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The De-imFAR Phase II Project: A study protocol for a randomized implementation trial to evaluate the effectiveness of de-implementation strategies to reduce low-value statin prescribing in the primary prevention of Cardiovascular Disease.

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Complete List of Authors:	<p>Sanchez , Alvaro; Osakidetza-Basque Health Service, Primary Care Research Unit of Bizkaia, Deputy Directorate of Healthcare Assistance; Biocruces Bizkaia Health Research Institute</p> <p>Pijoan, Jose; Osakidetza-Basque Health Service, Clinical Epidemiology Unit; Biocruces Bizkaia Health Research Institute</p> <p>Sainz de Rozas, Rita; Osakidetza-Basque Health Service, Primary Care Pharmacy Unit, Ezkerraldea-Enkarterri-Cruces Integrated Health Organization; Biocruces Bizkaia Health Research Institute</p> <p>Lekue, Itxasne; Osakidetza-Basque Health Service, Primary Care Pharmacy Unit, Ezkerraldea-Enkarterri-Cruces Integrated Health Organization; Biocruces Bizkaia Health Research Institute</p> <p>San Vicente, Ricardo; Osakidetza-Basque Health Service, Zumarraga Health Center, Goierri-Alto Urola Integrated Health Organization</p> <p>Quindimil, Jose Antonio; Osakidetza-Basque Health Service, Sestao Health Center, Barakaldo-Sestao Integrated Health Organization</p> <p>Rotaeche, Rafael; Osakidetza-Basque Health Service, Primary Care Research Unit of Gipuzkoa, Organization of Integrated Health Services of Gipuzkoa</p> <p>Etxeberria, Arritxu ; Osakidetza-Basque Health Service, Primary Care Pharmacy, Donostialdea Integrated Health Organization</p> <p>Mozo, Carmela; Osakidetza-Basque Health Service, Primary Care Pharmacy, Donostialdea Integrated Health Organization</p> <p>Martinez-Cengotitabengoa, Monica; University of the Basque Country, School of Pharmacy; Osakidetza-Basque Health Service</p> <p>Monge, Monica; Osakidetza-Basque Health Service, Corporate Pharmacy Service, Directorate of Healthcare Assistance</p> <p>Gómez-Ramírez, Cristina; Osakidetza-Basque Health Service, Cardiology Department, Cruces University Hospital, Ezkerraldea-Enkarterri-Cruces Integrated Health Organization</p> <p>Samper, Ricardo; Osakidetza-Basque Health Service, Corporate Pharmacy Service, Directorate of Healthcare Assistance</p> <p>Ogueta Lana, Mikel ; Osakidetza-Basque Health Service, Subdirectorate of Quality and Health Information Systems</p> <p>Celorrio, Sara; Osakidetza-Basque Health Service, Barakaldo-Sestao Integrated Health Organization</p> <p>Merino-Inda, Nerea; Biocruces Bizkaia Health Research Institute</p> <p>Llarena, Marta; Biocruces Bizkaia Health Research Institute</p>

	Gonzalez Saenz de Tejada, Marta; Biocruces Bizkaia Health Research Institute García-Alvarez, Arturo; Osakidetza-Basque Health Service, Primary Care Research Unit of Bizkaia. Deputy Directorate of Healthcare Assistance; Biocruces Bizkaia Health Research Institute Grandes, Gonzalo; Osakidetza-Basque Health Service, Primary Care Research Unit of Bizkaia. Deputy Directorate of Healthcare Assistance; Biocruces Bizkaia Health Research Institute
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TITLE PAGE

Title

The De-imFAR Phase II Project: A study protocol for a randomized implementation trial to evaluate the effectiveness of de-implementation strategies to reduce low-value statin prescribing in the primary prevention of Cardiovascular Disease.

Author's details Alvaro Sanchez^{1*}, Jose I. Pijoan², Rita Sainz de Rozas³, Itxasne Lekue³, Ricardo San Vicente⁴, Jose Antonio Quindimil⁵, Rafael Rotaecche⁶, Arritxu Etxeberria⁷, Carmela Mozo⁷, Monica Martinez-Cengotitabengoa⁸, Monica Monge⁹, Cristina Gómez-Ramírez¹⁰, Ricardo Samper¹¹, Mikel Ogueta Lana¹², Sara Celorrio¹³, Nerea Merino-Inda¹⁴, Marta Llarena¹⁵, Marta Gonzalez Saenz de Tejada¹⁵, Arturo Garcia-Alvarez¹, and Gonzalo Grandes¹

¹ Primary Care Research Unit of Bizkaia, Deputy Directorate of Healthcare Assistance, Biocruces Bizkaia Health Research Institute, Basque Health Service - Osakidetza, Network for Research on Chronicity, Primary Care, and Health Promotion (RICAPPS), Barakaldo, Bizkaia, Spain.

² Clinical Epidemiology Unit, Biocruces Bizkaia Health Research Institute, Basque Health Service - Osakidetza, Barakaldo, Bizkaia, Spain. CIBER de Epidemiología y Salud Pública (CIBERESP), Instituto de Salud Carlos III, Spain.

³ Primary Care Pharmacy Unit, Ezkerraldea-Enkarterri-Cruces Integrated Health Organization, Basque Health Service – Osakidetza, Biocruces Bizkaia Health Research Institute, Barakaldo, Bizkaia, Spain.

⁴ Zumarraga Health Center, Goierri-Alto Urola Integrated Health Organization, Basque Health Service – Osakidetza, Zumárraga, Gipuzkoa, Spain.

⁵ Sestao Health Center, Barakaldo-Sestao Integrated Health Organization, Basque Health Service – Osakidetza, Sestao, Bizkaia, Spain.

1
2
3 29 ⁶ Primary Care Research Unit of Gipuzkoa, Organization of Integrated Health Services
4
5 30 of Gipuzkoa, Donostia-San Sebastian, Gipuzkoa, Spain

6
7 31 ⁷ Primary Care Pharmacy, Donostialdea Integrated Health Organization, Hernani,
8
9 32 Gipuzkoa, Spain

10
11 33 ⁸ School of Pharmacy, University of the Basque Country UPV/EHU, Vitoria-Gasteiz,
12
13 34 Spain. Psychology Clinic of East Anglia, Norwich, UK. Osakidetza Basque Health
14
15 35 Service, Barakaldo, Spain.

16
17 36 ⁹ Corporate Pharmacy Service, Directorate of Healthcare Assistance, Osakidetza-
18
19 37 Basque Health Service Central Services, Vitoria-Gasteiz, Spain

20
21 38 ¹⁰ Cardiology Department, Cruces University Hospital, Ezkerraldea-Enkarterri-Cruces
22
23 39 Integrated Health Organization, Basque Health Service – Osakidetza, Barakaldo,
24
25 40 Bizkaia, Spain.

26
27 41 ¹¹ Corporate Pharmacy Service, Directorate of Healthcare Assistance, Osakidetza-
28
29 42 Basque Health Service Central Services, Vitoria-Gasteiz, Spain

30
31 43 ¹² Subdirectorate of Quality and Health Information Systems, Osakidetza-Basque Health
32
33 44 Service Central Services, Vitoria-Gasteiz, Spain

34
35 45 ¹³ Barakaldo-Sestao Integrated Health Organization, Basque Health Service –
36
37 46 Osakidetza, Barakaldo, Spain

38
39 47 ¹⁴ Biocruces Bizkaia Health Research Institute, Barakaldo, Bizkaia, Spain.

40
41 48 ¹⁵ Biocruces Bizkaia Health Research Institute, Network for Research on Chronicity,
42
43 49 Primary Care, and Health Promotion (RICAPPS), Barakaldo, Bizkaia, Spain.

44
45
46
47 50

48
49 51 *** Corresponding author:**

50
51 52 Alvaro Sánchez

52
53 53 E-mail: Alvaro.sanchezperez@osakidetza.eus

54
55 54 Primary Care Research Unit of Bizkaia, Deputy Directorate of Healthcare Assistance,
56
57 55 Biocruces Bizkaia Health Research Institute, Basque Health Service – Osakidetza,
58
59
60

1
2
3 56 Network for Research on Chronicity, Primary Care, and Health Promotion (RICAPPS).
4
5 57 Plaza Cruces s/n, E-48903 Barakaldo, Bizkaia, Spain.
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59 **ABSTRACT**

60 **Introduction**

61 This study aims to reduce potentially inappropriate prescribing (PIP) of statins and foster
62 healthy lifestyle promotion in cardiovascular disease (CVD) primary prevention in low
63 risk patients. To this end, the study will compare the effectiveness and feasibility of
64 several de-implementation strategies developed following the structured design process
65 of the Behavior Change Wheel targeting key determinants of clinical decision-making
66 process in CVD prevention.

67 **Methods and analysis**

68 A randomized implementation trial, with an additional control group, will be launched,
69 involving family physicians (FPs) from 13 Integrated Healthcare Organizations (IHOs) of
70 Osakidetza – Basque Health Service with non-zero incidence rates of PIP of statins in
71 2021. All FPs will be exposed to a non-reflective decision assistance strategy based on
72 reminders and decision support tools. Additionally, FPs from two of the IHOs will be
73 randomly assigned to one of two increasingly intensive implementation strategies:
74 adding a decision information strategy based on knowledge dissemination, and a
75 reflective decision structure strategy through audit/feedback. The target population
76 comprises 45- to 74-year-old women and 40- to 74-year-old men with moderately
77 elevated cholesterol levels but no diagnosed CVD and a low cardiovascular risk
78 (REGICOR <7.5%), who attend at least one appointment with any of the participating
79 FPs (May 2022-May 2023), and will be followed until May 2024. The main
80 implementation outcome will be the change in the incidence rate of PIP of statins and
81 healthy lifestyle counseling in the study population 12 and 24 months after health
82 professionals' exposure to the strategies. Fidelity of the de-implementation strategies,

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2
3 83 FPs' perception of their feasibility and acceptability, and patient experience regarding the
4
5 84 quality of treatment received will also be evaluated.
6

7 85 **Ethics and dissemination**
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9 86 The study was approved by the Basque Country Clinical Research Ethics Committee
10
11 87 and was registered in ClinicalTrials.gov (NCT04022850). The results will be
12
13 88 disseminated in scientific peer-reviewed journals.
14
15

16 89 **Keywords:** Inappropriate Prescribing, Cardiovascular Diseases / prevention & control,
17
18 90 Hypercholesterolemia / drug therapy, Implementation Science, Research Design,
19
20 91 Primary care.
21
22

23 92

24
25 93 **STRENGTHS AND LIMITATIONS OF THIS STUDY**
26

- 27 94 • The goal of the present study is to assess the effectiveness of several de-
28
29 95 implementation strategies targeting primary care family physicians' (FPs)
30
31 96 decision-making process to reduce potentially inappropriate prescribing (PIP) of
32
33 97 statins and to increase healthy lifestyle promotion as the recommended treatment
34
35 98 option in cardiovascular disease (CVD) primary prevention through a randomized
36
37 99 implementation trial with an additional control group conducted in real-world
38
39 100 conditions of Primary Care.
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41
42 101 • The present study proposes an efficient design that combines experimental and
43
44 102 non-experimental comparisons through two randomized and one non-
45
46 103 randomized control (reference) arm that will allow: a) to capture the secular
47
48 104 trends across all FPs within the healthcare system that are exposed to a
49
50 105 reference intervention and estimating its effect on reducing PIP of statins and
51
52 106 increasing healthy lifestyle promotion; and b) to compare this reference strategy
53
54 107 with the two experimental de-implementation strategies.
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56
57 108 • The main limitation of the study lies in the planned comparisons of the
58
59 109 randomized groups with respect to the control arm. Therefore, in addition to
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3 110 evaluating the change in PIP incidence in all eligible FPs, a matching strategy
4
5 111 with the selection of one matched FP from this non-randomized group for each
6
7 112 of the randomized FPs will be performed seeking to increase comparability and
8
9 113 reduce potential bias.

