hypertension-
12 123 related hospital admissions (about 12,000 annually) and 40% of diabetes-related hospitalizations
13 124 (about 5,000 annually) could be prevented through strengthened primary health care for these
14 125 conditions.(11)

15 126 As such, strengthening primary health care is one of the commitments set out in the Action
16 127 Program of the Government of Republic of Moldova 2016–2018.(12) To do this requires the
17 128 development of simplified clinical protocols, in-person training programs for nurses and doctors,
18 129 and a core set of indicators to monitor and evaluate changes in the quality of care.
19 130

20 131 **Essential interventions to prevent cardiovascular diseases in primary health care**

21 132 In order to build capacity in primary health care and ultimately prevent premature mortality from
22 133 CVD in MDA, a study was envisioned to adapt and pilot the World Health Organization Package
23 134 of Essential NCD Intervention from Primary Healthcare in Low Resource Settings (WHO
24 135 PEN).(3) WHO PEN includes simplified clinical protocols which together cover the integrated
25 136 management of hypertension and diabetes, as well as education and counselling on healthy
26 137 behaviours aimed to prevent CVD. The central strategy of this integrated approach is the use of
27 138 total cardiovascular risk assessment to stratify and target individuals at high CVD risk, a process
28 139 considered to be a “best buy” intervention by the WHO.(5)
29 140

30 141 Since these approaches were unprecedented in MDA, the Ministry of Health, Labour and Social
31 142 Protection convened a national steering group to lead the adaptation and pilot process, with the
32 143 goal of using the findings for future health systems development. Led by the primary health care
33 144 division of the Ministry of Health, the steering group is comprised of representatives from the
34 145 Nicolae Testemitanu State University of Medicine and Pharmacy and the National Public Health
35 146 Agency. The national steering group is supported by an international team of experts coordinated
36 147 jointly by the WHO Regional Office for Europe and WHO Country Office in the Republic of
37 148 Moldova.
38 149

39 150 **AIM AND OBJECTIVES**

40 151 **Aim**

41 152 The aim of the evaluation is to determine the feasibility of implementing and evaluating essential
42 153 interventions for the prevention of cardiovascular disease in primary health care in MDA, with a
43 154 view toward national scale-up.
44 155

45 156 **Objectives**

46 157 In order to achieve this aim, the four overarching objectives of the evaluation are to:
47 158

- 1 159 1. Determine the baseline performance of primary health care services with respect to
- 2 160 essential interventions for the prevention and management of CVD
- 3 161 2. Assess the ability to implement MDA-adapted WHO PEN protocols one and two in pilot
- 4 162 primary health care centres
- 5 163 3. Estimate the change in performance of pilot primary health care centres after 12 months
- 6 164 of protocol implementation and compare this to control clinics using usual care
- 7 165 4. Determine the feasibility of collecting quantitative data required for future studies of
- 8 166 effectiveness from the existing informal paper clinical record system
- 9 167

13 168 **METHODS AND ANALYSIS**

14 169 **Overview of Process and Design**

15 170 An overview of the methods used to adapt, pilot, and evaluate essential interventions for CVD in
16 171 primary health care in MDA are summarized by the following seven steps.

17 172 Step One: Adaptation of WHO PEN Protocols to the National Context

18 173 Under the direction of the national steering group, WHO PEN protocols one and two will be
19 174 compared and contrasted to national disease specific guidelines. The WHO PEN protocols will
20 175 then be adapted to ensure consistency with the organization, culture, and availability of resources
21 176 of the health system, while ensuring that they remain simple clinical decision support tools.

22 177 Step Two: Development of a Training Package for Primary Health Care Workers

23 178 A three-day training package will be developed under the direction of the national steering group
24 179 in order to provide in-person theoretical and practical training to nurses and doctors working in
25 180 primary health care. This will include lectures, clinical case studies, and practical exercises that
26 181 embrace the experience and knowledge of participants.

27 182 Step Three: Collection of Baseline Data

28 183 According to the Ministry of Health process, a list of 20 primary health care clinics will be
29 184 nominated and provided to the working group. They will then be randomized into an intervention
30 185 group arm (n=10) and control arm (n=10). Data for quantitative indicators will be extracted from
31 186 all 20 clinics by randomly sampling individual paper-based patient records from all primary
32 187 health care units using a standardized data collection instrument. This will be done by a specially
33 188 trained group of postgraduate medical trainees.

34 189 Step Four: Training Staff in Pilot Clinics

35 190 All doctors and nurses from the primary health care centres in the intervention arm will be
36 191 invited to be trained together by a national team of experts in groups of approximately 30. It is
37 192 estimated that up to 200 health workers will be trained in total. At the end of training each PHC
38 193 team will pass through evaluation at the University Centre for Simulation in Medical Training
39 194 using objective structured clinical exams and get feedback from trainers and peers.

40 195 Step Five: Implementation of Protocols

41 196 Trained participants from the ten primary health care clinics in the intervention arm will then be
42 197 free to implement the clinical protocols and change their clinical practice, without incentives, for
43 198 12 months. During this time, a team of national experts will be created to offer support (distance
44 199

205 and on-the-job) to the primary health care centres in the intervention arm. All ten clinics in the
206 intervention arm will receive at least one in-person follow-up support visit.

207

208 Step Six: Collection of Follow-up Data

209 After 12 months, using the same method and data collection instruments used to collect baseline
210 quantitative data (Step Three), data will again be extracted from randomly selected individual
211 paper-based patient records from all 20 health care centres. Five primary health care centres
212 from the intervention arm will be selected by the national steering group for one-on-one semi
213 structured interviews with health staff. This will be supplemented by inviting a selection of staff
214 from all ten health centres in the intervention arm to participate in focus groups. Together, these
215 qualitative data will be analysed thematically for explanatory themes.

216

217 Step Seven: Evaluation of Results and Sharing Experience

218 The findings of the quantitative and qualitative analyses will be integrated in a final report and
219 shared with key stakeholders, including health staff from the participating primary health care
220 centres. The results will also be shared at a national conference and in an open-access peer
221 reviewed journal, in order to inform the future development of primary health care capacity in
222 MDA.

223

224 **Methodological Design**

225 A pragmatic, sequential mixed methods explanatory design, composed of quantitative and
226 qualitative strands of equal weight, will be used (Figure 1). This design was chosen for because it
227 allows for the use of qualitative data to enlighten and explain the quantitative findings, including
228 but not limited to the feasibility of collecting data from paper-based records, the contextual
229 factors affecting guideline implementation, changes in clinical practice, and optimization for the
230 future.

231

232 **Figure 1.** Illustration using the GATE frame structure (13) of the mixed methods evaluation
233 design

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235 A sample size of 20 primary health care centres was chosen because it was seen as a good
236 balance of allowing for variation in clinic geography and demography, while still remaining
237 feasible for the pilot implementation. Half of the centres (n=10) will be randomly allocated to the
238 intervention arm and half (n=10) to the control arm. Baseline data will be collected from both
239 intervention and control clinics, ensuring that baseline data is collected before implementation
240 occurs.

241

242 Within clinic comparisons will be used to compare the 12 months before implementation with
243 the 12 months of implementation. Between clinics comparison will be used to compare the
244 intervention clinics with control clinics during the same time period.

245

246 **Eligibility Criteria for Primary Health Care Centres**

247 Health facilities will be nominated by the Ministry of Health for participation based on the
248 following eligibility criteria: (1) primary health care facilities must be operating in the public
249 sector as legal entities; (2) primary health care facilities must be sampled in a way such that they
250 are geographically distributed evenly across the country; equally from the Central, North and

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3 251 Southern regions of MDA; and (3) health facilities must be primary health care centres that are
4 252 managed by family doctors with no specialist doctors working in the facility.
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6 254 **Randomization**

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8 255 The clinics will be stratified based on the ratio of patients to family doctors to minimize possible
9 256 confounding by doctor caseload, and then randomized electronically into two groups of 10
10 257 primary health care centres.
11 258

12 259 **Comparison**

13 260 The 10 primary health care centres in the intervention arm will be compared to the 10 primary
14 261 health care centres in the control arm. The control arm will receive no intervention and proceed
15 262 with usual care.
16 263

17 264 **Quantitative Indicators**

18
19 265 Indicators were developed to balance input and process indicators, such as measurement of risk
20 266 factors and calculation of risk scores, with output (e.g. prescribing) and outcome (e.g. blood
21 267 pressure control) indicators. While one of the objectives of this evaluation is to determine the
22 268 ability to measure these indicators based on routine paper records, we used our existing
23 269 knowledge of the health system to design indicators which were valuable and likely to be
24 270 feasible to calculate. Table 1 shows the indicator, the question the indicator seeks to answer, and
25 271 the respective numerator and denominator definitions which will be used in the calculations.
26 272

27
28 273 **Table 1.** Indicators, their numerators and denominators, and questions the indicators answer
29 274

30 275 **Data Collection and Management**

31 276 Quantitative Data Collection Tool

32 277
33 278 A standardized data collection template has been developed for extracting anonymized patient
34 279 data from individual paper records (Table 2). An online version was also made to allow for data
35 280 entry on a computer or smartphone. It is estimated to take 15 minutes to extract data from one
36 281 patient record since the records are made of blank paper with no formal structure or organization
37 282 of health data.
38 283

39 284 **Table 2.** Standardized data collection form used to extract data from individual patient records
40 285

41 286 Method of Randomly Sampling Patient Records

42 287 A random sample of the records of patients aged over 40, who have visited the medical facility
43 288 within the past 12 months, will be taken. Since medical records in MDA are organized
44 289 alphabetically on shelves, we created a randomly generated list of alphanumeric combinations
45 290 that allowed for the selection of patient charts at random. For example, an alphanumeric code of
46 291 "C24" would correspond to the 24th patient chart in the section of last names starting with the
47 292 letter C.
48 293

49 294 The list will be followed in the order that it was generated so as to prevent selection bias. The
50 295 randomly selected chart will then be checked to see if it meets two inclusion criteria: (1) the
51 296 patient is aged 18 years or older and (2) the patient visited the health centre within the last 12
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3 297 months. If the record meets these criteria, data will then be extracted. If it does not, it will be
4 298 returned to the shelf and the next alphanumeric code on the randomly generated list will be used.
5 299 This process will be repeated in each clinic until a sample size of 1.2% of the patient population
6 300 in each clinic is sampled. This proportion was chosen pragmatically such that the average sample
7 301 per primary health care centre would equal 100 unique patients.
8 302

303 Data Analysis

11 304 The change in indicators from baseline to follow-up will be calculated for intervention clinics
12 305 and compared with control clinics. Subgroup analysis by age, gender, and other demographic
13 306 features may be done as deemed appropriate by the national steering committee. All analyses
14 307 will account for stratified sampling.
15 308

17 309 Qualitative Data Collection

18 310 **Follow-up Support Visits**

19 311 Follow-up visits will be made to each intervention clinic at least once during the implementation
20 312 timeframe (12 months) to provide ad hoc implementation support. These visits will be
21 313 conducted by members of the national steering group, who will keep field notes about each visit
22 314 and provide feedback and support to the health centres. The perspectives gained through follow-
23 315 up support visits will be used by the national steering group to develop preliminary data
24 316 collection tools for semi-structured interviews.
25 316
26

27 317 **Semi-Structured Interviews**

28 318 A maximum variation sample of half of the intervention clinics (n=5) will be chosen, based on
29 319 the perceived performance of each clinic by the evaluation steering committee. A pragmatic
30 320 sample of clinic managers (n=1 per clinic), doctors (n=3 per clinic), and nurses (n=3 per clinic)
31 321 will be interviewed one-on-one, using a semi-structured format. Interviews will proceed until
32 322 data saturation has been reached, to a maximum of 30 interviews. After obtaining written,
33 323 informed consent, interviews will be of 30 to 60 minutes in length, audio recorded, and be
34 324 transcribed verbatim and analysed thematically using framework thematic analysis.(14)
35 324
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37 325 **Focus Group Workshop**

38 326 Participants from all ten implementation clinics will be invited to a workshop to further collect
39 327 explanatory qualitative data and to critically reflect on the implementation process. Participants
40 328 will be a mix of doctors, nurses, and managers from the intervention clinics.
41 328
42 329

43 330 Participants will be placed into small groups based on their profession, and asked to complete a
44 331 standardized worksheet. Each group will be under the guidance of a facilitator, and emergent
45 332 themes from one-one-one interviews will be used as prompts to each group. The worksheet will
46 333 allow for each group to directly comment, modify, or add to the emergent themes, create new
47 334 themes, and organize themes into categories such as barriers and facilitators.
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49 336 The resulting qualitative data will be analysed thematically using the framework approach, and
50 337 used to help explain the findings of the quantitative strand.(14)
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339 **Patient and Public Involvement**

340 Neither patients nor the public were involved in the methodological design.

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343 **ETHICS AND DISSEMINATION**

344 **Ethical Review and Approval**

345 This project was reviewed by the Research Ethics Committee of the Nicolae Testemitanu State
346 University of Medicine and Pharmacy of the Republic of Moldova and granted permission on 31
347 May 2017.

348

349 **Dissemination**

350 Quantitative findings will be summarized and presented back to all intervention clinics during
351 follow-up workshops. A comprehensive project report will be written and shared with key
352 stakeholders. A final report of key findings of the evaluation will be written and submitted to an
353 open access peer-reviewed journal and made available to all study participants so they can use
354 the findings to improve their practice. The findings will be used to evaluate the feasibility of a
355 national scale-up of essential NCD interventions in primary health care in MDA.

356

357 **REFERENCES**

- 358 1. Benziger CP, Roth GA, Moran AE. The Global Burden of Disease Study and the
359 Preventable Burden of NCD. *Glob Heart*. England; 2016 Dec;11(4):393–7.
- 360 2. World Health Organization (WHO). World Health Statistics [Internet]. 2018. Available
361 from: http://www.who.int/gho/publications/world_health_statistics/2018/en/
- 362 3. World Health Organization (WHO). Package of Essential Noncommunicable (PEN)
363 disease interventions for primary health care in low-resource settings [Internet]. 2013.
364 Available from: http://www.who.int/ncds/management/pen_tools/en/
- 365 4. World Health Organization (WHO). Global action plan for the prevention and control of
366 NCDs 2013-2020. 2013.
- 367 5. Organization WH. Tackling NCDs: “Best buys” and other recommended interventions for
368 the prevention and control of noncommunicable diseases [Internet]. 2017. Available from:
369 [http://apps.who.int/iris/bitstream/handle/10665/259232/WHO-NMH-NVI-17.9-
370 eng.pdf;jsessionid=074ED8768EA1FFD0E632DB861E91A6FD?sequence=1](http://apps.who.int/iris/bitstream/handle/10665/259232/WHO-NMH-NVI-17.9-eng.pdf;jsessionid=074ED8768EA1FFD0E632DB861E91A6FD?sequence=1)
- 371 6. World Health Organization (WHO). Evaluation of the structure and provision of primary
372 care in the Republic of Moldova. 2012.
- 373 7. National Center for Health Management. Health Yearbook: Public Health in Moldova
374 [Internet]. 2015. Available from: <http://www.cnms.md/ro/rapoarteo>
- 375 8. World Health Organization. Global Health Observatory data repository [Internet]. [cited
376 2018 Jul 10]. Available from: <http://apps.who.int/gho/data/node.home>
- 377 9. World Health Organization (WHO). Prevalence of Noncommunicable Disease Risk
378 Factors in the Republic of Moldova (STEPS) [Internet]. 2014. Available from:
379 http://www.who.int/ncds/surveillance/steps/Moldova_2013_STEPS_Report.pdf
- 380 10. Turcanu C, Domente S, Buga M, Richardson E. Health Systems in Transition: Republic of
381 Moldova [Internet]. 2012. Available from:
382 http://www.euro.who.int/__data/assets/pdf_file/0006/178053/HiT-Moldova.pdf
- 383 11. World Health Organization (WHO). Ambulatory care sensitive conditions in the Republic
384 of Moldova [Internet]. 2015. Available from:

- 1
2
3 385 <http://www.euro.who.int/en/countries/republic-of-moldova/publications/ambulatory-care-sensitive-conditions-in-the-republic-of-moldova-2015>
4 386
5 387 12. Government of the Republic of Moldova. Action Program of the Government of the
6 388 Republic of Moldova 2016–2018 [Internet]. 2016. Available from:
7 389 [http://gov.md/sites/default/files/document/attachments/guvernul_republicii_moldova_-](http://gov.md/sites/default/files/document/attachments/guvernul_republicii_moldova_-_programul_de_activitate_al_guvernului_republicii_moldova_2016-2018.pdf)
8 390 [_programul_de_activitate_al_guvernului_republicii_moldova_2016-2018.pdf](http://gov.md/sites/default/files/document/attachments/guvernul_republicii_moldova_-_programul_de_activitate_al_guvernului_republicii_moldova_2016-2018.pdf)
9 391 13. Jackson R, Ameratunga S, Broad J, Connor J, Lethaby A, Robb G, et al. The GATE
10 392 frame: critical appraisal with pictures. Vol. 144, ACP journal club. United States; 2006. p.
11 393 A8-11.
12 394 14. Gale NK, Heath G, Cameron E, Rashid S, Redwood S. Using the framework method for
13 395 the analysis of qualitative data in multi-disciplinary health research. BMC Med Res
14 396 Methodol. England; 2013 Sep;13:117.
15 397

18 398 **AUTHORS AND CONTRIBUTIONS**

19 399 DC, AC, TL, GC, VS, TZ, AA, and JF contributed to the methodological design. DC, AC, TL,
20 400 and JF contributed to writing the manuscript.
21 401

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23 403 This study is funded jointly by the Swiss Agency for Development and Cooperation (SDC) and WHO
24 404 Regional Office for Europe.
25 405

26 406 **COMPETING INTERESTS STATEMENT**

27 407 DC, AC, TL, GC, VS, TZ, AA, JF declare no competing interests.
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409 **Table 1.** Indicators, their numerators and denominators, and questions the indicators answer

Question	Indicator	Numerator	Denominator
Are risk factors being measured?	Proportion of eligible patients who have all risk factor values recorded as required for calculation of risk score	Patients aged 40 or older who have visited in the last 12 months who have all measurements required for calculation of risk score within 12 months of the most recent date of visit	Patients aged 40 or older who have visited in the last 12 months
Are risk factor measurements being converted to a total risk score?	Proportion of patients aged 40 or older who have visited in the last 12 months who have all measurements required for calculation of risk score within 12 months of the most recent date of visit, that have a documented risk score	Patients aged 40 or older who have visited in the last 12 months who have all measurements required for calculation of risk score within 12 months of the most recent date of visit, that have a documented risk score	Patients aged 40 or older who have visited in the last 12 months who have all measurements required for calculation of risk score within 12 months of the most recent date of visit
Are risk scores calculated correctly?	Proportion of patients aged 40 or older who have visited in the last 12 months who have all measurements required for calculation of risk score within 12 months of the most recent date of visit, that have a documented risk score that is correct	Patients aged 40 or older who have visited in the last 12 months who have all measurements required for calculation of risk score within 12 months of the most recent date of visit, that have a documented risk score that is correct	Patients aged 40 or older who have visited in the last 12 months who have all measurements required for calculation of risk score within 12 months of the most recent date of visit, that have a documented risk score
Are patients being risk scored?	Proportion of eligible patients with a documented risk score	Patients aged 40 or older who have visited in the last 12 months with a documented risk score	Patients aged 40 or older who have visited in the last 12 months
Are risk scores calculated correctly?	Proportion of eligible patients with a documented risk score that is correct	Patients aged 40 or older who have visited in the last 12 months with a documented risk score that is correct	Patients aged 40 or older who have visited in the last 12 months with a documented risk score
Are statins prescribed to the correct patients?	Proportion of eligible patients prescribed a statin	Patients with existing CVD, diabetics 40 or older with high LDL values (as defined based on total CVD risk of SCORE 10-14% in LDL ≥ 2.6 mmol/L; with very high risk SCORE $\geq 15\%$ in LDL ≥ 1.8 mmol/L), or patients with a SCORE of $\leq 9\%$ and LDL ≥ 2.6 or total cholesterol ≥ 7.2 , or patients with a SCORE of 10-14% and a LDL ≥ 1.8 or total cholesterol ≥ 7.2 mmol/L, or patients with a SCORE of $\geq 15\%$, prescribed a statin	Patients with existing CVD, diabetics 40 or older with high LDL values (as defined based on total CVD risk of SCORE 10-14% in LDL ≥ 2.6 mmol/L; with very high risk SCORE $\geq 15\%$ in LDL ≥ 1.8 mmol/L), or patients with a SCORE of $\leq 9\%$ and LDL ≥ 2.6 or total cholesterol ≥ 7.2 , or patients with a SCORE of 10-14% and a LDL ≥ 1.8 or total cholesterol ≥ 7.2 mmol/L, or patients with a SCORE of $\geq 15\%$
Are statins prescribed correctly based on documented risk score?	Proportion of patients eligible based on documented risk score prescribed a statin	Patients with a documented risk score as very high risk SCORE $\geq 15\%$ prescribed a statin	Patients with a documented risk score as very high risk SCORE $\geq 15\%$
Are patients with existing disease, who do not require the calculation of a risk score to prescribe statins, prescribed statins?	Proportion of patients with existing CVD prescribed a statin	Patients with existing CVD prescribed a statin	Patients with existing CVD
Is the blood pressure of high risk patients controlled?	Proportion of high risk patients (SCORE $\geq 15\%$ or DM and age over 40)	Patients with a true risk score indicating a very high risk (SCORE $\geq 15\%$) or DM and age	Patients with a true risk score indicating a very high risk (SCORE $\geq 15\%$) or DM and

	whose last two recorded blood pressure measurements were <130/80 mmHg	over 40 whose last two documented blood pressure readings were <130/80	age over 40
Is the blood pressure of lower risk patients controlled?	Proportion of lower risk patients (SCORE<15%) whose last two recorded blood pressure measurements were <140/90 mmHg	Patients with a true risk score indicating <15% whose last two documented blood pressure readings were <140/90	Patients with a true risk score indicating <15%
Are patients with existing CVD prescribed basic medications to reduce risk?	Proportion of patients with existing CVD prescribed a statin and aspirin and blood pressure lowering treatment	Patients with existing CVD prescribed a statin and aspirin and blood pressure lowering treatment	Patients with existing CVD
Is the blood glucose of diabetic patients controlled?	Proportion of diabetic patients with glycaemic control as defined by last two HbA1c measurements	Patients with diabetes 2 whose last two HbA1c measurements were below personal target as defined by MDA adapted WHO PEN 1	Patients with diabetes type 2
Is the blood pressure of hypertensive patients controlled?	Proportion of confirmed hypertensive patients whose SBP is <140/90 at last two visits	Patients with confirmed hypertension whose last two blood pressure readings were <140/90	Patients with confirmed hypertension
What is the prevalence of high blood pressure?	Proportion of people whose last two systolic blood pressure reading are 140 mmHg or above	Patients whose last two systolic blood pressure readings were \geq 140	All patients over 18

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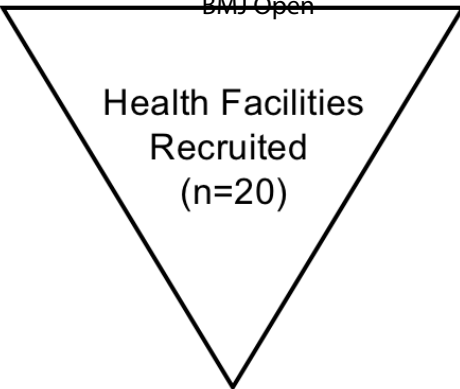
413 **Table 2.** Standardized data collection form used to extract data from individual patient records
 414

Data Collection Question	Answer
What is your name? (Name of person extracting data)	
Date of Data Extraction (MM-DD-YYYY)	
Write the Clinic Name	
Is this a duplicate extraction?	
If it is a duplicate extraction, enter the number you and your extraction partner have assigned to this file.	
Date of Birth (MM-DD-YYYY)	
Sex (M/F)	
Smoking Status (Y/M)	
Diagnosis of Hypertension (Y/N)	
Date of Hypertension Diagnosis (MM-DD-YYYY)	
Can you find one or more blood pressure readings? (Y/N)	
Most Recent Systolic Blood Pressure	
Most Recent Diastolic Blood Pressure	
Date of the Most Recent Blood Pressure Measurement (MM-DD-YYYY)	
Can you find a second most recent blood pressure reading? (Y/N)	
Second most recent systolic blood pressure	
Second most recent diastolic blood pressure	
Date of the second most recent systolic blood pressure (MM-DD-YYYY)	
Diagnosis of Diabetes (Type 1, Type 2, No)	
Can you find one or more HbA1c measurements? (Y/N)	
Most recent HbA1c reading (mmol/mol)	
Date of the most recent HbA1c measurement? (MM-DD-YYYY)	
Can you find another HbA1c measurement? (Y/N)	
Second most recent HbA1c reading (mmol/mol, otherwise specify unit)	
Date of the second most recent HbA1c reading? (MM-DD-YYYY)	
Can you find one or more total cholesterol measurements? (Y/N)	
Most recent total cholesterol reading (mmol/L)	
Date of the most recent cholesterol reading (MM-DD-YYYY)	
Can you find another cholesterol measurement? (Y/N)	
Second most recent cholesterol reading (mmol/L)	
Date of the second most recent cholesterol reading (MM-DD-YYYY)	
Was the patient prescribed a statin? (Y/N)	
What was the date of the statin prescription? (MM-DD-YYYY)	

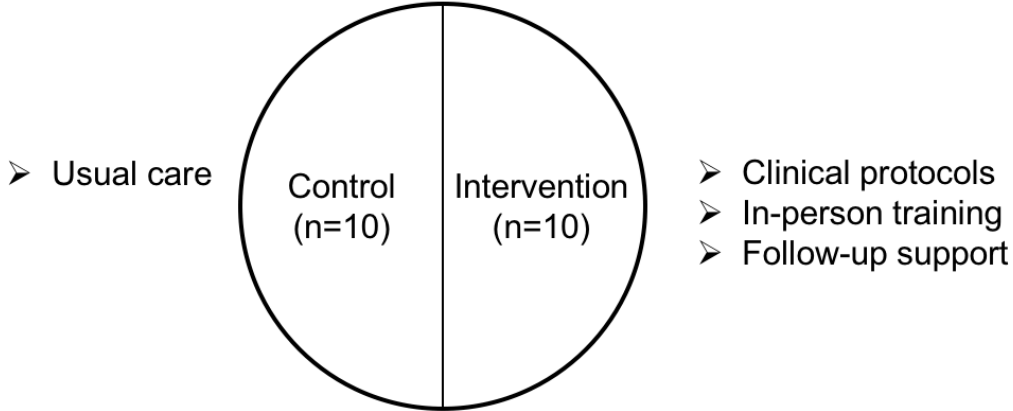
1	What was the drug and dose?	
2	Does the patient have existing CVD? (Y/N)	
3	State the type of CVD	
4	Has the patient been prescribed acetylsalicylic acid (ASA or aspirin)? (Y/N)	
5	What was the most recent date that ASA was prescribed? (MM-DD-YYYY)	
6	Has the patient been prescribed anti-hypertensives? (Y/N)	
7	What was the most recent date that anti-hypertensives were prescribed? (MM-DD-YYYY)	
8	Can you find a documented ESC SCORE risk score? (Y/N)	
9	Enter the most recent documented ESC SCORE risk score (%)	
10	What was the date the risk score was documented? (MM-DD-YYYY)	
11	Please record any important notes about the data extraction here. Examples include an error you think may have been made, clarification of the units for measurements (e.g. mmol/L vs mg/dL). Or notes that you would like for yourself.	