- 11 114 • In order to better understand from the perspective of the study participants the
12
13 115 reasons why (why not) the strategies work, to explain the variations in the results
14
15 116 achieved and to identify the essential components and those that will require to
16
17 117 be optimized, qualitative methods will also be used to assess i) professionals'
18
19 118 perception of the feasibility and acceptability of the de-implementation strategies
20
21 119 aimed at reducing their unnecessary prescribing and favoring recommended
22
23 120 practice in the primary prevention of CVD in patients with low cardiovascular risk
24
25 121 (CVR); and ii) patients' perception and experiences related to receiving clinical
26
27 122 care derived from the exposure of their healthcare professionals to the different
28
29 123 de-implementation strategies.
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39 127 **INTRODUCTION**

40
41 128 Low-value healthcare may be considered a major global problem due to the widespread
42
43 129 empirical evidence of its high prevalence across healthcare systems and its impact on
44
45 130 patient safety, resource use, and social inefficiency [1,2]. It is becoming a global priority
46
47 131 to reduce low-value care, that is, clinical practices (e.g., diagnostic and therapeutic
48
49 132 procedures) that are ineffective, have not been shown to be efficient or effective, are not
50
51 133 the best available option, or have a poor cost- and/or risk-to-benefit balance.
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56 135 Nonetheless, reducing or eliminating low-value practices is a complex matter, as drivers
57
58 136 fostering or maintaining them seem, in most cases, to operate at multiple levels and be
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60 137 context specific; therefore, there is a need for a careful process of formal analysis of the

1
2
3 138 problems and their mechanisms of action to design and guide effective and efficient
4
5 139 corrective measures. This can be achieved using models or theories that cover a wide
6
7 140 range of possible influences or determinants of the clinical behavior in question. In this
8
9 141 context, behavior change theory has been extensively applied to understand the factors
10
11 142 that may influence clinical behavior, identify and design possible techniques and
12
13 143 interventions that could be used to change it, and explain the mechanisms through which
14
15 144 such interventions operate [3,4].
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20 146 The DE-imFAR (from the Spanish for de-implementation of low-value pharmacological
21
22 147 prescribing) project [5] aims to apply behavioral science theory within a structured
23
24 148 process involving the main stakeholders (health professionals, patients, and
25
26 149 researchers) in the design, deployment, and evaluation of targeted de-implementation
27
28 150 strategies for reducing potentially inappropriate prescribing (PIP). Specifically, we have
29
30 151 applied a combination of the Theoretical Domains Framework and Behavior Change
31
32 152 Wheel [6] methods to a) understand the factors that may influence problematic clinical
33
34 153 behavior (PIP of statins in low cardiovascular risk (CVR) patients within the context of
35
36 154 cardiovascular disease [CVD] primary prevention in primary care), and b) map targeted
37
38 155 de-implementation and implementation strategies conducive to reducing or stopping the
39
40 156 low-value practice in question.
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44
45 158 Briefly, having prioritized a specific target behavior (clinician decision-making on
46
47 159 intervention/treatment to be provided based on objective clinical information and
48
49 160 subjective schemas and heuristics), identified determinants (facilitators of statin PIP and
50
51 161 barriers to recommended activities promoting healthy lifestyles), and mapped specific
52
53 162 behavior change techniques, three types of de-implementation/implementation
54
55 163 strategies were selected for influencing decision-making through different mechanisms.
56
57 164 The behavior change interventions selected were those judged to be the most potentially
58
59 165 effective, feasible, and acceptable by the DE-imFAR Phase I working group: a) a non-

1
2
3 166 reflective decision assistance strategy based on providing evidence-based information
4
5 167 communication technology tools to help and guide decision-making; b) a decision
6
7 168 information strategy based on the dissemination of the evidence concerning CVD
8
9 169 primary prevention framed in a corporate campaign encouraging family physicians (FPs)
10
11 170 to move away from PIP; and c) a reflective decision structure strategy encouraging
12
13 171 reflection on actual performance based on an audit/feedback system [7].
14
15
16 172

17
18 173 According to the evidence reviewed in Phase I of the DE-imFAR project [8-17] regarding
19
20 174 the evaluation of interventions for the reduction of low-value prescribing, the three
21
22 175 prioritized de-implementation strategies seem to be non-innovative interventions but do
23
24 176 address the main determinants of clinical decisions processes that perpetuate the PIP
25
26 177 of statins in our public healthcare setting (Osakidetza/Basque Health Service). On the
27
28 178 other hand, these strategies are supported by evidence as multicomponent interventions
29
30 179 that —combining passive dissemination interventions, based on training in or
31
32 180 dissemination of clinical practice guidelines (CPGs), with more proactive interventions
33
34 181 incorporating decision-making aids or the sending of audit/feedback— achieve the most
35
36 182 positive results. Specifically, in the context of PIP of statins, a positive impact has been
37
38 183 observed on documentation of CVR and prescription adequacy using a) multi-
39
40 184 component dissemination strategies including informative web pages, and
41
42 185 implementation of electronic CPGs compared to routine practice and training activities,
43
44 186 and b) interventions based on sending clinical scenarios and cases, and audit/feedback
45
46 187 to professionals, and decision support tools [12-16]. Research is needed, however, to
47
48 188 determine whether these evidence-based and barrier-specific strategies for de-
49
50 189 implementation identified in DE-imFAR Phase I are also effective in our context.
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55
56 191 Thus, the goal of the present study is to assess the potential effectiveness and feasibility
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58 192 of a set of de-implementation strategies to reduce the PIP of statins in the primary
59
60 193 prevention of CVD (low-risk patients, REGICOR [18] CVR score <7.5%, with moderately

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3 194 elevated cholesterol levels, low-density lipoprotein (LDL) cholesterol levels between 70
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5 195 and 189 mg/dL and/or total cholesterol (TC) between 200 and 289 mg/dL, but without
6
7 196 ischemic heart disease/CVD). The de-implementation strategies are derived from a
8
9 197 systematic theory- and evidence-based intervention design process and composed of a
10
11 198 set of active components targeting the facilitators of the non-desired behavior (PIP of
12
13 199 statins) while tackling the barriers to applying the recommended clinical practice behavior
14
15 200 (healthy lifestyle promotion) [7].
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19
20 202 Specifically, we aim to answer the following research questions:

21
22 203 1. Observational comparison questions:

23
24 204 As compared to a reference/control non-reflective decision assistance strategy based on
25
26 205 reminders and decision support tools incorporated into the electronic health record
27
28 206 (EHR) for helping clinical decision-making, what is the effect on the incidence of PIP of
29
30 207 statins in CVD primary prevention and the rate of delivery of healthy lifestyle counseling
31
32 208 of a) a decision information strategy comprising a corporate “Stopping Low-Value
33
34 209 Prescribing” campaign and the dissemination of evidence-based CPGs for the primary
35
36 210 prevention of CVD; b) a reflective decision structure strategy based on an audit/feedback
37
38 211 system; and c) any intervention based on a reflective de-implementation strategy (a or
39
40 212 b)?
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43 213

44
45 214 2. Experimental comparison question:

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47 215 As compared to a decision information strategy comprising a corporate “Stopping Low-
48
49 216 Value Prescribing” campaign and the dissemination of evidence-based CPGs for the
50
51 217 primary prevention of CVD, together with the non-reflective decision assistance
52
53 218 intervention based on reminders and decision support tools incorporated into the EHR
54
55 219 for helping clinical decision-making, what is the effect on the incidence of PIP of statins
56
57 220 in CVD primary prevention and the rate of delivery of healthy lifestyle counseling of
58
59 221 adding a reflective decision structure strategy based on an audit/feedback system?
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3 2224
5 223 **METHODS AND ANALYSIS**6
7 224 **Design**

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9 225 A randomized implementation trial with an additional control group will be conducted for
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11 226 evaluating the potential effectiveness and feasibility of three de-implementation
12
13 227 strategies (Figure 1). A mixed methods evaluation will be undertaken: quantitative for
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15 228 assessing the implementation results at the professional level (implementation outcomes
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17 229 regarding changes in rates of PIP and healthy lifestyle counseling) and qualitative for
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19 230 assessing the feasibility and perceived impact of the de-implementation strategies from
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21 231 the FPs' perspective and the experience and satisfaction of patients concerning the
22
23 232 clinical care received. The unit of intervention will be the primary care FP, while
24
25 233 observation and analysis will be performed at professional and patient levels. The DE-
26
27 234 imFAR research protocol was reviewed and approved by the Basque Country Clinical
28
29 235 Research Ethics Committee (Reference: EOM2022018, approved on 30 March 2022)
30
31 236 and was registered in the U.S. NLM ClinicalTrials.gov database (ClinicalTrials.gov
32
33 237 Identifier NCT04022850, Registered 17 July 2019; Last update 28 July 2023).

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38 239 Osakidetza provides universal coverage and services are free at the point of use, aside
39
40 240 from co-payment for drugs, funded through regional general taxation. Primary,
41
42 241 specialized, and social health-related service provision is organized around 13
43
44 242 Integrated Healthcare Organizations (IHOs) that cover the 3 provinces of the region of
45
46 243 the Basque Country: Araba, Bizkaia, and Gipuzkoa. Each resident is on the list of one
47
48 244 FP or pediatrician who offers comprehensive primary care and refers patients for hospital
49
50 245 and specialty services. Primary care professionals work in full-time teams, including FPs,
51
52 246 pediatricians, nurses, and administrative staff based at local centers providing access to
53
54 247 healthcare for users in a defined geographical area.

55
56 248 We used the SPIRIT reporting guidelines and the SPIRIT checklist when writing the
57
58 249 present study [19].
59
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250

251 Participants

252 1. Professionals: FPs belonging to any of the 13 IHOs of Osakidetza with a non-zero
253 annual incidence rate of PIP of statins at baseline (2021) with a minimum cluster size of
254 $n \geq 10$ patients

255 2. Patients: All 40- to 74-year-old men and 45- to 74-year-old women with no history of
256 statin use, LDL cholesterol levels between 70 and 189 mg/dL and/or TC between 200
257 and 289 mg/dL but without ischemic heart disease/CVD, and an estimated CVR
258 REGICOR $< 7.5\%$ who attend at least one appointment at the participating FPs' practices
259 during the study period from May 2022 to May 2023, and followed until May 2024.