415

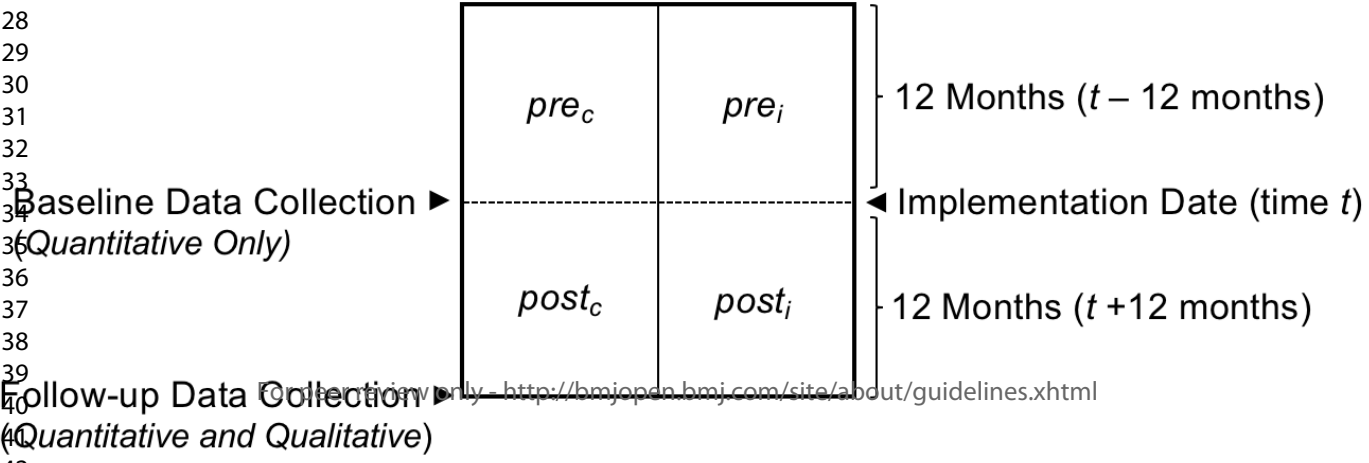
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Randomization



Data Collection



BMJ Open

Protocol for the Evaluation of a Pilot Implementation of Essential Interventions for the Prevention of Cardiovascular Diseases in Primary Health Care in the Republic of Moldova

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3 1 **Protocol for the Evaluation of a Pilot Implementation of Essential Interventions for the**
4 2 **Prevention of Cardiovascular Diseases in Primary Health Care in the Republic of Moldova**
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8 5 Dylan R. J. Collins¹, Angela Ciobanu², Tiina Laatikainen³, Ghenadie Curocichin⁴, Virginia
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23 ABSTRACT

25 Introduction

26 Nearly 90% of all deaths in Republic of Moldova are caused by NCDs, the majority of which
27 (55%) are caused by CVD. In addition to reducing premature mortality from CVD, it is estimated
28 that strengthening primary health care could cut the number hypertension-related hospital
29 admissions and diabetes-related hospitalizations in half. The aim of this evaluation is to determine
30 the feasibility of implementing and evaluating essential interventions for the prevention of CVD
31 in primary health care in Republic of Moldova, with a view toward national scale-up.

33 Methods and Analysis

34 A national steering group including international experts will be convened to adapt WHO PEN
35 protocols one and two to the health system of Republic of Moldova, develop and conduct training
36 of primary health care workers, and test a core set of indicators to monitor the quality of care and
37 change in clinical practice. To evaluate the impact of this pilot implementation, a pragmatic,
38 sequential mixed methods explanatory design, composed of quantitative and qualitative strands of
39 equal weight, will be used. Twenty primary health care centres will be selected and randomized to
40 the training and implementation arm (n=10) and the usual care arm (n=10). At baseline and 12
41 months follow-up, a standardized data collection form will be piloted to extract data directly from
42 patient paper records in order to estimate the change in clinical practice. Semi-structured
43 interviews and inter-clinic peer workshops will be conducted at 12 months follow-up, and
44 qualitative data collected from these formats will be analysed thematically for explanatory themes
45 that relate to the quantitative findings.

47 Ethics and Dissemination

48 Ethical review and approval has been obtained. Findings of the evaluation will be shared in a
49 project report to key stakeholders, presented back to participants, and written into a manuscript for
50 an open access peer-reviewed scientific journal.

53 STRENGTHS AND LIMITATIONS OF THIS STUDY

- 55 • To our knowledge, this is the first description of adapting and piloting WHO essential NCD
56 interventions in primary health care in a low- or middle-income country and provides a
57 methodological example to other jurisdictions
- 58 • A mixed methods design allows for a greater understanding of the potential barriers and
59 facilitators to implementation and can inform future health systems development
- 60 • Primary health care facilities will be selected from different regions of Republic of
61 Moldova in order to pilot implementation in a variety of contexts throughout the country
- 62 • Since this is an evaluation of a pilot implementation, the sample size is based on
63 pragmatism and not statistical power
- 64 • We are unable to include patient perspectives and experience in the evaluation, which is an
65 important aspect of health care quality

67 INTRODUCTION

68
69 Globally, non-communicable diseases (NCDs) account for more than one-half of the global burden
70 of disease.(1) In 2016, an estimated 41 million deaths were due to NCDs, of which nearly half
71 were due to cardiovascular diseases (CVD).(2) Primary health care systems play an important role
72 in the prevention, early detection, and appropriate management of these diseases, but many nations
73 lack primary health care capacity.(3,4)

74
75 To support national governments to realize their commitments in reducing the burden of NCDs,
76 as agreed in the United Nations Political Declaration on NCDs, the World Health Assembly
77 endorsed the WHO Global Action Plan for the Prevention and Control of NCDs 2013-2020. To
78 support implementation of this Action Plan, WHO has identified a set of cost-effective policy
79 options (“best buys”) for the prevention and control of NCDs within countries.(5)

80
81 The Republic of Moldova (henceforth “MDA”) is located in Eastern Europe, between Ukraine and
82 Romania; the Capital and largest city is Chisinau. By gross domestic product per capita, MDA is
83 one of the poorest countries in the WHO European Region and it is estimated that 21.9% of citizens
84 live below the absolute poverty line of 1 US Dollar per day.(6)

86 **Non-communicable diseases are a leading cause of death in MDA**

87 While NCDs are a global epidemic, MDA ranks amongst the countries most affected. Nearly 90%
88 of all deaths in MDA are caused by NCDs, the majority of which (55%) are caused by CVD.(7)
89 In 2016, the probability of dying prematurely from any of the four major NCDs (CVDs, cancer,
90 diabetes, chronic respiratory disease) was 24.9%,; almost twice as high for men (33.7%) as women
91 (17.3%).(8) Men and people residing in rural areas are disproportionately impacted by CVD and
92 represent key populations for public health intervention.(7)

93
94 This burden is driven by some of the highest rates of NCD risk factors, including tobacco and
95 alcohol use, in the WHO European region indicated by a 2013 STEPS survey.(9) One-in-four
96 (25.3%) Moldovans smoke tobacco and this rate nearly doubles in men.(9) Among adults aged 18
97 to 69, 61.9% currently consume alcohol and one in five people have engaged in heavy episodic
98 drinking (six or more drinks on any one occasion in the past 30 days).(9)

99
100 The overall prevalence of obesity amongst adults is 22.9%, being higher among women (28.5%)
101 as compared with men (17.8%).(9) The prevalence of raised blood pressure (defined as SBP \geq
102 140 mmHg and/or DBP \geq 90 mmHg or currently taking medication for raised blood pressure)
103 among MDA’s adult population is 39.8%, and 76.2% of these patients are not on blood pressure
104 lowering medication.(9) A total of 12.3% of the population have a blood glucose level of \geq 6.1
105 mmol/L, and 29.4% of the population has a total blood cholesterol level of \geq 5 mmol/L.(9) It is
106 estimated that one in five (23.0%) people aged 40–69 years have a 10-year fatal or non-fatal CVD
107 risk of over 30% (including those with an existing CVD).(9)

109 **Primary health care in MDA and commitment to NCDs**

110 According to the Constitution of Republic of Moldova of 1994, citizens are entitled to a free of
111 charge minimum package of essential health services, including primary health care. However,
112 resource constraints have made it difficult to offer these services and significant gaps in care

1
2
3 113 exist.(10) According to the most recent data (2010), there were 5.3 family doctors per 10,000
4 114 inhabitants and 25.9 specialist doctors per 10,000 inhabitants. In rural areas these rates are halved,
5 115 leading to human resource shortages in primary care.(10) Approximately 17% of practicing
6 116 physicians in MDA work in primary health care, and 92% of them rely on paper clinical records.(6)
7 117 The most recent estimate (2009) states that there are approximately 630 primary health care centres
8 118 throughout the country, or 21.2 centres per 100,000 people.(6)
9 119

10 119
11 120 Despite these health system challenges, the Government of Republic of Moldova is committed to
12 121 improving primary health care capacity for NCDs. It is estimated that 60% of hypertension-related
13 122 hospital admissions (about 12,000 annually) and 40% of diabetes-related hospitalizations (about
14 123 5,000 annually) could be prevented through strengthened primary health care for these conditions,
15 124 including better identification and management of those at increased CVD risk.(11)
16 125

17 125
18 126 Given the need and international policy support for addressing this gap in NCD care, there was a
19 127 favourable window of opportunity to act with impact. As such, strengthening primary health care
20 128 was set out as one of the main commitments in the Action Program of the Government of Republic
21 129 of Moldova 2016–2018.(12) To do this requires the development of simplified clinical protocols,
22 130 in-person training programs for nurses and doctors, and a core set of indicators to monitor and
23 131 evaluate changes in the quality of care.
24 132

25 132 26 133 **Essential interventions to prevent cardiovascular diseases in primary health care**

27 134 In order to build capacity in primary health care and ultimately prevent premature mortality from
28 135 CVD in MDA, a study was envisioned to adapt and pilot the World Health Organization Package
29 136 of Essential NCD Intervention from Primary Healthcare in Low Resource Settings (WHO
30 137 PEN).(3) WHO PEN includes simplified clinical protocols which together cover the integrated
31 138 management of hypertension and diabetes, as well as education and counselling on healthy
32 139 behaviours aimed to prevent CVD. The central strategy of this integrated approach is the use of
33 140 total cardiovascular risk assessment to stratify and target individuals at high CVD risk, a process
34 141 considered to be a “best buy” intervention by the WHO.(5)
35 142

36 142
37 143 These interventions are aimed at tackling areas identified in a 2014 WHO assessment of challenges
38 144 and opportunities for better NCD outcomes in Moldova. (13) This includes shortcomings amongst
39 145 health workers in the identification and management of individuals with increased cardiovascular
40 146 risk. The interventions are expected to add to the current quality of care by targeting interventions
41 147 (non-pharmacological and/or pharmacological) to those at highest risk who stand to gain the most
42 148 in absolute cardiovascular risk reduction, while also emphasizing improvements in the
43 149 organization of care. The intervention also includes practical face-to-face training and follow-up
44 150 implementation support. Current practice underutilizes these medical strategies and guidelines
45 151 (e.g. CVD risk score directed primary prevention), in addition to limited task sharing with non-
46 152 physician health works (e.g. nurses) in these care pathways. (13) At the study’s inception, there
47 153 were no known developments beyond the scope of this project that could change clinical practice
48 154 for NCDs in primary health care.
49 155

50 155
51 156 Since the use of WHO PEN was unprecedented in MDA, the Ministry of Health, Labour and Social
52 157 Protection convened a national steering group to lead the adaptation and pilot process, with the
53 158 goal of using the findings for future health systems development. Led by the primary health care
54 159
55 160

1
2
3 159 division of the Ministry of Health, the steering group is comprised of representatives from the
4 160 Nicolae Testemitanu State University of Medicine and Pharmacy and the National Public Health
5 161 Agency. The national steering group is supported by an international team of experts coordinated
6 162 jointly by the WHO Regional Office for Europe and WHO Country Office in the Republic of
7 163 Moldova.
8 164

10 165 **AIM AND OBJECTIVES**

11 166 **Aim**

12 167
13 168 The aim of the evaluation is to determine the feasibility of implementing and evaluating essential
14 169 interventions for the prevention of cardiovascular disease in primary health care in MDA, with a
15 170 view toward national scale-up.
16 171

17 172 **Objectives**

18 173 Primary Objectives

- 19 174 1. Assess the ability to implement MDA-adapted WHO PEN protocols one and two in pilot
20 175 primary health care centres
- 21 176 2. Determine the feasibility of collecting quantitative data required for future studies of
22 177 effectiveness from the existing informal paper clinical record system
23 178

24 179 Secondary Objectives

- 25 180 1. Determine the baseline performance of primary health care services with respect to
26 181 essential interventions for the prevention and management of CVD
- 27 182 2. Estimate the change in performance of pilot primary health care centres after 12 months
28 183 of protocol implementation and compare this to control clinics using usual care
29 184

30 185 **METHODS AND ANALYSIS**

31 186 **Overview of Process and Design**

32 187
33 188 An overview of the methods used to adapt, pilot, and evaluate essential interventions for CVD in
34 189 primary health care in MDA are summarized by the following seven steps, which are planned to
35 190 occur from September 2016 to May 2019.
36 191

37 192 Step One: Adaptation of WHO PEN Protocols to the National Context

38 193 Under the direction of the national steering group, WHO PEN protocols one and two will be
39 194 compared and contrasted to national disease specific guidelines. The WHO PEN protocols will
40 195 then be adapted to ensure consistency with the organization, culture, and availability of resources
41 196 of the health system, while ensuring that they remain simple clinical decision support tools.
42 197

43 198 Step Two: Development of a Training Package for Primary Health Care Workers

44 199 A three-day training package will be developed under the direction of the national steering group
45 200 in order to provide in-person theoretical and practical training to nurses and doctors working in
46 201 primary health care. This will include lectures, clinical case studies, and practical exercises that
47 202 embrace the experience and knowledge of participants.
48 203

49 204 Step Three: Collection of Baseline Data

205 According to the Ministry of Health process, a list of 20 primary health care clinics will be
206 nominated and provided to the working group. They will then be randomized into an intervention
207 group arm (n=10) and control arm (n=10). Data for quantitative indicators will be extracted from
208 all 20 clinics by randomly sampling individual paper-based patient records from all primary health
209 care units using a standardized data collection instrument. This will be done before randomization
210 by a specially trained group of postgraduate medical trainees, such that neither the clinics nor the
211 data extractors will know the allocation of each clinic to intervention or control arm.

212 213 Step Four: Training Staff in Pilot Clinics

214 All doctors and nurses from the primary health care centres in the intervention arm will be invited
215 to be trained together by a national team of experts in groups of approximately 30. It is estimated
216 that up to 200 health workers will be trained in total. At the end of training each PHC team will
217 pass through evaluation at the University Centre for Simulation in Medical Training using
218 objective structured clinical exams and get feedback from trainers and peers.

219 220 Step Five: Implementation of Protocols

221 Trained participants from the ten primary health care clinics in the intervention arm will then be
222 free to implement the clinical protocols and change their clinical practice, without incentives, for
223 12 months. During this time, a team of national experts will be created to offer support (distance
224 and on-the-job) to the primary health care centres in the intervention arm. All ten clinics in the
225 intervention arm will receive at least one in-person follow-up support visit.

226 227 Step Six: Collection of Follow-up Data

228 After 12 months, using the same method and data collection instruments used to collect baseline
229 quantitative data (Step Three), data will again be extracted from randomly selected individual
230 paper-based patient records from all 20 health care centres. Five primary health care centres from
231 the intervention arm will be selected by the national steering group for one-on-one semi structured
232 interviews with health staff. This will be supplemented by inviting a selection of staff from all ten
233 health centres in the intervention arm to participate in focus groups. Together, these qualitative
234 data will be analysed thematically for explanatory themes.

235 236 Step Seven: Evaluation of Results and Sharing Experience

237 The findings of the quantitative and qualitative analyses will be integrated in a final report and
238 shared with key stakeholders, including health staff from the participating primary health care
239 centres. The results will also be shared at a national conference and in an open-access peer
240 reviewed journal, in order to inform the future development of primary health care capacity in
241 MDA.

242 243 **Methodological Design**

244 A pragmatic, sequential mixed methods explanatory design, composed of quantitative and
245 qualitative strands of equal weight, will be used (Figure 1). This design was chosen because it
246 allows for the use of qualitative data to enlighten and explain the quantitative findings, including
247 but not limited to the feasibility of collecting data from paper-based records, the contextual factors
248 affecting guideline implementation, changes in clinical practice, and optimization for the future.

249
250 **Figure 1.** Illustration using the GATE frame structure (14) of the mixed methods evaluation design

251
252 A sample size of 20 primary health care centres was chosen because it was seen as a good balance
253 of allowing for variation in clinic geography and demography, while still remaining feasible for
254 the pilot implementation. Half of the centres (n=10) will be randomly allocated to the intervention
255 arm and half (n=10) to the control arm. Baseline data will be collected from both intervention and
256 control clinics, ensuring that baseline data is collected before implementation occurs.

257
258 Within clinic comparisons will be used to compare the 12 months before randomization with the
259 12 months of implementation. Between clinics comparison will be used to compare the
260 intervention clinics with control clinics during the same time period.

261 262 **Eligibility Criteria for Primary Health Care Centres**

263 Health facilities will be nominated by the Ministry of Health for participation based on the
264 following eligibility criteria: (1) primary health care facilities must be operating in the public sector
265 as legal entities; (2) primary health care facilities must be sampled in a way such that they are
266 geographically distributed evenly across the country; equally from the Central, North and Southern
267 regions of MDA; and (3) health facilities must be primary health care centres that are managed by
268 family doctors with no specialist doctors working in the facility. These criteria were chosen in
269 order to select a group of clinics that sufficiently reflect the majority of primary health care
270 facilities in Moldova.

271 272 **Randomization**

273 The clinics will be stratified based on the ratio of patients to family doctors to minimize possible
274 confounding by doctor caseload, and then randomized electronically into two groups of 10 primary
275 health care centres.

276 277 **Comparison**

278 The 10 primary health care centres in the intervention arm will be compared to the 10 primary
279 health care centres in the control arm. The control arm will receive no intervention and proceed
280 with usual care.

281 282 **Quantitative Indicators**

283 Indicators were developed to balance input and process indicators, such as measurement of risk
284 factors and calculation of risk scores, with output (e.g. prescribing) and outcome (e.g. blood
285 pressure control) indicators. While one of the objectives of this evaluation is to determine the
286 ability to measure these indicators based on routine paper records, we used our existing knowledge
287 of the health system to design indicators which were valuable and likely to be feasible to calculate.
288 Table 1 shows the indicator, the question the indicator seeks to answer, and the respective
289 numerator and denominator definitions which will be used in the calculations.

290
291 **Table 1.** Indicators, their numerators and denominators, and questions the indicators answer

292 293 **Data Collection and Management**

294 295 Quantitative Data Collection Tool

1
2
3 296 A standardized data collection template has been developed for extracting anonymized patient data
4 297 from individual paper records (Table 2). An online version was also made to allow for data entry
5 298 on a computer or smartphone. It is estimated to take 15 minutes to extract data from one patient
6 299 record since the records are made of blank paper with no formal structure or organization of health
7 300 data.
8 301

9 302 **Table 2.** Standardized data collection form used to extract data from individual patient records
10 303

11 304 Method of Randomly Sampling Patient Records

12 305 A random sample of the records of patients aged over 18, who have visited the medical facility
13 306 within the past 12 months, will be taken. Since medical records in MDA are organized
14 307 alphabetically on shelves, we created a randomly generated list of alphanumeric combinations that
15 308 allowed for the selection of patient charts at random. For example, an alphanumeric code of “C24”
16 309 would correspond to the 24th patient chart in the section of last names starting with the letter C.
17 310

18 311 The list will be followed in the order that it was generated so as to prevent selection bias. The
19 312 randomly selected chart will then be checked to see if it meets two inclusion criteria: (1) the patient
20 313 is aged 18 years or older and (2) the patient visited the health centre within the last 12 months. If
21 314 the record meets these criteria, data will then be extracted. If it does not, it will be returned to the
22 315 shelf and the next alphanumeric code on the randomly generated list will be used. This process
23 316 will be repeated in each clinic until a sample size of 1.2% of the patient population in each clinic
24 317 is sampled. This proportion was chosen pragmatically such that the average sample per primary
25 318 health care centre would equal 100 unique patients.
26 319

27 320 Data Analysis

28 321 The change in indicators from baseline to follow-up will be calculated for intervention clinics
29 322 and compared with control clinics (Table 1). Subgroup analysis by age, gender, and other
30 323 demographic features may be done as deemed appropriate by the national steering committee.
31 324 All analyses will account for stratified sampling. Since the health centre is the unit of inference
32 325 for the outcomes (e.g. health centre proportion of eligible patients with a documented CVD risk
33 326 score), use of an intraclass correlation coefficient is not required for analyses of these
34 327 outcomes. Age and gender adjusted logistic regression models will be used to analyse the
35 328 differences in pre-defined indicators between intervention and control clinics and between
36 329 baseline and follow-up. The differences in means of continuous variables between the
37 330 intervention and control clinics and baseline and follow-up will be analysed using age and
38 331 gender adjusted analysis of variance.
39 332

40 333 Qualitative Data Collection

41 334 **Follow-up Support Visits**

42 335 Follow-up visits will be made to each intervention clinic at least once during the implementation
43 336 timeframe (12 months) to provide ad hoc implementation support. These visits will be conducted
44 337 by members of the national steering group, who will keep field notes about each visit and provide
45 338 feedback and support to the health centres. The perspectives gained through follow-up support
46 339 visits will be used by the national steering group to develop preliminary data collection tools for
47 340 semi-structured interviews.
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341 **Semi-Structured Interviews**

342 A maximum variation sample of half of the intervention clinics (n=5) will be chosen, based on the
343 perceived performance of each clinic by the evaluation steering committee. A pragmatic sample
344 of clinic managers (n=1 per clinic), doctors (n=3 per clinic), and nurses (n=3 per clinic) will be
345 interviewed one-on-one, using a semi-structured format. Interviews will proceed until data
346 saturation has been reached, to a maximum of 30 interviews. After obtaining written, informed
347 consent, interviews will be of 30 to 60 minutes in length, audio recorded, and be transcribed
348 verbatim and analysed thematically using framework thematic analysis.(15) The interviews will
349 be conducted by members of the steering group, but the interviewers will be allocated to
350 participants from health centres with whom they did not provide follow-up support visits.

351 **Focus Group Workshop**

352 Participants from all ten implementation clinics will be invited to a workshop to further collect
353 explanatory qualitative data and to critically reflect on the implementation process. Participants
354 will be a mix of doctors, nurses, and managers from the intervention clinics.

356 Participants will be placed into small groups based on their profession, and asked to complete a
357 standardized worksheet. Each group will be under the guidance of a facilitator, and emergent
358 themes from one-one-one interviews will be used as prompts to each group. The worksheet will
359 allow for each group to directly comment, modify, or add to the emergent themes, create new
360 themes, and organize themes into categories such as barriers and facilitators.

362 Integration of Quantitative and Qualitative Strands

363 The resulting qualitative data will be analysed thematically using the framework approach, and
364 used to help explain the findings of the quantitative strand.(15) Following the sequential mixed
365 method design, integration of the qualitative findings with quantitative findings will allow for the
366 interpretation of the results in light of each other. This may include post-hoc analysis of
367 effectiveness of some of the quantitative outcomes as appropriate, to further add meaning to the
368 integration of qualitative and quantitative strands.

369 **Patient and Public Involvement**

370 Neither patients nor the public were involved in the methodological design.

373 **ETHICS AND DISSEMINATION**

374 **Ethical Review and Approval**

375 This project was reviewed by the Research Ethics Committee of the Nicolae Testemitanu State
376 University of Medicine and Pharmacy of the Republic of Moldova and granted permission on 31
377 May 2017.

379 **Dissemination**

380 Quantitative findings will be summarized and presented back to all intervention clinics during
381 follow-up workshops. A comprehensive project report will be written and shared with key
382 stakeholders. A final report of key findings of the evaluation will be written and submitted to an
383 open access peer-reviewed journal and made available to all study participants so they can use the
384 findings to improve their practice. The findings will be used to evaluate the feasibility of a national
385 scale-up of essential NCD interventions in primary health care in MDA.