260

261 Clinical interventions

262 According to clinical practice recommendations in Osakidetza and the Spanish National
263 Health System [20], although there is evidence that statins reduce the risk of
264 cardiovascular events in secondary prevention and individuals with high CVR, for primary
265 prevention in low-risk patients (REGICOR $< 10\%$), the risk-benefit balance is uncertain.
266 Specifically, in patients with low CVR, preventive activities should be focused on the
267 promotion of healthy lifestyles through optimizing diet, increasing physical activity, and
268 stopping smoking. Moreover, the NICE guideline on CVR management and reduction
269 [21] and the 2019 ACC/AHA guideline on the primary prevention of CVD [22] encourage
270 discussion with patients concerning the benefits of lifestyle modification for the
271 prevention of CVD, as well as other modifiable risk factors, before considering
272 pharmacological treatment. They also stress the importance of discussing the risks and
273 benefits of pharmacological treatment, taking into account patient preferences and
274 conditions. Similarly, the 2019 ESC/EAS guidelines for the management of dyslipidemias
275 [23] recommend healthy eating, regular exercise, and smoking cessation as the first line
276 of treatment for hyperlipidemia.

277

278 **De-implementation strategies evaluated**

279 There is plenty of evidence demonstrating that it is possible to de-implement
280 inappropriate medical practices through the lens of clinician cognition [24-26]. In this
281 context, the growing field of choice architecture aims to explore how the structure and
282 framing of decision situations influence the choice of certain behaviors over alternative
283 ones. On the one hand, FPs' decision-making ability can be influenced by unconscious
284 processes that occur in response to environmental or emotive cues, that is, through type
285 1 (or automatic) cognition. On the other, clinicians' conscious intention to change can be
286 promoted by engaging their reflective cognition to consciously evaluate and correct their
287 inappropriate behavior, that is, using type 2 (or reflective) cognition [27].

288

289 Within the present study, three types of strategies that purportedly affect FPs' decision-
290 making process will be set up. The strategies can be theoretically differentiated as a
291 function of the way they may affect clinicians' decision-making [28] and will be
292 cumulatively deployed (see Supplemental file 1 for a more detailed description):

293 1) *A non-reflective decision assistance strategy*, that targets type 1 cognitive processes
294 through decision support systems that prompt and remind FPs about the recommended
295 practice in a simplified way, thereby reducing the cognitive burden. In short, pop-up
296 reminders and alerts with associated messages were incorporated into the REGICOR
297 CVR calculator in OSABIDE (Osakidetza's EHR system) and within the prescription
298 pathway in PRESBIDE (the electronic drug prescribing component). The tools devised
299 include an interactive media-based algorithm stating the recommended practice for the
300 primary prevention of CVD in low-risk patients developed by an expert panel, and a
301 patient information sheet depicting and promoting evidence-based practice for
302 addressing cholesterol in the primary prevention of CVD in low-risk patients.

303 2) *A both reflective and non-reflective decision information strategy*, targeting both types
304 1 and 2 cognitive processes, based on the principle of knowledge dissemination and
305 consisting of a "Stopping Low-Value Prescribing" campaign run by the organization that

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3 306 also eases access (decreasing the physical effort required) to the evidence-based CPGs
4
5 307 for the primary prevention of CVD in low-risk patients.

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7 308 3) *A reflective decision structure strategy*, that targets type 2 cognition through an
8
9 309 audit/feedback system reporting data with practice- and organizational-level
10
11 310 performance indicators regarding PIP of statins and healthy lifestyle promotion to prompt
12
13 311 reflection about their own care practice, provided along with intention formation and goal-
14
15 312 setting-focused messages.

17 313 **Allocation of intervention units to compared groups**

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19
20 314 All FPs from all 13 IHOs will be exposed to the first of the aforementioned strategies,
21
22 315 namely, the provision of non-reflective decision assistance strategy. Further, in addition
23
24 316 to this first strategy, FPs belonging to two IHOs (Barakaldo-Sestao and Ezkerraldea-
25
26 317 Enkarterri-Cruces) in which the DE-imFAR project has been previously commissioned
27
28 318 [7] will be randomly assigned to exposure to either the second (provision of decision
29
30 319 information strategy) or second and third (provision of decision information and reflective
31
32 320 decision structure strategies). The allocation sequence within these two groups will be
33
34 321 generated using a specific restricted randomization scheme by one member of the
35
36 322 research team. The sequence will be concealed at the coordinating center. In all cases,
37
38 323 FPs will only be allocated to the study groups after they have provided informed consent
39
40 324 to participate through an opt-out strategy. The data analyst and the staff in charge of
41
42 325 measurements will be blind to FP allocation to study arms. Given that the audit/feedback
43
44 326 strategy will involve regular reports sent privately to individuals, participants in the
45
46 327 experimental arms are also expected to be blind to group allocation.

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51 329 **Outcome measures**

52
53 330 To assess the effectiveness of the de-implementation strategies compared in terms of
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55 331 public health impact, we will use the following dimensions of the Reach, Effectiveness,
56
57 332 Adoption, Implementation, and Maintenance (RE-AIM) framework [29]:

58
59 333 *Reach*

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2
3 334 • Percentage of patients in the target population exposed to the recommended CVD
4
5 335 primary prevention practice (e.g., assessment and advice regarding healthy lifestyles
6
7 336 instead of statins), 12 months following FP's exposure to the experimental or control de-
8
9 337 implementation strategies; and their representativeness.

11 338 *Adoption*

13 339 • Percentage of FPs who improve their CVD prevention practice, by reducing PIP of
14
15 340 statins and/or increasing health promotion activities in the target population eligible for
16
17 341 CVD prevention, 12 months following FP's exposure to the allocated or control de-
18
19 342 implementation strategies; and their representativeness.

22 343 *Implementation*

24 344 The study's main outcome measures will compare the change in the incidence of both
25
26 345 the PIP of statins and the health promotion activities in patients of the target population
27
28 346 eligible for CVD primary prevention, from baseline to 12 months after exposure of
29
30 347 collaborating FPs to the de-implementation strategies. Specifically, the two following
31
32 348 measures will be compared:

34 349 • Change in the incidence of PIP of statins

36 350 and

38 351 • Change in the incidence of provision of advice regarding healthy lifestyles, in both
39
40 352 cases, considering the change, from baseline to 12 months after exposure of FPs to the
41
42 353 de-implementation strategies compared, in the target population.

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46 355 As a secondary implementation outcome, we will compare the change in the incidence
47
48 356 of CVR score documentation in the EHR, from baseline to 12 months after exposure of
49
50 357 FPs to the de-implementation strategies compared, in 40- to 74-year-old men and 45- to
51
52 358 74-year-old women with no history of statin use and without ischemic heart disease/CVD
53
54 359 but who have been newly prescribed statins during the fieldwork period.

56 360

58 361 *Maintenance and Spreading*

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3 362 • Change in the incidence of PIP of statins and provision of healthy lifestyle counseling
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5 363 in eligible patients, 24 months after exposure of FPs to the de-implementation strategies
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7 364 compared to levels observed at the 12-month assessment.
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9 365

11 366 **Fidelity and Feasibility Evaluation**

13 367 The fidelity of the delivery of each de-implementation strategy under study (i.e., the
14
15 368 degree to which they have been executed as planned) will be evaluated. To this end, a
16
17 369 complete record and subsequent description of the execution process, documentation of
18
19 370 adaptations made to the planned strategies, and process indicators of the delivery of and
20
21 371 exposure to the interventions (see Supplemental file 1 for specification of the exposure
22
23 372 to each strategy), will be used to assess the following components of fidelity: adherence,
24
25 373 dose, quality of delivery, professionals' responsiveness and program differentiation [30].
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29
30 375 The professionals' perception of the feasibility of and satisfaction with the de-
31
32 376 implementation strategies to enhance the provision of the recommended CVD
33
34 377 prevention clinical practice will be assessed through key-informant semi-structured
35
36 378 interviews. At least 12 interviews with professionals will be carried out: 6 professionals
37
38 379 (3 from each randomized arm) who reduced their PIP and 6 who did not. Exposed
39
40 380 patients' perception and experience regarding the quality of CVD prevention care
41
42 381 received will also be assessed through key-informant semi-structured interviews: at least
43
44 382 five interviews will be carried out with patients who have and five with patients who have
45
46 383 not been clinically managed according to recommended practice.
47
48 384

51 385 **Analysis**

53 386 Frequencies and proportions along with the corresponding 95% confidence intervals
54
55 387 (CIs) will be used to describe the prevalence and cumulative incidence of PIP of statins
56
57 388 and healthy lifestyle counseling in the primary prevention of CVD by FPs. The primary
58
59 389 effectiveness outcomes will be the changes in the cumulative incidence of PIP of statins

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3 390 and healthy lifestyle counseling in patients from the target population (individuals with no
4
5 391 history of statin use, LDL cholesterol levels between 70 and 189 mg/dL and/or TC
6
7 392 between 200 and 289 mg/dL without past or current ischemic heart disease/CVD, and
8
9 393 an estimated CVR REGICOR <7.5% attending at least one clinical appointment with their
10
11 394 FP in the study period), from baseline to 12 months after exposure of FPs to the de-
12
13 395 implementation strategies. Therefore, to evaluate the impact of the three de-
14
15 396 implementation strategies, we will estimate the relative reduction in the risk of receiving
16
17 397 PIP of statins in patients from the target population assigned to the experimental
18
19 398 interventions over that in patients from the non-randomized group (non-reflective
20
21 399 decision assistance strategy group). With respect to this group and seeking to increase
22
23 400 comparability and reduce potential bias, in addition to evaluating the change in PIP
24
25 401 incidence in all eligible FPs, we will select one matched FP from this non-randomized
26
27 402 group for each of the randomized FPs taking into account both FP-related characteristics
28
29 403 (e.g., baseline rate of PIP, etc.) and characteristics of the population of patients assigned
30
31 404 to the FP (e.g., average socioeconomic status, etc.). Change in PIP incidence rates from
32
33 405 baseline to those observed 12 and 24 months after FPs' exposure to the de-
34
35 406 implementation strategies and the relative risk reduction will be estimated with the
36
37 407 corresponding 95% CIs. To adjust for potential confounding factors, stratified statistical
38
39 408 analyses and logistic models will be used. These models will be extended to generalized
40
41 409 mixed effects models to take into account the hierarchical structure of data (patients
42
43 410 nested in FPs and FPs in primary care teams), with fixed effects (comparison group,
44
45 411 effect of time on outcome indicators, and time-group interactions) and random effects on
46
47 412 the intercept and the time slope (for each patient, FP, center, etc.). These models will be
48
49 413 adjusted for potential confounders, following a backward strategy, guided by the stratified
50
51 414 analyses. A similar approach will be taken to analyze the secondary outcomes. The
52
53 415 analyses will be carried out with SAS (v. 9.2, SAS Institute, Cary, NC, USA), and R (R
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55 416 Development Core Team, 2014).
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3 418 Calculation of the required sample size for the most unfavorable scenario, this being the
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5 419 comparison between the two randomized de-implementation strategies, was based on:
6
7 420 i) a baseline incidence of statin PIP of 7.4% estimated among the patients of the target
8
9 421 population seen in 2021 by FPs with an incidence of PIP > 0% with a minimum cluster
10
11 422 size $n \geq 10$ patients, ii) an intra-class correlation coefficient of 0.01, iii) an average cluster
12
13 423 size of 39 patients with a coefficient of variation of 0.63, iv) $\alpha = 0.05$ and statistical power
14
15 424 of 80%, and v) hypothetical decreases in annual PIP rates of 20% in the decision
16
17 425 information strategy group and 50% in the decision structure strategy group. With these
18
19 426 assumptions, it was estimated that at least 58 FPs were required for each experimental
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21
22 427 arm.
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26 429 **Management, quality, and safety in data processing**