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REFERENCES

1. Benziger CP, Roth GA, Moran AE. The Global Burden of Disease Study and the Preventable Burden of NCD. *Glob Heart*. 2016 Dec;11(4):393–7.
2. World Health Organization (WHO). World Health Statistics [Internet]. 2018. Available from: http://www.who.int/gho/publications/world_health_statistics/2018/en/
3. World Health Organization (WHO). Package of Essential Noncommunicable (PEN) disease interventions for primary health care in low-resource settings [Internet]. 2013. Available from: http://www.who.int/ncds/management/pen_tools/en/
4. World Health Organization (WHO). Global action plan for the prevention and control of NCDs 2013-2020. 2013.
5. Organization WH. Tackling NCDs: “Best buys” and other recommended interventions for the prevention and control of noncommunicable diseases [Internet]. 2017. Available from: <http://www.who.int/ncds/management/best-buys/en/>
6. World Health Organization (WHO). Evaluation of the structure and provision of primary care in the Republic of Moldova. 2012.
7. National Center for Health Management. Health Yearbook: Public Health in Moldova [Internet]. 2015. Available from: <http://www.cnms.md/ro/rapoarte>
8. World Health Organization. Global Health Observatory data repository [Internet]. [cited 2018 Jul 10]. Available from: <http://apps.who.int/gho/data/node.home>
9. World Health Organization (WHO). Prevalence of Noncommunicable Disease Risk Factors in the Republic of Moldova (STEPS) [Internet]. 2014. Available from: http://www.who.int/ncds/surveillance/steps/Moldova_2013_STEPS_Report.pdf
10. Turcanu C, Domente S, Buga M, Richardson E. Health Systems in Transition: Republic of Moldova [Internet]. 2012. Available from: http://www.euro.who.int/__data/assets/pdf_file/0006/178053/HiT-Moldova.pdf
11. World Health Organization (WHO). Ambulatory care sensitive conditions in the Republic of Moldova [Internet]. 2015. Available from: <http://www.euro.who.int/en/countries/republic-of-moldova/publications/ambulatory-care-sensitive-conditions-in-the-republic-of-moldova-2015>
12. Government of the Republic of Moldova. Action Program of the Government of the Republic of Moldova 2016–2018 [Internet]. 2016. Available from: http://gov.md/sites/default/files/document/attachments/guvernul_republicii_moldova_-_programul_de_activitate_al_guvernului_republicii_moldova_2016-2018.pdf
13. World Health Organization Regional Office for Europe. Better noncommunicable disease outcomes: challenges and opportunities for health systems -- Country Assessment of Republic of Moldova [Internet]. Copenhagen; 2014. Available from: http://www.euro.who.int/__data/assets/pdf_file/0008/255464/BetterNCDoutcomesChallengesOpportunitiesHealthSystemsMoldovaCountryAssessmentEng.pdf?ua=1
14. Jackson R, Ameratunga S, Broad J, Connor J, Lethaby A, Robb G, et al. The GATE frame: critical appraisal with pictures. Vol. 144, ACP journal club. United States; 2006. p. A8-11.
15. Gale NK, Heath G, Cameron E, Rashid S, Redwood S. Using the framework method for the analysis of qualitative data in multi-disciplinary health research. *BMC Med Res Methodol*. 2013 Sep;13:117.

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3 432 **AUTHORS AND CONTRIBUTIONS**

4 433 DC, AC, TL, GC, VS, TZ, AA, and JF contributed to the methodological design. DC, AC, TL, and
5 434 JF contributed to writing the manuscript.

6 435

7
8 436 **FUNDING STATEMENT**

9 437 This study is funded jointly by the Swiss Agency for Development and Cooperation (SDC) and WHO
10 438 Regional Office for Europe.

11 439

12 440 **COMPETING INTERESTS STATEMENT**

13 441 DC, AC, TL, GC, VS, TZ, AA, JF declare no competing interests.

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443 **Table 1.** Indicators, their numerators and denominators, and questions the indicators answer

Question	Indicator	Numerator	Denominator
Are risk factors being measured?	Proportion of eligible patients who have all risk factor values recorded as required for calculation of risk score	Patients aged 40 or older who have visited in the last 12 months who have all measurements required for calculation of risk score within 12 months of the most recent date of visit	Patients aged 40 or older who have visited in the last 12 months
Are risk factor measurements being converted to a total risk score?	Proportion of patients aged 40 or older who have visited in the last 12 months who have all measurements required for calculation of risk score within 12 months of the most recent date of visit, that have a documented risk score	Patients aged 40 or older who have visited in the last 12 months who have all measurements required for calculation of risk score within 12 months of the most recent date of visit, that have a documented risk score	Patients aged 40 or older who have visited in the last 12 months who have all measurements required for calculation of risk score within 12 months of the most recent date of visit
Are risk scores calculated correctly?	Proportion of patients aged 40 or older who have visited in the last 12 months who have all measurements required for calculation of risk score within 12 months of the most recent date of visit, that have a documented risk score that is correct	Patients aged 40 or older who have visited in the last 12 months who have all measurements required for calculation of risk score within 12 months of the most recent date of visit, that have a documented risk score that is correct	Patients aged 40 or older who have visited in the last 12 months who have all measurements required for calculation of risk score within 12 months of the most recent date of visit, that have a documented risk score
Are patients being risk scored?	Proportion of eligible patients with a documented risk score	Patients aged 40 or older who have visited in the last 12 months with a documented risk score	Patients aged 40 or older who have visited in the last 12 months
Are risk scores calculated correctly?	Proportion of eligible patients with a documented risk score that is correct	Patients aged 40 or older who have visited in the last 12 months with a documented risk score that is correct	Patients aged 40 or older who have visited in the last 12 months with a documented risk score
Are statins prescribed to the correct patients?	Proportion of eligible patients prescribed a statin	Patients with existing CVD, diabetics 40 or older with high LDL values (as defined based on total CVD risk of SCORE 10-14% in LDL \geq 2.6 mmol/L; with very high risk SCORE \geq 15% in LDL \geq 1.8 mmol/L), or patients with a SCORE of \leq 9% and LDL \geq 2.6 or total cholesterol \geq 7.2, or patients with a SCORE of 10-14% and a LDL \geq 1.8 or total cholesterol \geq 7.2 mmol/L, or patients with a SCORE of \geq 15%, prescribed a statin	Patients with existing CVD, diabetics 40 or older with high LDL values (as defined based on total CVD risk of SCORE 10-14% in LDL \geq 2.6 mmol/L; with very high risk SCORE \geq 15% in LDL \geq 1.8 mmol/L), or patients with a SCORE of \leq 9% and LDL \geq 2.6 or total cholesterol \geq 7.2, or patients with a SCORE of 10-14% and a LDL \geq 1.8 or total cholesterol \geq 7.2 mmol/L, or patients with a SCORE of \geq 15%
Are statins prescribed correctly based on documented risk score?	Proportion of patients eligible based on documented risk score prescribed a statin	Patients with a documented risk score as very high risk SCORE \geq 15% prescribed a statin	Patients with a documented risk score as very high risk SCORE \geq 15%
Are patients with existing disease, who do not require the calculation of a risk score to prescribe statins, prescribed statins?	Proportion of patients with existing CVD prescribed a statin	Patients with existing CVD prescribed a statin	Patients with existing CVD

Is the blood pressure of high risk patients controlled?	Proportion of high risk patients (SCORE \geq 15% or DM and age over 40) whose last two recorded blood pressure measurements were <130/80 mmHg	Patients with a true risk score indicating a very high risk (SCORE \geq 15%) or DM and age over 40 whose last two documented blood pressure readings were <130/80	Patients with a true risk score indicating a very high risk (SCORE \geq 15%) or DM and age over 40
Is the blood pressure of lower risk patients controlled?	Proportion of lower risk patients (SCORE <15%) whose last two recorded blood pressure measurements were <140/90 mmHg	Patients with a true risk score indicating <15% whose last two documented blood pressure readings were <140/90	Patients with a true risk score indicating <15%
Are patients with existing CVD prescribed basic medications to reduce risk?	Proportion of patients with existing CVD prescribed a statin and aspirin and blood pressure lowering treatment	Patients with existing CVD prescribed a statin and aspirin and blood pressure lowering treatment	Patients with existing CVD
Is the blood glucose of diabetic patients controlled?	Proportion of diabetic patients with glycaemic control as defined by last two HbA1c measurements	Patients with diabetes 2 whose last two HbA1c measurements were below personal target as defined by MDA adapted WHO PEN 1	Patients with diabetes type 2
Is the blood pressure of hypertensive patients controlled?	Proportion of confirmed hypertensive patients whose SBP is <140/90 at last two visits	Patients with confirmed hypertension whose last two blood pressure readings were <140/90	Patients with confirmed hypertension
What is the prevalence of high blood pressure?	Proportion of people whose last two systolic blood pressure reading are 140 mmHg or above	Patients whose last two systolic blood pressure readings were \geq 140	All patients over 18

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447 **Table 2.** Standardized data collection form used to extract data from individual patient records
 448

Data Collection Question	Answer
What is your name? (Name of person extracting data)	
Date of Data Extraction (MM-DD-YYYY)	
Write the Clinic Name	
Is this a duplicate extraction?	
If it is a duplicate extraction, enter the number you and your extraction partner have assigned to this file.	
Date of Birth (MM-DD-YYYY)	
Sex (M/F)	
Smoking Status (Y/M)	
Diagnosis of Hypertension (Y/N)	
Date of Hypertension Diagnosis (MM-DD-YYYY)	
Can you find one or more blood pressure readings? (Y/N)	
Most Recent Systolic Blood Pressure	
Most Recent Diastolic Blood Pressure	
Date of the Most Recent Blood Pressure Measurement (MM-DD-YYYY)	
Can you find a second most recent blood pressure reading? (Y/N)	
Second most recent systolic blood pressure	
Second most recent diastolic blood pressure	
Date of the second most recent systolic blood pressure (MM-DD-YYYY)	
Diagnosis of Diabetes (Type 1, Type 2, No)	
Can you find one or more HbA1c measurements? (Y/N)	
Most recent HbA1c reading (mmol/mol)	
Date of the most recent HbA1c measurement? (MM-DD-YYYY)	
Can you find another HbA1c measurement? (Y/N)	
Second most recent HbA1c reading (mmol/mol, otherwise specify unit)	
Date of the second most recent HbA1c reading? (MM-DD-YYYY)	
Can you find one or more total cholesterol measurements? (Y/N)	
Most recent total cholesterol reading (mmol/L)	
Date of the most recent cholesterol reading (MM-DD-YYYY)	
Can you find another cholesterol measurement? (Y/N)	
Second most recent cholesterol reading (mmol/L)	
Date of the second most recent cholesterol reading (MM-DD-YYYY)	
Was the patient prescribed a statin? (Y/N)	
What was the date of the statin prescription? (MM-DD-YYYY)	

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3	What was the drug and dose?
4	Does the patient have existing CVD? (Y/N)
5	State the type of CVD
6	Has the patient been prescribed acetylsalicylic acid (ASA or aspirin)? (Y/N)
7	What was the most recent date that ASA was prescribed? (MM-DD-YYYY)
8	Has the patient been prescribed anti-hypertensives? (Y/N)
9	What was the most recent date that anti-hypertensives were prescribed? (MM-DD-YYYY)
10	Can you find a documented ESC SCORE risk score? (Y/N)
11	Enter the most recent documented ESC SCORE risk score (%)
12	What was the date the risk score was documented? (MM-DD-YYYY)
13	Please record any important notes about the data extraction here. Examples include an error you think may have been made, clarification of the units for measurements (e.g. mmol/L vs mg/dL). Or notes that you would like for yourself.
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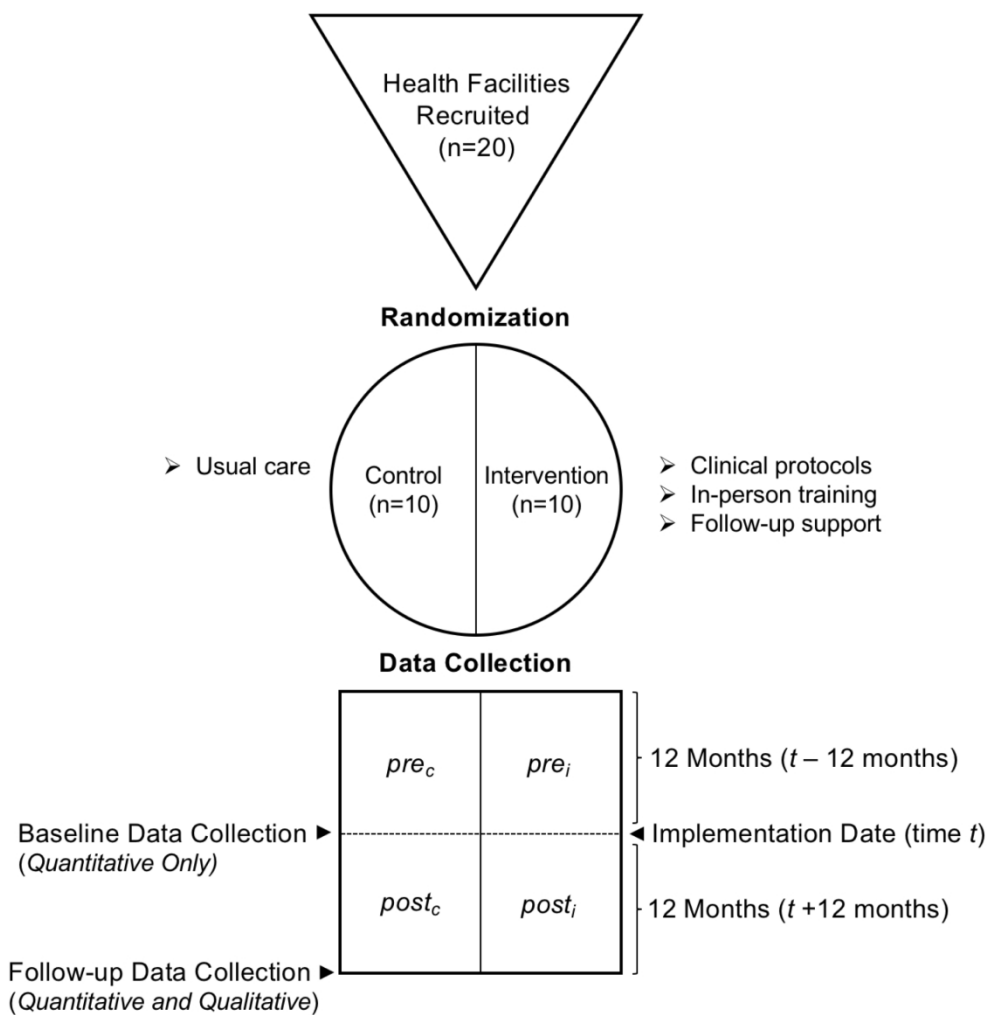


Figure 1. Illustration using the GATE frame structure (14) of the mixed methods evaluation design

184x193mm (300 x 300 DPI)

BMJ Open

Protocol for the Evaluation of a Pilot Implementation of Essential Interventions for the Prevention of Cardiovascular Diseases in Primary Health Care in the Republic of Moldova

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Primary Subject Heading:	Cardiovascular medicine
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Manuscripts

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3 **1 Protocol for the Evaluation of a Pilot Implementation of Essential Interventions for the**
4 **2 Prevention of Cardiovascular Diseases in Primary Health Care in the Republic of Moldova**
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23 ABSTRACT

25 Introduction

26 Nearly 90% of all deaths in Republic of Moldova are caused by NCDs, the majority of which
27 (55%) are caused by CVD. In addition to reducing premature mortality from CVD, it is estimated
28 that strengthening primary health care could cut the number hypertension-related hospital
29 admissions and diabetes-related hospitalizations in half. The aim of this evaluation is to determine
30 the feasibility of implementing and evaluating essential interventions for the prevention of CVD
31 in primary health care in Republic of Moldova, with a view toward national scale-up.

33 Methods and Analysis

34 A national steering group including international experts will be convened to adapt WHO PEN
35 protocols one and two to the health system of Republic of Moldova, develop and conduct training
36 of primary health care workers, and test a core set of indicators to monitor the quality of care and
37 change in clinical practice. To evaluate the impact of this pilot implementation, a pragmatic,
38 sequential mixed methods explanatory design, composed of quantitative and qualitative strands of
39 equal weight, will be used. Twenty primary health care centres will be selected and randomized to
40 the training and implementation arm (n=10) and the usual care arm (n=10). At baseline and 12
41 months follow-up, a standardized data collection form will be piloted to extract data directly from
42 patient paper records in order to estimate the change in clinical practice. Semi-structured
43 interviews and inter-clinic peer workshops will be conducted at 12 months follow-up, and
44 qualitative data collected from these formats will be analysed thematically for explanatory themes
45 that relate to the quantitative findings.

47 Ethics and Dissemination

48 Ethical review and approval has been obtained. Findings of the evaluation will be shared in a
49 project report to key stakeholders, presented back to participants, and written into a manuscript for
50 an open access peer-reviewed scientific journal.

53 STRENGTHS AND LIMITATIONS OF THIS STUDY

- 55 • To our knowledge, this is the first description of adapting and piloting WHO essential NCD
56 interventions in primary health care in a low- or middle-income country and provides a
57 methodological example to other jurisdictions
- 58 • A mixed methods design allows for a greater understanding of the potential barriers and
59 facilitators to implementation and can inform future health systems development
- 60 • Primary health care facilities will be selected from different regions of Republic of
61 Moldova in order to pilot implementation in a variety of contexts throughout the country
- 62 • Since this is an evaluation of a pilot implementation, the sample size is based on
63 pragmatism and not statistical power
- 64 • We are unable to include patient perspectives and experience in the evaluation, which is an
65 important aspect of health care quality

67 INTRODUCTION

68
69 Globally, non-communicable diseases (NCDs) account for more than one-half of the global burden
70 of disease.(1) In 2016, an estimated 41 million deaths were due to NCDs, of which nearly half
71 were due to cardiovascular diseases (CVD).(2) Primary health care systems play an important role
72 in the prevention, early detection, and appropriate management of these diseases, but many nations
73 lack primary health care capacity.(3,4)

74
75 To support national governments to realize their commitments in reducing the burden of NCDs,
76 as agreed in the United Nations Political Declaration on NCDs, the World Health Assembly
77 endorsed the WHO Global Action Plan for the Prevention and Control of NCDs 2013-2020. To
78 support implementation of this Action Plan, WHO has identified a set of cost-effective policy
79 options (“best buys”) for the prevention and control of NCDs within countries.(5)

80
81 The Republic of Moldova (henceforth “MDA”) is located in Eastern Europe, between Ukraine and
82 Romania; the Capital and largest city is Chisinau. By gross domestic product per capita, MDA is
83 one of the poorest countries in the WHO European Region and it is estimated that 21.9% of citizens
84 live below the absolute poverty line of 1 US Dollar per day.(6)

86 **Non-communicable diseases are a leading cause of death in MDA**

87 While NCDs are a global epidemic, MDA ranks amongst the countries most affected. Nearly 90%
88 of all deaths in MDA are caused by NCDs, the majority of which (55%) are caused by CVD.(7)
89 In 2016, the probability of dying prematurely from any of the four major NCDs (CVDs, cancer,
90 diabetes, chronic respiratory disease) was 24.9%,; almost twice as high for men (33.7%) as women
91 (17.3%).(8) Men and people residing in rural areas are disproportionately impacted by CVD and
92 represent key populations for public health intervention.(7)

93
94 This burden is driven by some of the highest rates of NCD risk factors, including tobacco and
95 alcohol use, in the WHO European region indicated by a 2013 STEPS survey.(9) One-in-four
96 (25.3%) Moldovans smoke tobacco and this rate nearly doubles in men.(9) Among adults aged 18
97 to 69, 61.9% currently consume alcohol and one in five people have engaged in heavy episodic
98 drinking (six or more drinks on any one occasion in the past 30 days).(9)

99
100 The overall prevalence of obesity amongst adults is 22.9%, being higher among women (28.5%)
101 as compared with men (17.8%).(9) The prevalence of raised blood pressure (defined as SBP \geq
102 140 mmHg and/or DBP \geq 90 mmHg or currently taking medication for raised blood pressure)
103 among MDA’s adult population is 39.8%, and 76.2% of these patients are not on blood pressure
104 lowering medication.(9) A total of 12.3% of the population have a blood glucose level of \geq 6.1
105 mmol/L, and 29.4% of the population has a total blood cholesterol level of \geq 5 mmol/L.(9) It is
106 estimated that one in five (23.0%) people aged 40–69 years have a 10-year fatal or non-fatal CVD
107 risk of over 30% (including those with an existing CVD).(9)

109 **Primary health care in MDA and commitment to NCDs**

110 According to the Constitution of Republic of Moldova of 1994, citizens are entitled to a free of
111 charge minimum package of essential health services, including primary health care. However,
112 resource constraints have made it difficult to offer these services and significant gaps in care

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3 113 exist.(10) According to the most recent data (2010), there were 5.3 family doctors per 10,000
4 114 inhabitants and 25.9 specialist doctors per 10,000 inhabitants. In rural areas these rates are halved,
5 115 leading to human resource shortages in primary care.(10) Approximately 17% of practicing
6 116 physicians in MDA work in primary health care, and 92% of them rely on paper clinical records.(6)
7 117 The most recent estimate (2009) states that there are approximately 630 primary health care centres
8 118 throughout the country, or 21.2 centres per 100,000 people.(6)
9 119

10 119
11 120 Despite these health system challenges, the Government of Republic of Moldova is committed to
12 121 improving primary health care capacity for NCDs. It is estimated that 60% of hypertension-related
13 122 hospital admissions (about 12,000 annually) and 40% of diabetes-related hospitalizations (about
14 123 5,000 annually) could be prevented through strengthened primary health care for these conditions,
15 124 including better identification and management of those at increased CVD risk.(11)
16 125

17 125
18 126 Given the need and international policy support for addressing this gap in NCD care, there was a
19 127 favourable window of opportunity to act with impact. As such, strengthening primary health care
20 128 was set out as one of the main commitments in the Action Program of the Government of Republic
21 129 of Moldova 2016–2018.(12) To do this requires the development of simplified clinical protocols,
22 130 in-person training programs for nurses and doctors, and a core set of indicators to monitor and
23 131 evaluate changes in the quality of care.
24 132

25 132 26 133 **Essential interventions to prevent cardiovascular diseases in primary health care**

27 134 In order to build capacity in primary health care and ultimately prevent premature mortality from
28 135 CVD in MDA, a study was envisioned to adapt and pilot the World Health Organization Package
29 136 of Essential NCD Intervention from Primary Healthcare in Low Resource Settings (WHO
30 137 PEN).(3) WHO PEN includes simplified clinical protocols which together cover the integrated
31 138 management of hypertension and diabetes, as well as education and counselling on healthy
32 139 behaviours aimed to prevent CVD. The central strategy of this integrated approach is the use of
33 140 total cardiovascular risk assessment to stratify and target individuals at high CVD risk, a process
34 141 considered to be a “best buy” intervention by the WHO.(5)
35 142

36 142
37 143 These interventions are aimed at tackling areas identified in a 2014 WHO assessment of challenges
38 144 and opportunities for better NCD outcomes in Moldova. (13) This includes shortcomings amongst
39 145 health workers in the identification and management of individuals with increased cardiovascular
40 146 risk. The interventions are expected to add to the current quality of care by targeting interventions
41 147 (non-pharmacological and/or pharmacological) to those at highest risk who stand to gain the most
42 148 in absolute cardiovascular risk reduction, while also emphasizing improvements in the
43 149 organization of care. The intervention also includes practical face-to-face training and follow-up
44 150 implementation support. Current practice underutilizes these medical strategies and guidelines
45 151 (e.g. CVD risk score directed primary prevention), in addition to limited task sharing with non-
46 152 physician health works (e.g. nurses) in these care pathways. (13) At the study’s inception, there
47 153 were no known developments beyond the scope of this project that could change clinical practice
48 154 for NCDs in primary health care.
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51 155
52 156 Since the use of WHO PEN was unprecedented in MDA, the Ministry of Health, Labour and Social
53 157 Protection convened a national steering group to lead the adaptation and pilot process, with the
54 158 goal of using the findings for future health systems development. Led by the primary health care
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3 159 division of the Ministry of Health, the steering group is comprised of representatives from the
4 160 Nicolae Testemitanu State University of Medicine and Pharmacy and the National Public Health
5 161 Agency. The national steering group is supported by an international team of experts coordinated
6 162 jointly by the WHO Regional Office for Europe and WHO Country Office in the Republic of
7 163 Moldova.
8 164

10 165 **AIM AND OBJECTIVES**

11 166 **Aim**

12 167
13 168 The aim of the evaluation is to determine the feasibility of implementing and evaluating essential
14 169 interventions for the prevention of cardiovascular disease in primary health care in MDA, with a
15 170 view toward national scale-up.
16 171

17 172 **Objectives**

18 173 Primary Objectives

- 19 174 1. Assess the ability to implement MDA-adapted WHO PEN protocols one and two in pilot
20 175 primary health care centres
- 21 176 2. Determine the feasibility of collecting quantitative data required for future studies of
22 177 effectiveness from the existing informal paper clinical record system
23 178

24 179 Secondary Objectives

- 25 180 1. Determine the baseline performance of primary health care services with respect to
26 181 essential interventions for the prevention and management of CVD
- 27 182 2. Estimate the change in performance of pilot primary health care centres after 12 months
28 183 of protocol implementation and compare this to control clinics using usual care
29 184

30 185 **METHODS AND ANALYSIS**

31 186 **Overview of Process and Design**

32 187
33 188 An overview of the methods used to adapt, pilot, and evaluate essential interventions for CVD in
34 189 primary health care in MDA are summarized by the following seven steps, which are planned to
35 190 occur from September 2016 to May 2019.
36 191

37 192 Step One: Adaptation of WHO PEN Protocols to the National Context

38 193 Under the direction of the national steering group, WHO PEN protocols one and two will be
39 194 compared and contrasted to national disease specific guidelines. The WHO PEN protocols will
40 195 then be adapted to ensure consistency with the organization, culture, and availability of resources
41 196 of the health system, while ensuring that they remain simple clinical decision support tools.
42 197

43 198 Step Two: Development of a Training Package for Primary Health Care Workers

44 199 A three-day training package will be developed under the direction of the national steering group
45 200 in order to provide in-person theoretical and practical training to nurses and doctors working in
46 201 primary health care. This will include lectures, clinical case studies, and practical exercises that
47 202 embrace the experience and knowledge of participants.
48 203

49 204 Step Three: Collection of Baseline Data

205 According to the Ministry of Health process, a list of 20 primary health care clinics will be
206 nominated and provided to the working group. They will then be randomized into an intervention
207 group arm (n=10) and control arm (n=10). Data for quantitative indicators will be extracted from
208 all 20 clinics by randomly sampling individual paper-based patient records from all primary health
209 care units using a standardized data collection instrument. This will be done before randomization
210 by a specially trained group of postgraduate medical trainees, such that neither the clinics nor the
211 data extractors will know the allocation of each clinic to intervention or control arm.