28 430 This study will be carried out in accordance with the international standards for
29
30 431 conducting epidemiological studies, included in the International Guidelines for Ethical
31
32 432 Review of Epidemiological Studies [31]. This is a prospective intervention study focused
33
34 433 mainly on the collection of information from data recorded by health professionals in the
35
36 434 Osakidetza EHR (OSABIDE) under routine clinical practice conditions. The process
37
38 435 indicators related to the clinical practice of the professionals, and patients'
39
40 436 sociodemographic and clinical characteristics (age, sex, socioeconomic status, active
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42 437 health problems, etc.) and clinical outcomes will be extracted from OSABIDE through the
43
44 438 corporate Oracle Business Intelligence platform. The Primary Care Research Unit of
45
46 439 Bizkaia is formally authorized to extract and use data from the EHR for research
47
48 440 purposes by the Healthcare Directorate of Osakidetza. On the other hand, it will be
49
50 441 necessary to inform participants about the study and obtain their written informed
51
52 442 consent concerning the information collected directly from the professionals and patients
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54 443 under study through the key-informant semi-structured interviews. All the information
55
56 444 regarding the study subjects, either extracted from EHRs or collected from the
57
58 445 participants expressly for this research, will be protected and treated confidentially for all
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3 446 purposes, in accordance with the provisions of the Spanish Organic Law 3/2018, of 5
4
5 447 December, on Personal Data Protection and digital rights guarantee (LOPD-GDD) and
6
7 448 the provisions of Regulation (EU) 2016/679 of the European Parliament and of the
8
9 449 Council of 27 April 2016, on the protection of natural persons with regard to the
10
11 450 processing of personal data and on the free movement of such data (General Data
12
13 451 Protection Regulation, RGPD). Specifically, all data will be documented anonymously
14
15 452 and de-identified, linked to a unique key that is meaningless outside the context of the
16
17 453 system. The final resulting database will be exported to a formatted plain text file that will
18
19 454 then be compressed and encrypted using a secure algorithm and subsequently be
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21 455 processed and included in a robust and secure database server.
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26 457 **Patient and public involvement**

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28 458 Patients were involved in the DE-imFAR Phase I project as one of the main stakeholders
29
30 459 (health professionals, patients, and researchers) in the formative process conducted to
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32 460 map and design de-implementation strategies to reduce PIP, which will be evaluated in
33
34 461 the DE-imFAR Phase II project. Specifically, during the Phase I project, a focus group
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36 462 with six patients was conducted to ascertain patients' experience regarding the clinical
37
38 463 practice of statin prescription and triangulate physicians discourse.
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42 464 During the Phase II project, semi-structured interviews will be conducted with patients to
43
44 465 assess their perception and experience of the clinical care received as a result of their
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46 466 healthcare professionals' exposure to the different de-implementation strategies. These
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48 467 interviews will help to better understand from the perspective of the study participants
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50 468 the reasons why the strategies work (or do not work), to explain the variations in the
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52 469 outcomes achieved and to identify the key components and those that need to be
53
54 470 optimized.
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58 59 472 **ETHICS AND DISSEMINATION**

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3 473 The research protocol (version 1; 170221) has been approved by the Basque Country
4
5 474 Clinical Research Ethics Committee (Reference: EOM2022018, approved on 30 March
6
7 475 2022) and was registered in the U.S. NLM ClinicalTrials.gov database (ClinicalTrials.gov
8
9 476 Identifier NCT04022850, Registered 17 July 2019; Last update 28 July 2023).The
10
11 477 Primary Care Research Unit of Bizkaia is explicitly authorized by the Healthcare
12
13 478 Directorate of Osakidetza - Basque Health Service to extract and use data from EHRs
14
15 479 for research purposes. Since data supporting the present study will mostly concern
16
17 480 routine data retrieved from the EHR of the Basque Health Service-Osakidetza, it will be
18
19 481 only shared on justified request to the study guarantors. The results of this study will be
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21 482 disseminated via publication in scientific peer-reviewed journals.
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484 **LIST OF ABBREVIATIONS**

485 EHR: Electronic health record

486 CI: Confidence interval

487 CVD: Cardiovascular disease

488 CVR: Cardiovascular risk

489 CPG: Clinical practice guideline

490 FP: Family physician

491 IHO: Integrated Healthcare Organization

492 LDL: Low-density lipoprotein

493 PIP: Potentially inappropriate prescribing

494 RE-AIM: Reach, Effectiveness, Adoption, Implementation, and Maintenance

495 TC: Total cholesterol

496

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621 **AUTHORS' CONTRIBUTIONS**

622 AS, JIP, and GG conceived the idea and are the study guarantors. They are primarily
623 responsible for the study design and planning, obtained funding, will be responsible for
624 project coordination and supervision, analysis and interpretation of results, and were
625 responsible for manuscript preparation. RSR, IL, RSV, JAQ, RR, AE, CM, MMC, MM,
626 CGR, RS, MOL, SC, NMI, ML, MGST, and AGA are co-investigators of the projects and
627 collaborated in the study design and/or manuscript preparation; and they will be
628 responsible for study coordination and interpretation of results. AS, JIP, and AGA will be

1
2
3 629 responsible for the analysis of results. All authors read and approved the final version of
4
5 630 the manuscript.

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10
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18
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22
23 639 Department of the Basque Government (funded projects 2018111085 and 2021111024).
24
25 640 The funding bodies have had no role in the design of the study, collection, analysis, or
26
27 641 interpretation of data or the writing of the manuscript.
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32 33 643 **COMPETING INTERESTS STATEMENT**

34
35 644 The authors declare that they have no competing interests.
36
37 645

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48
49 651 (Medical Directorate) and Vanesa Martín (Quality Unit) at Barakaldo-Sestao Integrated
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51 652 Health Organization.
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56 57 654 **WORD COUNT**

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2
3 655 3763 words excluding title page, abstract, strengths and limitations of this study, list of
4
5 656 abbreviations, full references, authors' contributions, funding statement, competing
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7 657 interests statement and acknowledgements.
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658 **FIGURES**

659 **Figure 1. Study design diagram. (PDF format)**

660 Note: FP: Family Physician; IHO: Integrated Healthcare Organization; R: Randomization.

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3 661 **SUPPLEMENTAL FILES**
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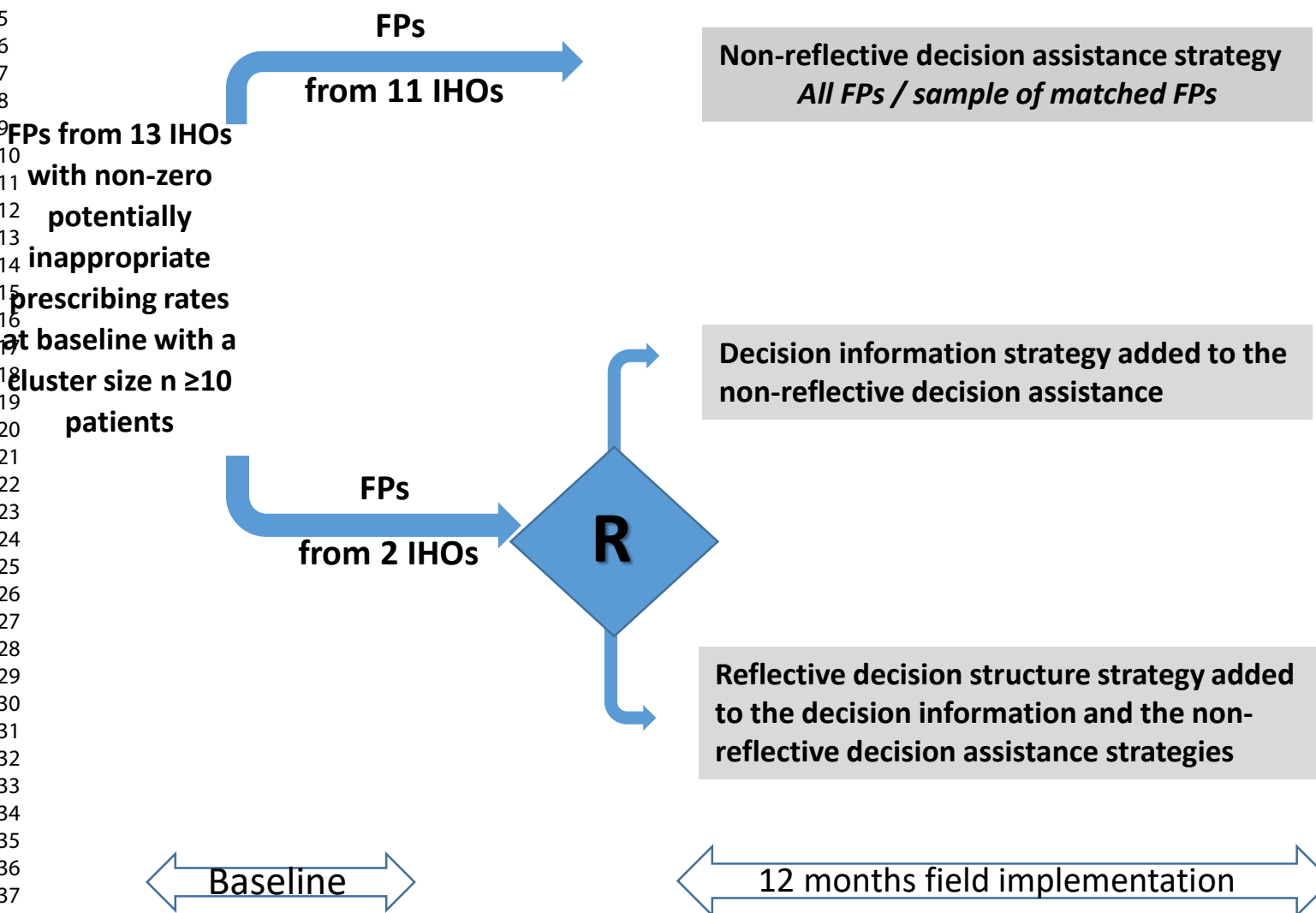
5 662 **Supplemental File 1 [DE-imFAR de-implementation strategies] (PDF format)**
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Experimental implementation trial with an additional control group

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Change in the incidence of potentially inappropriate prescriptions and provision of lifestyle advice from baseline to 12 months after exposure of physicians to the compared strategies, in 40- to 74-year-old men and 45- to 74-year-old women with no history of statin use, with LDL-cholesterol levels between 70 and 189 mg/dl and/or Total Cholesterol between 200 and 289 mg/dl but without ischemic heart/cardiovascular disease and with an estimated cardiovascular risk <7.5% attending during the field-work period

Outcome

The DE-imFAR de-implementation strategies

1. Strategy - Non-reflective decision assistance strategy

Support for clinical decision-making on the primary prevention of cardiovascular disease (CVD) in low cardiovascular risk (CVR) patients integrated into the electronic health record (EHR) of the Basque Health Service (Osakidetza), based on pop-up reminders and alerts, together with an interactive media-based algorithm stating the recommended practice and a patient information sheet.

1.1. Target audience

This strategy targets all family physicians (FPs) from all 13 Integrated Healthcare Organizations (IHOs) of the Basque Health Service (Osakidetza), both in primary and specialist or hospital care.

1.2. Active components (actions) of the intervention

- “Lighthouse” guiding alert in the REGICOR CVR calculator. Reminders of recommended clinical practice in the primary prevention of CVD that pop-up in the REGICOR CVR calculator when the CVR is estimated in patients aged between 35 and 74 years old. The alert varies depending on the CVR score (<10% or ≥10%).

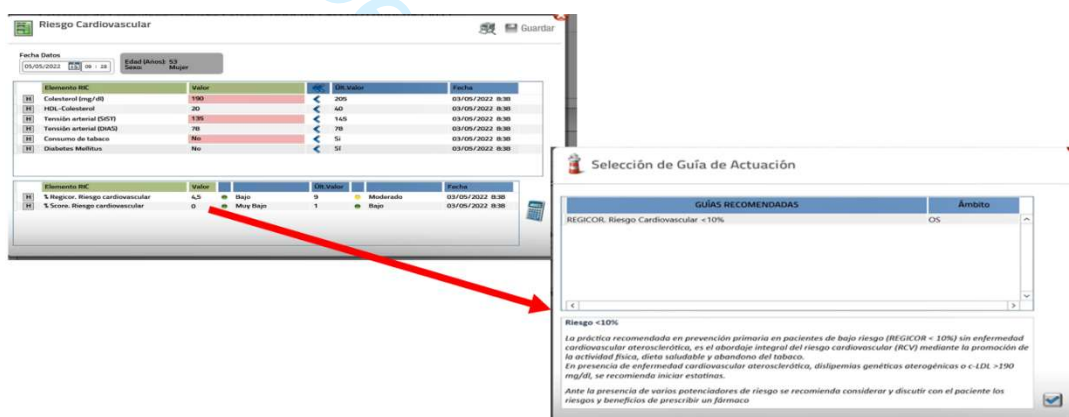


Figure 1. Pop-up reminder (“Lighthouse” guiding alert) in the REGICOR cardiovascular risk calculator when estimated cardiovascular risk score is <10%.

- Alerts in PRESBIDE. Pop-up reminders that appear when the PRESBIDE software is used to prescribe statins. There are three types of alerts depending on the patient’s age group (<35, 35-74, and ≥75 years old). Further, links are provided to a decision-making algorithm and a patient information sheet (i-botika).
- Decision-making algorithm: “Management of cholesterol as a risk factor in primary prevention of cardiovascular disease”. Clinical decision tree presenting potential courses of action based on clinical practice guidelines (CPGs), specifically for reducing cholesterol for the primary prevention of CVD in patients of different age groups and levels of CVR. Interactive decision-making support tool, developed by researchers collaborating in the DE-imFAR project, that also includes links for downloading two further documents: one providing information on CVD risk factors and the other on the 5As “Ask, Assess, Advise, Assist, Arrange” clinical intervention, recommended for promoting healthy lifestyles.

- Patient information sheet on cholesterol levels (i-botika: “Cholesterol levels are not the only thing”, developed in the framework of this project, providing information on high cholesterol levels and their role together with other risk factors associated with CVD)

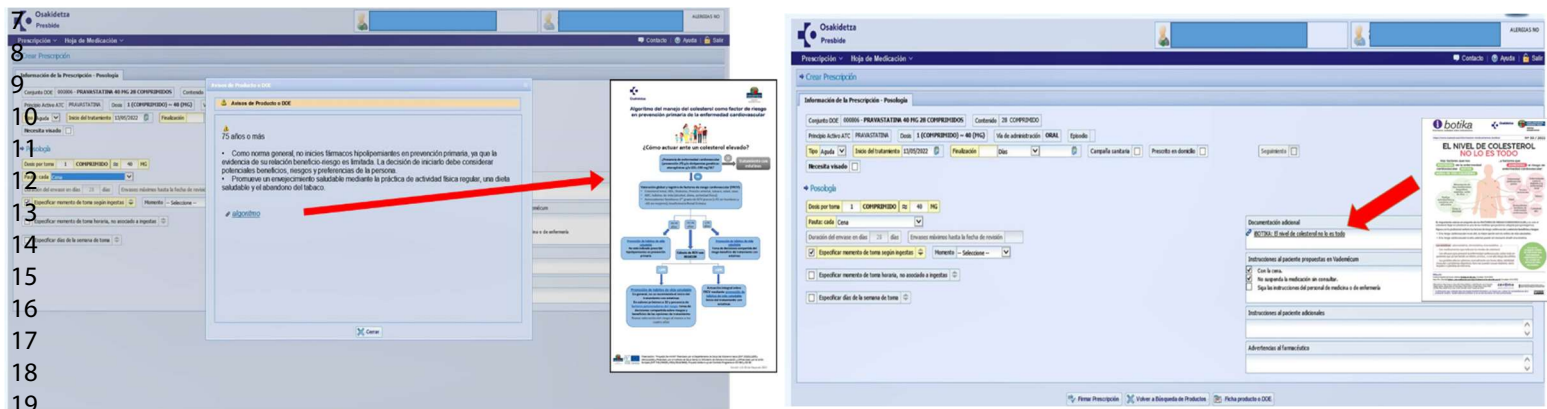


Figure 2. a). Pop-up reminder in the PRESBIDE software with recommendations on the prescribing of statins in people ≥ 75 years old that includes a link to the “Management of cholesterol as a risk factor in primary prevention of cardiovascular disease” algorithm, b) PRESBIDE form for prescribing statins, with a link to the patient information sheet (i-botika).

1.3. Objectives: *Determinant - What needs to change*

Pop-up alerts, reminders, and an algorithm

Cognitive and interpersonal skills:

- ✓ Enhance skills to enable appropriate prescribing of statins based on clinical practice recommendations

Attention, memory, and decision-making processes:

- ✓ Promote recall of recommended clinical practice in the primary prevention of CVD, reducing the impact of therapeutic inertia

Context and resources:

- ✓ Develop support systems in the EHR as reminders of and to promote the practices recommended in CPGs for the primary prevention of CVD (avoiding statins and encouraging healthy lifestyles)
- ✓ Restrict or impede inappropriate prescribing of statins due to clinical prescribing behavior driven by simplicity and speed

Emotion/Reinforcement:

- ✓ Reduce the likelihood of inappropriate prescribing due to habit, routine, or inertia (to “treat” cholesterol), through the experiencing of negative emotions when going against the recommended practice and this is made evident by alerts

Patient information sheet

Social influence (patient involvement):

- ✓ Increase patient awareness of the problems associated with the inappropriate prescribing of statins: risks vs benefits
- ✓ Increase patient knowledge of the criteria and courses of action recommended in CPGs (concerning cholesterol, CVD, and CVR)

1.4. Choice architecture techniques

A. Decision Information

A1. Translate information: change the format or presentation of information but not the content.

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3 **Reframe:** present the (same) information in several ways, e.g., Presenting the contents of CPGs
4 in several different ways (i.e., text within alerts, in the form of an algorithm, etc.).

5 **Simplify:** reduce the burden of cognitive effort necessary to process the information available
6 and increase its usefulness in the decision-making process, e.g., algorithm.

7 **A2. Make information visible:** make necessary information readily accessible.

8 **Make external information visible:** make decision-relevant information visible, e.g., text within
9 alerts recalling the CPGs.

10 11 **B. Decision structure**

12 **B1. Change choice defaults**

13 **Prompted choice:** avoid the status quo bias or default effects because of inertia or assumed
14 recommendations, e.g., pop-up alerts.

15 **B2. Change option-related effort:** change physical effort.

16 **Increase physical effort:** e.g., pop-up alerts.

17 18 **C. Decision assistance**

19 **C1. Provide reminders:** provide positive reminders that heighten the salience of a desired option
20 and/or diminish the salience of an undesired option, e.g., Pop-up alerts with the
21 recommendation to not prescribe statins.

22 23 **1.5. Exposure**

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- “Lighthouse” guiding alert in the REGICOR CVR calculator: by clicking to “save” the result after estimating CVR
 - Alerts in PRESBIDE: by starting to prescribe statins or clicking on the links to the algorithm or the patient information sheet

2. Strategy - Reflective/non-reflective decision information strategy

Corporate campaign entitled “Stopping low-value prescribing” (in Spanish: “*Abandono de prescripciones farmacológicas de escaso valor*”), promoted through a knowledge dissemination strategy based on circulars and notifications (e.g., mass mailing and internal newsletters) concerning content, informative material and documents on recommended clinical practice and improving the appropriateness and/or optimization in prescribing drug treatments, including that of statins for the primary prevention of CVD, made available to FPs on the corporate intranets of the Ezkerraldea-Enkarterri-Cruces (EEC) and Barakaldo-Sestao (BS) IHOs, part of the Basque Health Service (Osakidetza).

2.1. Target audience

This strategy targets all FPs from the EEC and BS IHOs, who will also be exposed to the first strategy, namely, non-reflective decision assistance.

2.2. Active components (actions) of the intervention

- Adherence to and implementation of best practice pages on the EEC and BS IHO intranets which have dedicated sections focused on improving the appropriateness of the use of statins providing easy access to the CPGs and recommended practice for the primary prevention of CVD.



Figure 3. Main page of the adherence to and implementation of best practice (“*Adecuación e Implementación de Buenas Prácticas*”) section on the Ezkerraldea-Enkarterri-Cruces Integrated Healthcare Organization intranet and main page of the dedicated “Stopping inappropriate prescribing of statins for the primary prevention of cardiovascular disease” section. Equivalent pages were also created on the Barakaldo-Sestao Integrated Healthcare Organization intranet.