212 213 Step Four: Training Staff in Pilot Clinics

214 All doctors and nurses from the primary health care centres in the intervention arm will be invited
215 to be trained together by a national team of experts in groups of approximately 30. It is estimated
216 that up to 200 health workers will be trained in total. At the end of training each PHC team will
217 pass through evaluation at the University Centre for Simulation in Medical Training using
218 objective structured clinical exams and get feedback from trainers and peers.

219 220 Step Five: Implementation of Protocols

221 Trained participants from the ten primary health care clinics in the intervention arm will then be
222 free to implement the clinical protocols and change their clinical practice, without incentives, for
223 12 months. During this time, a team of national experts will be created to offer support (distance
224 and on-the-job) to the primary health care centres in the intervention arm. All ten clinics in the
225 intervention arm will receive at least one in-person follow-up support visit.

226 227 Step Six: Collection of Follow-up Data

228 After 12 months, using the same method and data collection instruments used to collect baseline
229 quantitative data (Step Three), data will again be extracted from randomly selected individual
230 paper-based patient records from all 20 health care centres. Five primary health care centres from
231 the intervention arm will be selected by the national steering group for one-on-one semi structured
232 interviews with health staff. This will be supplemented by inviting a selection of staff from all ten
233 health centres in the intervention arm to participate in focus groups. Together, these qualitative
234 data will be analysed thematically for explanatory themes.

235 236 Step Seven: Evaluation of Results and Sharing Experience

237 The findings of the quantitative and qualitative analyses will be integrated in a final report and
238 shared with key stakeholders, including health staff from the participating primary health care
239 centres. The results will also be shared at a national conference and in an open-access peer
240 reviewed journal, in order to inform the future development of primary health care capacity in
241 MDA.

242 243 **Methodological Design**

244 A pragmatic, sequential mixed methods explanatory design, composed of quantitative and
245 qualitative strands of equal weight, will be used (Figure 1). This design was chosen because it
246 allows for the use of qualitative data to enlighten and explain the quantitative findings, including
247 but not limited to the feasibility of collecting data from paper-based records, the contextual factors
248 affecting guideline implementation, changes in clinical practice, and optimization for the future.

249
250 **Figure 1.** Illustration using the GATE frame structure (14) of the mixed methods evaluation design

251
252 A sample size of 20 primary health care centres was chosen because it was seen as a good balance
253 of allowing for variation in clinic geography and demography, while still remaining feasible for
254 the pilot implementation. Half of the centres (n=10) will be randomly allocated to the intervention
255 arm and half (n=10) to the control arm. Baseline data will be collected from both intervention and
256 control clinics, ensuring that baseline data is collected before implementation occurs.

257
258 Within clinic comparisons will be used to compare the 12 months before randomization with the
259 12 months of implementation. Between clinics comparison will be used to compare the
260 intervention clinics with control clinics during the same time period.

261 262 **Eligibility Criteria for Primary Health Care Centres**

263 Health facilities will be nominated by the Ministry of Health for participation based on the
264 following eligibility criteria: (1) primary health care facilities must be operating in the public sector
265 as legal entities; (2) primary health care facilities must be sampled in a way such that they are
266 geographically distributed evenly across the country; equally from the Central, North and Southern
267 regions of MDA; and (3) health facilities must be primary health care centres that are managed by
268 family doctors with no specialist doctors working in the facility. These criteria were chosen in
269 order to select a group of clinics that sufficiently reflect the majority of primary health care
270 facilities in Moldova.

271 272 **Randomization**

273 The clinics will be stratified based on the ratio of patients to family doctors to minimize possible
274 confounding by doctor caseload, and then randomized electronically into two groups of 10 primary
275 health care centres.

276 277 **Comparison**

278 The 10 primary health care centres in the intervention arm will be compared to the 10 primary
279 health care centres in the control arm. The control arm will receive no intervention and proceed
280 with usual care.

281 282 **Quantitative Indicators**

283 Indicators were developed to balance input and process indicators, such as measurement of risk
284 factors and calculation of risk scores, with output (e.g. prescribing) and outcome (e.g. blood
285 pressure control) indicators. While one of the objectives of this evaluation is to determine the
286 ability to measure these indicators based on routine paper records, we used our existing knowledge
287 of the health system to design indicators which were valuable and likely to be feasible to calculate.
288 Table 1 shows the indicator, the question the indicator seeks to answer, and the respective
289 numerator and denominator definitions which will be used in the calculations.

290
291 **Table 1.** Indicators, their numerators and denominators, and questions the indicators answer

292 293 **Data Collection and Management**

294 295 Quantitative Data Collection Tool

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2
3 296 A standardized data collection template has been developed for extracting anonymized patient data
4 297 from individual paper records (Table 2). An online version was also made to allow for data entry
5 298 on a computer or smartphone. It is estimated to take 15 minutes to extract data from one patient
6 299 record since the records are made of blank paper with no formal structure or organization of health
7 300 data.
8 301

9 302 **Table 2.** Standardized data collection form used to extract data from individual patient records
10 303

11 304 Method of Randomly Sampling Patient Records

12 305 A random sample of the records of patients aged over 18, who have visited the medical facility
13 306 within the past 12 months, will be taken. Since medical records in MDA are organized
14 307 alphabetically on shelves, we created a randomly generated list of alphanumeric combinations that
15 308 allowed for the selection of patient charts at random. For example, an alphanumeric code of “C24”
16 309 would correspond to the 24th patient chart in the section of last names starting with the letter C.
17 310

18 311 The list will be followed in the order that it was generated so as to prevent selection bias. The
19 312 randomly selected chart will then be checked to see if it meets two inclusion criteria: (1) the patient
20 313 is aged 18 years or older and (2) the patient visited the health centre within the last 12 months. If
21 314 the record meets these criteria, data will then be extracted. If it does not, it will be returned to the
22 315 shelf and the next alphanumeric code on the randomly generated list will be used. This process
23 316 will be repeated in each clinic until a sample size of 1.2% of the patient population in each clinic
24 317 is sampled. This proportion was chosen pragmatically such that the average sample per primary
25 318 health care centre would equal 100 unique patients.
26 319

27 320 Data Analysis

28 321 The change in indicators from baseline to follow-up will be calculated for intervention clinics
29 322 and compared with control clinics (Table 1). Subgroup analysis by age, gender, and other
30 323 demographic features may be done as deemed appropriate by the national steering committee.
31 324 All analyses will account for stratified sampling. Since the health centre is the unit of inference
32 325 for the outcomes (e.g. health centre proportion of eligible patients with a documented CVD risk
33 326 score), use of an intraclass correlation coefficient is not required for analyses of these
34 327 outcomes. Age and gender adjusted logistic regression models will be used to analyse the
35 328 differences in pre-defined indicators between intervention and control clinics and between
36 329 baseline and follow-up. The differences in means of continuous variables between the
37 330 intervention and control clinics and baseline and follow-up will be analysed using age and
38 331 gender adjusted analysis of variance.
39 332

40 333 Qualitative Data Collection

41 334 **Follow-up Support Visits**

42 335 Follow-up visits will be made to each intervention clinic at least once during the implementation
43 336 timeframe (12 months) to provide ad hoc implementation support. These visits will be conducted
44 337 by members of the national steering group, who will keep field notes about each visit and provide
45 338 feedback and support to the health centres. The perspectives gained through follow-up support
46 339 visits will be used by the national steering group to develop preliminary data collection tools for
47 340 semi-structured interviews.
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341 **Semi-Structured Interviews**

342 A maximum variation sample of half of the intervention clinics (n=5) will be chosen, based on the
343 perceived performance of each clinic by the evaluation steering committee. A pragmatic sample
344 of clinic managers (n=1 per clinic), doctors (n=3 per clinic), and nurses (n=3 per clinic) will be
345 interviewed one-on-one, using a semi-structured format. Interviews will proceed until data
346 saturation has been reached, to a maximum of 30 interviews. After obtaining written, informed
347 consent, interviews will be of 30 to 60 minutes in length, audio recorded, and be transcribed
348 verbatim and analysed thematically using framework thematic analysis.(15) The interviews will
349 be conducted by members of the steering group, but the interviewers will be allocated to
350 participants from health centres with whom they did not provide follow-up support visits.

351 **Focus Group Workshop**

352 Participants from all ten implementation clinics will be invited to a workshop to further collect
353 explanatory qualitative data and to critically reflect on the implementation process. Participants
354 will be a mix of doctors, nurses, and managers from the intervention clinics.

356 Participants will be placed into small groups based on their profession, and asked to complete a
357 standardized worksheet. Each group will be under the guidance of a facilitator, and emergent
358 themes from one-one-one interviews will be used as prompts to each group. The worksheet will
359 allow for each group to directly comment, modify, or add to the emergent themes, create new
360 themes, and organize themes into categories such as barriers and facilitators.

362 Integration of Quantitative and Qualitative Strands

363 The resulting qualitative data will be analysed thematically using the framework approach, and
364 used to help explain the findings of the quantitative strand.(15) Following the sequential mixed
365 method design, integration of the qualitative findings with quantitative findings will allow for the
366 interpretation of the results in light of each other. This may include post-hoc analysis of
367 effectiveness of some of the quantitative outcomes as appropriate, to further add meaning to the
368 integration of qualitative and quantitative strands.

369 **Patient and Public Involvement**

370 Neither patients nor the public were involved in the methodological design.

373 **ETHICS AND DISSEMINATION**

374 **Ethical Review and Approval**

375 This project was reviewed by the Research Ethics Committee of the Nicolae Testemitanu State
376 University of Medicine and Pharmacy of the Republic of Moldova and granted permission on 31
377 May 2017.

379 **Dissemination**

380 Quantitative findings will be summarized and presented back to all intervention clinics during
381 follow-up workshops. A comprehensive project report will be written and shared with key
382 stakeholders. A final report of key findings of the evaluation will be written and submitted to an
383 open access peer-reviewed journal and made available to all study participants so they can use the
384 findings to improve their practice. The findings will be used to evaluate the feasibility of a national
385 scale-up of essential NCD interventions in primary health care in MDA.

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REFERENCES

1. Benziger CP, Roth GA, Moran AE. The Global Burden of Disease Study and the Preventable Burden of NCD. *Glob Heart*. 2016 Dec;11(4):393–7.
2. World Health Organization (WHO). World Health Statistics [Internet]. 2018. Available from: http://www.who.int/gho/publications/world_health_statistics/2018/en/
3. World Health Organization (WHO). Package of Essential Noncommunicable (PEN) disease interventions for primary health care in low-resource settings [Internet]. 2013. Available from: http://www.who.int/ncds/management/pen_tools/en/
4. World Health Organization (WHO). Global action plan for the prevention and control of NCDs 2013-2020. 2013.
5. Organization WH. Tackling NCDs: “Best buys” and other recommended interventions for the prevention and control of noncommunicable diseases [Internet]. 2017. Available from: <http://www.who.int/ncds/management/best-buys/en/>
6. World Health Organization (WHO). Evaluation of the structure and provision of primary care in the Republic of Moldova. 2012.
7. National Center for Health Management. Health Yearbook: Public Health in Moldova [Internet]. 2015. Available from: <http://www.cnms.md/ro/rapoarteo>
8. World Health Organization. Global Health Observatory data repository [Internet]. [cited 2018 Jul 10]. Available from: <http://apps.who.int/gho/data/node.home>
9. World Health Organization (WHO). Prevalence of Noncommunicable Disease Risk Factors in the Republic of Moldova (STEPS) [Internet]. 2014. Available from: http://www.who.int/ncds/surveillance/steps/Moldova_2013_STEPS_Report.pdf
10. Turcanu C, Domente S, Buga M, Richardson E. Health Systems in Transition: Republic of Moldova [Internet]. 2012. Available from: http://www.euro.who.int/__data/assets/pdf_file/0006/178053/HiT-Moldova.pdf
11. World Health Organization (WHO). Ambulatory care sensitive conditions in the Republic of Moldova [Internet]. 2015. Available from: <http://www.euro.who.int/en/countries/republic-of-moldova/publications/ambulatory-care-sensitive-conditions-in-the-republic-of-moldova-2015>
12. Government of the Republic of Moldova. Action Program of the Government of the Republic of Moldova 2016–2018 [Internet]. 2016. Available from: http://gov.md/sites/default/files/document/attachments/guvernul_republicii_moldova_-_programul_de_activitate_al_guvernului_republicii_moldova_2016-2018.pdf
13. World Health Organization Regional Office for Europe. Better noncommunicable disease outcomes: challenges and opportunities for health systems -- Country Assessment of Republic of Moldova [Internet]. Copenhagen; 2014. Available from: http://www.euro.who.int/__data/assets/pdf_file/0008/255464/BetterNCDoutcomesChallengesOpportunitiesHealthSystemsMoldovaCountryAssessmentEng.pdf?ua=1
14. Jackson R, Ameratunga S, Broad J, Connor J, Lethaby A, Robb G, et al. The GATE frame: critical appraisal with pictures. Vol. 144, ACP journal club. United States; 2006. p. A8-11.
15. Gale NK, Heath G, Cameron E, Rashid S, Redwood S. Using the framework method for the analysis of qualitative data in multi-disciplinary health research. *BMC Med Res Methodol*. 2013 Sep;13:117.