- Corporate dissemination campaign: activities aimed at attracting FPs to the pages created on the EEC and BS IHO intranets, in order that they access the information and documents available
 - News story on the launch of the campaign with links to the pages on the corporate intranets, e.g.,

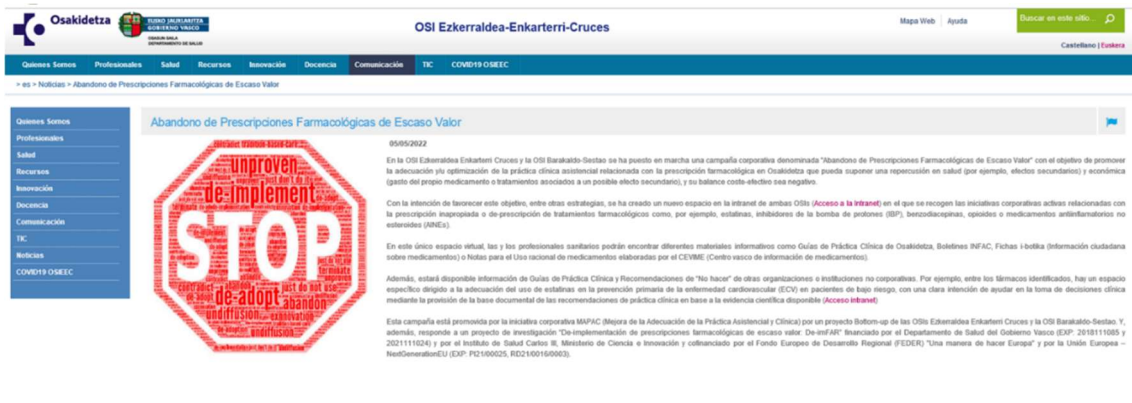


Figure 4. News story published on the Ezkerraldea-Enkarterri-Cruces Integrated Healthcare Organization intranet to announce the launch of the corporate “Stopping low-value prescribing” campaign and the development of pages on its intranet and that of the Barakaldo-Sestao Integrated Healthcare Organization, on May 5, 2022. The story was also published on the Barakaldo-Sestao Integrated Healthcare Organization intranet.

- **Monthly newsletter:** reporting of the launch of the campaign in the monthly newsletter circulated by the BS IHO to all its employees
- **Mass mailing** on the launch of the campaign with links to the pages on the corporate intranets
- **Revitalization of the corporate campaign:** periodic publication of news stories on the EEC and BS IHO intranets with content related to the campaign informing FPs of the updating of content/informative materials (for example, any changes in the recommendations in CPGs and INFAC [pharmacotherapy information] newsletters) on the dedicated pages on the intranets of both IHOs, aimed at improving the appropriateness of the use of statins in primary prevention of CVD, including links to these pages.
- **Justification email** from the Healthcare Management of the Basque Health Service, telling all FPs about the initiatives being put in place to improve the approach to the prevention of CVD, improving the appropriateness of statin prescribing, and encouraging the provision of healthy lifestyle advice, among other components.

2.3. Objectives: Determinant - *What needs to change*

Knowledge:

- ✓ Increase awareness of the problem of the inappropriate prescribing of statins
- ✓ Increase knowledge of the CPGs on the primary prevention of CVD, in particular, the appropriate or recommended care as a function of the estimated CVR
- ✓ Provide evidence-based standardized and up-to-date clinical guidelines

Behavior regulation:

- ✓ Encourage reflection on practice/performance in relation to inappropriate prescribing of statins in the primary prevention of CVD

Beliefs about capabilities:

- ✓ Strengthen the belief that the prescribing of statins is not as straightforward and safe as might be thought
- ✓ Strengthen the belief that statin treatment is not easy for patients (dosage)

Beliefs about consequences:

- ✓ Strengthen the belief that not prescribing statins for the primary prevention of CVD is not the same as “not treating”.
- ✓ Strengthen the belief that statins are not more effective in reducing cardiovascular events than healthy lifestyle promotion in the primary prevention of CVD
- ✓ Strengthen the belief that statins, in the primary prevention of CVD, may have adverse effects and are not risk-free.

Professional/social role and identity:

- ✓ Foster the belief that appropriate primary prevention of CVD is considered important at the organizational level and among peers.
- ✓ Strengthen understanding that the role of FPs goes beyond that of prescribing drugs.

Social influence:

- ✓ Increase awareness of the organizational goals for reducing inappropriate prescribing of statins in the primary prevention of CVD.
- ✓ Increase patient awareness of the problems associated with the inappropriate prescribing of statins: risks vs benefits
- ✓ Increase patient knowledge of the criteria and recommended courses of action (concerning cholesterol, CVD, and CVR)

Emotion/reinforcement:

- ✓ Reduce the likelihood of inappropriate prescribing due to habit, routine, or inertia (to “treat” cholesterol), through the experiencing of negative emotions when going against the recommended clinical practice and this is made evident by alerts.

Cognitive and interpersonal skills:

- ✓ Enhance skills to enable the appropriate prescribing of statins based on CPGs.

2.4. Choice architecture techniques

A. Decision Information

A1. Translate Information: change the format or presentation of information but not the content.

Reframe: present the (same) information in several ways, e.g., clinical guidelines, algorithm, patient information leaflet.

Simplify: reduce the burden of cognitive effort necessary to process the information available and increase its usefulness in the decision-making process, e.g., algorithm.

A2. Make information visible: make necessary information readily accessible.

Make external information visible: make decision-relevant information visible, e.g., Links about inappropriate statin prescription in the Basque Health Service (Osakidetza), adverse effects of statins and cholesterol treatment, and promotion of the campaign through emails and news.

A3. Provide social reference point: influence decision-making through other’s behavior.

Refer to descriptive norm: depict the observable behavior of other people to impact on the decision-making process, e.g., links about inappropriate statin prescription in the Basque Health Service (Osakidetza).

B. Decision structure

B2. Change option-related effort: modify the physical or financial effort involved in the decision-making process.

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3 **Change physical effort**, e.g., decreasing physical effort by making all theme-related information
4 accessible on the same website and including links to the website in the text of emails and news
5 stories.
6

7 **C. Decision assistance**

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9 **C1. Provide reminders:** provide positive reminders that heighten the salience of a desired option
10 and/or diminish the salience of an undesired option, e.g., links to clinical guidelines with
11 recommended practice about CVD primary prevention, and information about adverse effects
12 of statins.
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15 **C2. Provide social reference point:** influence decision-making through other's behavior.

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17 **Refer to opinion leader:** use them as information disseminators to improve the impact of the
18 campaign, e.g., Setting of goals in an email sent by an opinion leader, using the source as much
19 as the content of the message to improve the impact of the campaign.
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22 23 **2.5. Exposure**

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- By accessing the pages of the EEC and BS IHO corporate intranet and clicking on the links to the CPGs, INFAC newsletters, i-botika patient information sheets, recommendations, etc. available in the dedicated "Stopping inappropriate prescribing of statins for the primary prevention of cardiovascular disease" section
 - By accessing the news section on the dedicated pages on the intranets of EEC and BS IHOs

3. Strategy - Reflective decision structure strategy

Sending of regular personalized *Audit & Feedback (A&F)* reports with practice- and organizational-level performance indicators of the FPs regarding inappropriate prescribing of statins and healthy lifestyle promotion in the primary prevention of CVD in low-risk patients in the Basque Health Service

3.1. Target audience

This strategy targets a randomly selected set of FPs from the EEC and BS IHOs, who will also be exposed to the previously described interventions, namely, *non-reflective decision assistance and decision information*.

3.2. Active components (actions) of the intervention

- Informative email concerning the sending of A&F reports, including the possibility to opt out: email with information for primary care FPs of the EEC and BS IHOs on the sending of regular personalized A&F reports, in the framework of the corporate campaign, with the goal of encouraging adherence to recommendations and stopping inappropriate prescribing of statins
- A&F reports mailing: periodic A&F reports with indicators describing global performance across the Basque Health Service: a) rate of new potentially inappropriate prescribing of statins to people without CVD and with REGICOR CVR scores <7.5% and practice in the promotion of healthy habits in these patients; b) rate of documentation of CVR (in the 2 years before the prescription date) in all 40- to 75-year-olds with no clinical history of CVR who are newly prescribed statins. Future A&F reports are expected to contain a link to a short voluntary exercise on goal setting for improving the appropriateness of statin prescribing for the primary prevention of CVD

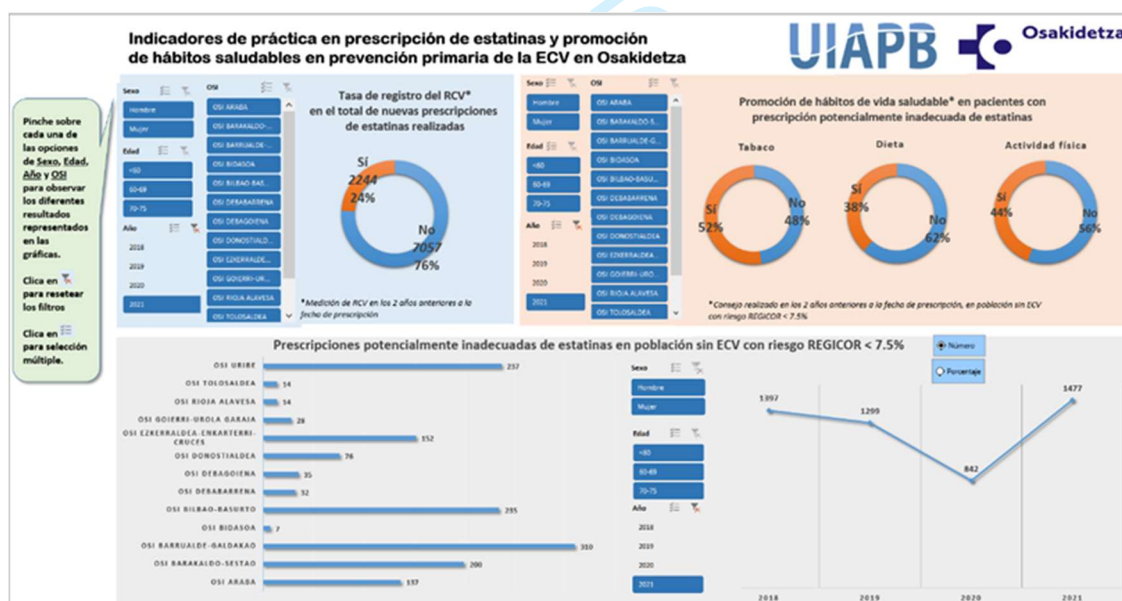


Figure 5. Draft of the Audit & Feedback report with practice- and organizational-level performance indicators of the family physicians regarding inappropriate prescribing of statins and healthy lifestyle promotion in the primary prevention of cardiovascular disease in low-risk patients in the Basque Health Service

3.3. Objectives: Determinant - What needs to change

Knowledge:

- ✓ Increase awareness of the problem of the inappropriate prescribing of statins

Behavior regulation:

- ✓ Make data available on inappropriate prescribing of statins for the primary prevention of CVD
- ✓ Provide tools for the setting of clear specific goals, at personal and organizational levels, regarding the reduction of inappropriate prescribing of statins for the primary prevention of CVD

Active reflection on personal practice:

- ✓ Encourage further reflection on practice/performance in relation to inappropriate prescribing of statins for the primary prevention of CVD

Intentions:

- ✓ Reduce the intention to prescribe statins inappropriately and increase the intention to promote healthy lifestyles for the primary prevention of CVD

Goals:

- ✓ Encourage commitment to practice in the primary prevention of CVD that is in accordance with recommendations
- ✓ Increase the motivation to promote healthy lifestyles in the primary prevention of CVD

Beliefs about capabilities:

- ✓ Strengthen self-efficacy and enhance the skills required for promoting healthy lifestyles

Emotion:

- ✓ Strengthen self-confidence about not prescribing statins for the primary prevention of CVD
- ✓ Foster belief in the safety of and trust in the courses of action recommended in the guidelines
- ✓ Experience a negative emotion after inappropriate prescribing

Professional/social role and identity:

- ✓ Foster the belief that appropriate primary prevention of CVD is considered important at the organizational level and among peers
- ✓ Strengthen understanding that the role of FPs goes beyond prescribing drugs

Reinforcement:

- ✓ Generate positive/negative reinforcement related to good/poor performance in the primary prevention of CVD.

3.4. Choice architecture techniques

A. Decision Information

A1. Translate Information: change the format or presentation of information but not the content.

Simplify: reduce the burden of cognitive effort necessary to process the information available and increase its usefulness in the decision-making process, e.g., presenting prescription rate data in a simple, user-friendly way, namely, on a dashboard.

A2. Make information visible: make necessary information readily accessible.

Make own behavior visible: feedback.

Make external information visible: make decision-relevant information visible, e.g., showing the prescription rates of other FPs and other IHOs.

A3. Provide social reference point: influence decision-making through the behavior of others.

Refer to descriptive norm: depict the observable behavior of other people to impact on the decision-making process, e.g., showing other FPs' prescribing behavior.

B. Decision structure

B2. Change opinion-related effort: modify the physical or financial effort involved in the decision-making process.

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3 **Decrease physical effort:** collect all prescribing data in one file, e.g., dashboard.

4 **C. Decision assistance**

5 **C2. Facilitate commitment:** overcome constrained self-control and bridge the intention-
6 behavior gap.

7 **Support self-commitment:** arrange with the aim of helping fulfill a plan, e.g., self-commitment
8 questionnaire
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11 **3.5. Exposure**

12 By opening the A&F reports received by email.
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For peer review only



STANDARD PROTOCOL ITEMS: RECOMMENDATIONS FOR INTERVENTIONAL TRIALS

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description	Addressed on page number
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	4
	2b	All items from the World Health Organization Trial Registration Data Set	N/A
Protocol version	3	Date and version identifier	18
Funding	4	Sources and types of financial, material, and other support	22
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	1-2
	5b	Name and contact information for the trial sponsor	2
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	22
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	N/A
Introduction			
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	5-7
	6b	Explanation for choice of comparators	6
Objectives	7	Specific objectives or hypotheses	7-8
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	9, 12

Methods: Participants, interventions, and outcomes

Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	9
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	10
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	11-12
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	N/A
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	N/A
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	N/A
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	13-14
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	N/A
Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	16
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	N/A

Methods: Assignment of interventions (for controlled trials)

Allocation:

Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	12
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1	Allocation		Mechanism of implementing the allocation sequence (eg, central	
2	concealment	16b	telephone; sequentially numbered, opaque, sealed envelopes),	12
3	mechanism		describing any steps to conceal the sequence until interventions are	
4			assigned	
5				
6	Implementati	16c	Who will generate the allocation sequence, who will enrol	12
7	on		participants, and who will assign participants to interventions	
8				
9	Blinding		Who will be blinded after assignment to interventions (eg, trial	
10	(masking)	17a	participants, care providers, outcome assessors, data analysts), and	12
11			how	
12				
13				
14		17b	If blinded, circumstances under which unblinding is permissible, and	
15			procedure for revealing a participant's allocated intervention during	N/A
16			the trial	
17				
18				

19 **Methods: Data collection, management, and analysis**

21	Data collection		Plans for assessment and collection of outcome, baseline, and	
22	methods	18a	other trial data, including any related processes to promote data	16-17
23			quality (eg, duplicate measurements, training of assessors) and a	
24			description of study instruments (eg, questionnaires, laboratory	
25			tests) along with their reliability and validity, if known. Reference to	
26			where data collection forms can be found, if not in the protocol	
27				
28				
29		18b	Plans to promote participant retention and complete follow-up,	N/A
30			including list of any outcome data to be collected for participants	
31			who discontinue or deviate from intervention protocols	
32				
33	Data		Plans for data entry, coding, security, and storage, including any	
34	management	19	related processes to promote data quality (eg, double data entry;	17
35			range checks for data values). Reference to where details of data	
36			management procedures can be found, if not in the protocol	
37				
38				
39	Statistical		Statistical methods for analysing primary and secondary outcomes.	
40	methods	20a	Reference to where other details of the statistical analysis plan can	15-16
41			be found, if not in the protocol	
42				
43		20b	Methods for any additional analyses (eg, subgroup and adjusted	15
44			analyses)	
45				
46				
47		20c	Definition of analysis population relating to protocol non-adherence	
48			(eg, as randomised analysis), and any statistical methods to handle	N/A
49			missing data (eg, multiple imputation)	
50				
51				

52 **Methods: Monitoring**

54	Data monitoring		Composition of data monitoring committee (DMC); summary of its	
55		21a	role and reporting structure; statement of whether it is independent	N/A
56			from the sponsor and competing interests; and reference to where	
57			further details about its charter can be found, if not in the protocol.	
58			Alternatively, an explanation of why a DMC is not needed	
59				
60				

1		Description of any interim analyses and stopping guidelines,	
2	21b	including who will have access to these interim results and make	N/A
3		the final decision to terminate the trial	
4			
5	Harms	Plans for collecting, assessing, reporting, and managing solicited	
6		and spontaneously reported adverse events and other unintended	N/A
7	22	effects of trial interventions or trial conduct	
8			
9	Auditing	Frequency and procedures for auditing trial conduct, if any, and	
10		whether the process will be independent from investigators and the	N/A
11	23	sponsor	
12			
13			
14			
15	Ethics and dissemination		
16	Research ethics	Plans for seeking research ethics committee/institutional review	
17	approval	board (REC/IRB) approval	18
18			
19	Protocol	Plans for communicating important protocol modifications (eg,	
20	amendments	changes to eligibility criteria, outcomes, analyses) to relevant parties	
21		(eg, investigators, REC/IRBs, trial participants, trial registries,	N/A
22	25	journals, regulators)	
23			
24			
25	Consent or	Who will obtain informed consent or assent from potential trial	
26	assent	participants or authorised surrogates, and how (see Item 32)	12,17
27			
28			
29	26b	Additional consent provisions for collection and use of participant	N/A
30		data and biological specimens in ancillary studies, if applicable	
31			
32	Confidentiality	How personal information about potential and enrolled participants	
33		will be collected, shared, and maintained in order to protect	16-17
34	27	confidentiality before, during, and after the trial	
35			
36	Declaration of	Financial and other competing interests for principal investigators	
37	interests	for the overall trial and each study site	22
38			
39	Access to data	Statement of who will have access to the final trial dataset, and	
40		disclosure of contractual agreements that limit such access for	18
41	29	investigators	
42			
43			
44	Ancillary and	Provisions, if any, for ancillary and post-trial care, and for	
45	post-trial care	compensation to those who suffer harm from trial participation	N/A
46			
47	Dissemination	Plans for investigators and sponsor to communicate trial results to	
48	policy	participants, healthcare professionals, the public, and other relevant	
49	31a	groups (eg, via publication, reporting in results databases, or other	18
50		data sharing arrangements), including any publication restrictions	
51			
52			
53	31b	Authorship eligibility guidelines and any intended use of	N/A
54		professional writers	
55			
56	31c	Plans, if any, for granting public access to the full protocol,	18
57		participant-level dataset, and statistical code	
58			
59			
60	Appendices		

1	Informed		Model consent form and other related documentation given to	
2	consent	32	participants and authorised surrogates	N/A
3	materials			
4				
5	Biological		Plans for collection, laboratory evaluation, and storage of biological	
6	specimens	33	specimens for genetic or molecular analysis in the current trial and	N/A
7			for future use in ancillary studies, if applicable	
8				

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "[Attribution-NonCommercial-NoDerivs 3.0 Unported](#)" license.

Reference: Chan A-W, Tetzlaff JM, Altman DG, et al. SPIRIT 2013 Statement: Defining standard protocol items for clinical trials. *Ann Intern Med.* 2013 Feb 5;158(3):200-207. doi: 10.7326/0003-4819-158-3-201302050-00583.

BMJ Open

The De-imFAR Phase II Project: A study protocol for a cluster randomized implementation trial to evaluate the effectiveness of de-implementation strategies to reduce low-value statin prescribing in the primary prevention of Cardiovascular Disease.