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3 432 **AUTHORS AND CONTRIBUTIONS**

4 433 DC, AC, TL, GC, VS, TZ, AA, and JF contributed to the methodological design. DC, AC, TL, and
5 434 JF contributed to writing the manuscript.

6 435

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8 436 **FUNDING STATEMENT**

9 437 This study is funded jointly by the Swiss Agency for Development and Cooperation (SDC) and WHO
10 438 Regional Office for Europe.

11 439

12 440 **COMPETING INTERESTS STATEMENT**

13 441 DC, AC, TL, GC, VS, TZ, AA, JF declare no competing interests.

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443 **Table 1.** Indicators, their numerators and denominators, and questions the indicators answer

Question	Indicator	Numerator	Denominator
Are risk factors being measured?	Proportion of eligible patients who have all risk factor values recorded as required for calculation of risk score	Patients aged 40 or older who have visited in the last 12 months who have all measurements required for calculation of risk score within 12 months of the most recent date of visit	Patients aged 40 or older who have visited in the last 12 months
Are risk factor measurements being converted to a total risk score?	Proportion of patients aged 40 or older who have visited in the last 12 months who have all measurements required for calculation of risk score within 12 months of the most recent date of visit, that have a documented risk score	Patients aged 40 or older who have visited in the last 12 months who have all measurements required for calculation of risk score within 12 months of the most recent date of visit, that have a documented risk score	Patients aged 40 or older who have visited in the last 12 months who have all measurements required for calculation of risk score within 12 months of the most recent date of visit
Are risk scores calculated correctly?	Proportion of patients aged 40 or older who have visited in the last 12 months who have all measurements required for calculation of risk score within 12 months of the most recent date of visit, that have a documented risk score that is correct	Patients aged 40 or older who have visited in the last 12 months who have all measurements required for calculation of risk score within 12 months of the most recent date of visit, that have a documented risk score that is correct	Patients aged 40 or older who have visited in the last 12 months who have all measurements required for calculation of risk score within 12 months of the most recent date of visit, that have a documented risk score
Are patients being risk scored?	Proportion of eligible patients with a documented risk score	Patients aged 40 or older who have visited in the last 12 months with a documented risk score	Patients aged 40 or older who have visited in the last 12 months
Are risk scores calculated correctly?	Proportion of eligible patients with a documented risk score that is correct	Patients aged 40 or older who have visited in the last 12 months with a documented risk score that is correct	Patients aged 40 or older who have visited in the last 12 months with a documented risk score
Are statins prescribed to the correct patients?	Proportion of eligible patients prescribed a statin	Patients with existing CVD, diabetics 40 or older with high LDL values (as defined based on total CVD risk of SCORE 10-14% in LDL \geq 2.6 mmol/L; with very high risk SCORE \geq 15% in LDL \geq 1.8 mmol/L), or patients with a SCORE of \leq 9% and LDL \geq 2.6 or total cholesterol \geq 7.2, or patients with a SCORE of 10-14% and a LDL \geq 1.8 or total cholesterol \geq 7.2 mmol/L, or patients with a SCORE of \geq 15%, prescribed a statin	Patients with existing CVD, diabetics 40 or older with high LDL values (as defined based on total CVD risk of SCORE 10-14% in LDL \geq 2.6 mmol/L; with very high risk SCORE \geq 15% in LDL \geq 1.8 mmol/L), or patients with a SCORE of \leq 9% and LDL \geq 2.6 or total cholesterol \geq 7.2, or patients with a SCORE of 10-14% and a LDL \geq 1.8 or total cholesterol \geq 7.2 mmol/L, or patients with a SCORE of \geq 15%
Are statins prescribed correctly based on documented risk score?	Proportion of patients eligible based on documented risk score prescribed a statin	Patients with a documented risk score as very high risk SCORE \geq 15% prescribed a statin	Patients with a documented risk score as very high risk SCORE \geq 15%
Are patients with existing disease, who do not require the calculation of a risk score to prescribe statins, prescribed statins?	Proportion of patients with existing CVD prescribed a statin	Patients with existing CVD prescribed a statin	Patients with existing CVD

Is the blood pressure of high risk patients controlled?	Proportion of high risk patients (SCORE \geq 15% or DM and age over 40) whose last two recorded blood pressure measurements were <130/80 mmHg	Patients with a true risk score indicating a very high risk (SCORE \geq 15%) or DM and age over 40 whose last two documented blood pressure readings were <130/80	Patients with a true risk score indicating a very high risk (SCORE \geq 15%) or DM and age over 40
Is the blood pressure of lower risk patients controlled?	Proportion of lower risk patients (SCORE <15%) whose last two recorded blood pressure measurements were <140/90 mmHg	Patients with a true risk score indicating <15% whose last two documented blood pressure readings were <140/90	Patients with a true risk score indicating <15%
Are patients with existing CVD prescribed basic medications to reduce risk?	Proportion of patients with existing CVD prescribed a statin and aspirin and blood pressure lowering treatment	Patients with existing CVD prescribed a statin and aspirin and blood pressure lowering treatment	Patients with existing CVD
Is the blood glucose of diabetic patients controlled?	Proportion of diabetic patients with glycaemic control as defined by last two HbA1c measurements	Patients with diabetes 2 whose last two HbA1c measurements were below personal target as defined by MDA adapted WHO PEN 1	Patients with diabetes type 2
Is the blood pressure of hypertensive patients controlled?	Proportion of confirmed hypertensive patients whose SBP is <140/90 at last two visits	Patients with confirmed hypertension whose last two blood pressure readings were <140/90	Patients with confirmed hypertension
What is the prevalence of high blood pressure?	Proportion of people whose last two systolic blood pressure reading are 140 mmHg or above	Patients whose last two systolic blood pressure readings were \geq 140	All patients over 18

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447 **Table 2.** Standardized data collection form used to extract data from individual patient records
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Data Collection Question	Answer
What is your name? (Name of person extracting data)	
Date of Data Extraction (MM-DD-YYYY)	
Write the Clinic Name	
Is this a duplicate extraction?	
If it is a duplicate extraction, enter the number you and your extraction partner have assigned to this file.	
Date of Birth (MM-DD-YYYY)	
Sex (M/F)	
Smoking Status (Y/M)	
Diagnosis of Hypertension (Y/N)	
Date of Hypertension Diagnosis (MM-DD-YYYY)	
Can you find one or more blood pressure readings? (Y/N)	
Most Recent Systolic Blood Pressure	
Most Recent Diastolic Blood Pressure	
Date of the Most Recent Blood Pressure Measurement (MM-DD-YYYY)	
Can you find a second most recent blood pressure reading? (Y/N)	
Second most recent systolic blood pressure	
Second most recent diastolic blood pressure	
Date of the second most recent systolic blood pressure (MM-DD-YYYY)	
Diagnosis of Diabetes (Type 1, Type 2, No)	
Can you find one or more HbA1c measurements? (Y/N)	
Most recent HbA1c reading (mmol/mol)	
Date of the most recent HbA1c measurement? (MM-DD-YYYY)	
Can you find another HbA1c measurement? (Y/N)	
Second most recent HbA1c reading (mmol/mol, otherwise specify unit)	
Date of the second most recent HbA1c reading? (MM-DD-YYYY)	
Can you find one or more total cholesterol measurements? (Y/N)	
Most recent total cholesterol reading (mmol/L)	
Date of the most recent cholesterol reading (MM-DD-YYYY)	
Can you find another cholesterol measurement? (Y/N)	
Second most recent cholesterol reading (mmol/L)	
Date of the second most recent cholesterol reading (MM-DD-YYYY)	
Was the patient prescribed a statin? (Y/N)	
What was the date of the statin prescription? (MM-DD-YYYY)	

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3	What was the drug and dose?
4	Does the patient have existing CVD? (Y/N)
5	State the type of CVD
6	Has the patient been prescribed acetylsalicylic acid (ASA or aspirin)? (Y/N)
7	What was the most recent date that ASA was prescribed? (MM-DD-YYYY)
8	Has the patient been prescribed anti-hypertensives? (Y/N)
9	What was the most recent date that anti-hypertensives were prescribed? (MM-DD-YYYY)
10	Can you find a documented ESC SCORE risk score? (Y/N)
11	Enter the most recent documented ESC SCORE risk score (%)
12	What was the date the risk score was documented? (MM-DD-YYYY)
13	Please record any important notes about the data extraction here. Examples include an error you think may have been made, clarification of the units for measurements (e.g. mmol/L vs mg/dL). Or notes that you would like for yourself.
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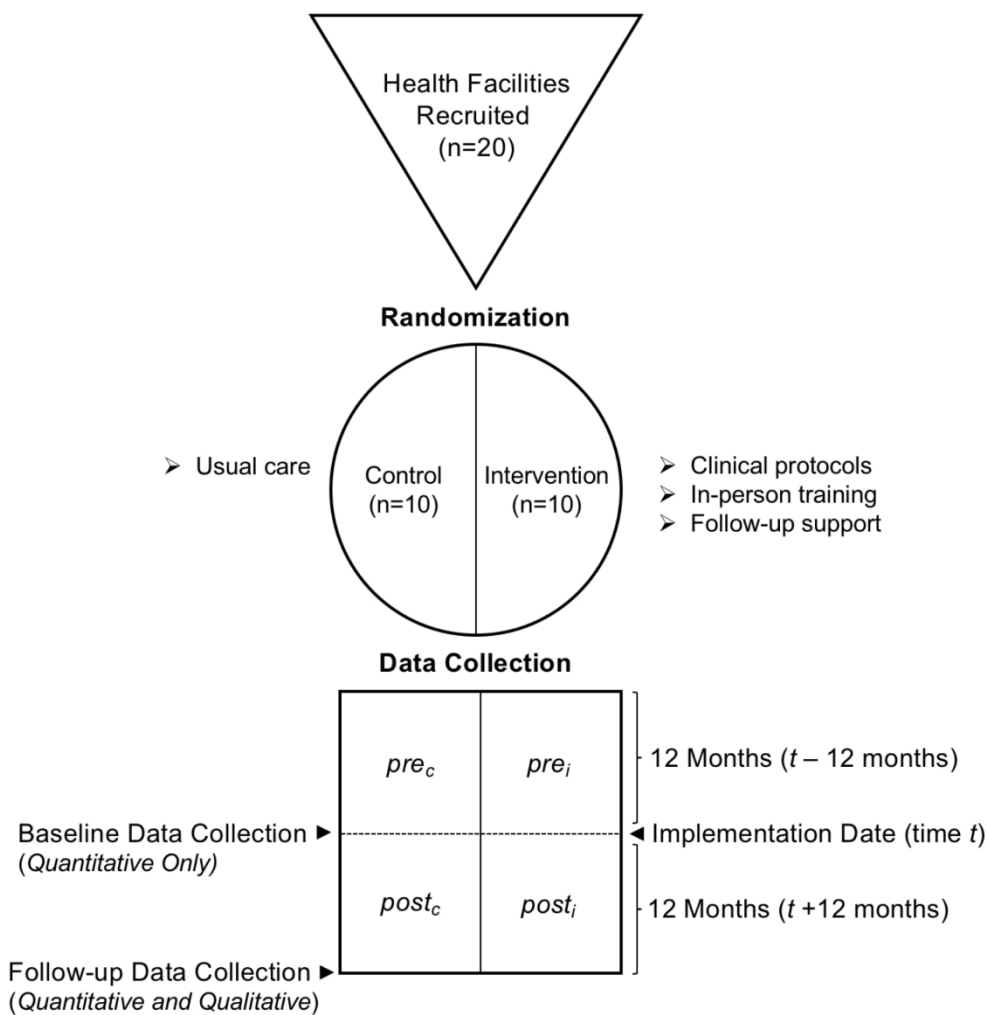


Figure 1. Illustration using the GATE frame structure (14) of the mixed methods evaluation design

184x193mm (300 x 300 DPI)