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2023-078692.R1
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Date Submitted by the Author:	02-Feb-2024
Complete List of Authors:	<p>Sanchez , Alvaro; Osakidetza-Basque Health Service, Primary Care Research Unit of Bizkaia, Deputy Directorate of Healthcare Assistance; Biocruces Bizkaia Health Research Institute</p> <p>Pi Joan, Jose Ignacio; Osakidetza-Basque Health Service, Clinical Epidemiology Unit; Biocruces Bizkaia Health Research Institute</p> <p>Sainz de Rozas, Rita; Osakidetza-Basque Health Service, Primary Care Pharmacy Unit, Ezkerraldea-Enkarterri-Cruces Integrated Health Organization; Biocruces Bizkaia Health Research Institute</p> <p>Lekue, Itxasne; Osakidetza-Basque Health Service, Primary Care Pharmacy Unit, Ezkerraldea-Enkarterri-Cruces Integrated Health Organization; Biocruces Bizkaia Health Research Institute</p> <p>San Vicente, Ricardo; Osakidetza-Basque Health Service, Zumarraga Health Center, Goierri-Alto Urola Integrated Health Organization</p> <p>Quindimil, Jose Antonio; Osakidetza-Basque Health Service, Sestao Health Center, Barakaldo-Sestao Integrated Health Organization</p> <p>Rotaeche, Rafael; Osakidetza-Basque Health Service, Primary Care Research Unit of Gipuzkoa, Organization of Integrated Health Services of Gipuzkoa</p> <p>Etxeberria, Arritxu ; Osakidetza-Basque Health Service, Primary Care Pharmacy, Donostialdea Integrated Health Organization</p> <p>Mozo, Carmela; Osakidetza-Basque Health Service, Primary Care Pharmacy, Donostialdea Integrated Health Organization</p> <p>Martinez-Cengotitabengoa, Monica; University of the Basque Country, School of Pharmacy; Osakidetza-Basque Health Service</p> <p>Monge, Monica; Osakidetza-Basque Health Service, Corporate Pharmacy Service, Directorate of Healthcare Assistance</p> <p>Gómez-Ramírez, Cristina; Osakidetza-Basque Health Service, Cardiology Department, Cruces University Hospital, Ezkerraldea-Enkarterri-Cruces Integrated Health Organization</p> <p>Samper, Ricardo; Osakidetza-Basque Health Service, Corporate Pharmacy Service, Directorate of Healthcare Assistance</p> <p>Ogueta Lana, Mikel ; Osakidetza-Basque Health Service, Subdirectorate of Quality and Health Information Systems</p> <p>Celorrio, Sara; Osakidetza-Basque Health Service, Barakaldo-Sestao Integrated Health Organization</p> <p>Merino-Inda, Nerea; Biocruces Bizkaia Health Research Institute</p> <p>Llarena, Marta; Biocruces Bizkaia Health Research Institute, Network for</p>

	<p>Research on Chronicity, Primary Care, and Health Promotion (RICAPPS) Gonzalez Saenz de Tejada, Marta; Biocruces Bizkaia Health Research Institute, Network for Research on Chronicity, Primary Care, and Health Promotion (RICAPPS)</p> <p>García-Alvarez, Arturo; Osakidetza-Basque Health Service, Primary Care Research Unit of Bizkaia. Deputy Directorate of Healthcare Assistance; Biocruces Bizkaia Health Research Institute</p> <p>Grandes, Gonzalo; Osakidetza-Basque Health Service, Primary Care Research Unit of Bizkaia. Deputy Directorate of Healthcare Assistance; Biocruces Bizkaia Health Research Institute</p>
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TITLE PAGE

Title

The De-imFAR Phase II Project: A study protocol for a cluster randomized implementation trial to evaluate the effectiveness of de-implementation strategies to reduce low-value statin prescribing in the primary prevention of Cardiovascular Disease.

Author's details Alvaro Sanchez^{1*}, Jose I. Pijoan², Rita Sainz de Rozas³, Itxasne Lekue³, Ricardo San Vicente⁴, Jose Antonio Quindimil⁵, Rafael Rotaecche⁶, Arritxu Etxeberria⁷, Carmela Mozo⁷, Monica Martinez-Cengotitabengoa⁸, Monica Monge⁹, Cristina Gómez-Ramírez¹⁰, Ricardo Samper¹¹, Mikel Ogueta Lana¹², Sara Celorrio¹³, Nerea Merino-Inda¹⁴, Marta Llarena¹⁵, Marta Gonzalez Saenz de Tejada¹⁵, Arturo Garcia-Alvarez¹, and Gonzalo Grandes¹

¹ Primary Care Research Unit of Bizkaia, Deputy Directorate of Healthcare Assistance, Biobizkaia Health Research Institute, Basque Health Service - Osakidetza, Network for Research on Chronicity, Primary Care, and Health Promotion (RICAPPS), Barakaldo, Bizkaia, Spain.

² Clinical Epidemiology Unit, Biobizkaia Health Research Institute, Basque Health Service - Osakidetza, Barakaldo, Bizkaia, Spain. CIBER de Epidemiología y Salud Pública (CIBERESP), Instituto de Salud Carlos III, Spain.

³ Primary Care Pharmacy Unit, Ezkerraldea-Enkarterri-Cruces Integrated Health Organization, Basque Health Service – Osakidetza, Biobizkaia Health Research Institute, Barakaldo, Bizkaia, Spain.

⁴ Zumarraga Health Center, Goierri-Alto Urola Integrated Health Organization, Basque Health Service – Osakidetza, Zumárraga, Gipuzkoa, Spain.

⁵ Sestao Health Center, Barakaldo-Sestao Integrated Health Organization, Basque Health Service – Osakidetza, Sestao, Bizkaia, Spain.

1
2
3 29 ⁶ Primary Care Research Unit of Gipuzkoa, Organization of Integrated Health Services
4
5 30 of Gipuzkoa, Biogipuzkoa Health Reseach Institute, Donostia-San Sebastian, Gipuzkoa,
6
7 31 Spain

8
9 32 ⁷ Primary Care Pharmacy, Donostialdea Integrated Health Organization, Hernani,
10
11 33 Gipuzkoa, Spain

12
13 34 ⁸ School of Pharmacy, University of the Basque Country UPV/EHU, Vitoria-Gasteiz,
14
15 35 Spain. Psychology Clinic of East Anglia, Norwich, UK. Osakidetza Basque Health
16
17 36 Service, Barakaldo, Spain.

18
19
20 37 ⁹ Corporate Pharmacy Service, Directorate of Healthcare Assistance, Osakidetza-
21
22 38 Basque Health Service Central Services, Vitoria-Gasteiz, Spain

23
24 39 ¹⁰ Cardiology Department, Cruces University Hospital, Ezkerraldea-Enkarterri-Cruces
25
26 40 Integrated Health Organization, Basque Health Service – Osakidetza, Barakaldo,
27
28 41 Bizkaia, Spain.

29
30 42 ¹¹ Corporate Pharmacy Service, Directorate of Healthcare Assistance, Osakidetza-
31
32 43 Basque Health Service Central Services, Vitoria-Gasteiz, Spain

33
34 44 ¹² Subdirectorate of Quality and Health Information Systems, Osakidetza-Basque Health
35
36 45 Service Central Services, Vitoria-Gasteiz, Spain

37
38
39 46 ¹³ Barakaldo-Sestao Integrated Health Organization, Basque Health Service –
40
41 47 Osakidetza, Barakaldo, Spain

42
43 48 ¹⁴ Biobizkaia Health Research Institute, Barakaldo, Bizkaia, Spain.

44
45 49 ¹⁵ Biobizkaia Health Research Institute, Network for Research on Chronicity, Primary
46
47 50 Care, and Health Promotion (RICAPPS), Barakaldo, Bizkaia, Spain.

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49 51

50
51 52 *** Corresponding author:**

52
53 53 Alvaro Sánchez

54
55 54 E-mail: Alvaro.sanchezperez@osakidetza.eus

56
57 55 Primary Care Research Unit of Bizkaia, Deputy Directorate of Healthcare Assistance,
58
59 56 Biobizkaia Health Research Institute, Basque Health Service – Osakidetza, Network for

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2
3 57 Research on Chronicity, Primary Care, and Health Promotion (RICAPPS). Plaza Cruces
4
5 58 s/n, E-48903 Barakaldo, Bizkaia, Spain.
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7 59

60 **ABSTRACT**

61 **Introduction**

62 This study aims to reduce potentially inappropriate prescribing (PIP) of statins and foster
63 healthy lifestyle promotion in cardiovascular disease (CVD) primary prevention in low-
64 risk patients. To this end, we will compare the effectiveness and feasibility of several de-
65 implementation strategies developed following the structured design process of the
66 Behavior Change Wheel targeting key determinants of clinical decision-making process
67 in CVD prevention.

68 **Methods and analysis**

69 A cluster randomized implementation trial, with an additional control group, will be
70 launched, involving family physicians (FPs) from 13 Integrated Healthcare Organizations
71 (IHOs) of Osakidetza-Basque Health Service with non-zero incidence rates of PIP of
72 statins in 2021. All FPs will be exposed to a non-reflective decision assistance strategy
73 based on reminders and decision support tools. Additionally, FPs from two of the IHOs
74 will be randomly assigned to one of two increasingly intensive de-implementation
75 strategies: adding a decision information strategy based on knowledge dissemination,
76 and a reflective decision structure strategy through audit/feedback. The target population
77 comprises 45- to 74-year-old women and 40- to 74-year-old men with moderately
78 elevated cholesterol levels but no diagnosed CVD and low cardiovascular risk
79 (REGICOR <7.5%), who attend at least one appointment with any of the participating
80 FPs (May 2022-May 2023), and will be followed until May 2024. We use the Reach,
81 Effectiveness, Adoption, Implementation and Maintenance (RE-AIM) framework to
82 evaluate outcomes. The main outcome will be the change in the incidence rate of PIP of
83 statins and healthy lifestyle counseling in the study population 12 and 24 months after
84 FPs' exposure to the strategies. Moreover, FPs' perception of their feasibility and

1
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3 85 acceptability, and patient experience regarding quality of treatment received will be
4
5 86 evaluated.

6
7 87 **Ethics and dissemination**

8
9 88 The study was approved by the Basque Country Clinical Research Ethics Committee
10
11 89 and was registered in ClinicalTrials.gov (NCT04022850). Results will be disseminated in
12
13 90 scientific peer-reviewed journals.

14
15
16 91 **Keywords:** Inappropriate Prescribing, Cardiovascular Diseases / prevention & control,
17
18 92 Hypercholesterolemia / drug therapy, Implementation Science, Research Design,
19
20 93 Primary care.

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25 95 **STRENGTHS AND LIMITATIONS OF THIS STUDY**

- 26
27 96 • An strength of the DE-imFAR study is that it involves an efficient design that
28
29 97 combines experimental and non-experimental comparisons through two randomly
30
31 98 assigned intervention arms and one non-randomized control arm to test the
32
33 99 comparative effectiveness on reducing potentially inappropriate prescribing (PIP)
34
35 100 of statins and increasing healthy lifestyle promotion of several de-implementation
36
37 101 strategies deployed in real-world settings.
- 38
39 102 • Counting with one non-randomized control arm is a strength because it allows
40
41 103 capturing the effect of temporal trends, regression to the mean, and the learning
42
43 104 curve due to the reference/background strategy to which all targeted family
44
45 105 physicians (FPs) are exposed, when comparing this reference strategy with the
46
47 106 two experimental de-implementation strategies.
- 48
49 107 • Another strength is the use of qualitative methods to better understand from the
50
51 108 perspective of the study participants the reasons why (why not) the strategies
52
53 109 work, to explain the variations in the results achieved and to identify the essential
54
55 110 components of the strategy and those that will require to be optimized.
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2
3 111 • To the best of our knowledge, the DE-imFAR study is one of the firsts of its kind
4
5 112 that specifically uses the RE-AIM framework for the evaluation of the study results
6
7 113 in terms of public health impacts.
8
9 114 • The main limitation lies in the planned comparisons of the randomized groups with
10
11 115 respect to the control arm, likely to differ to some extent at baseline because of
12
13 116 the non-random process of generation. To tackle this limitation, in addition to
14
15 117 evaluating the change in PIP incidence in all eligible FPs, a matching strategy with
16
17 118 the selection of one matched FP from this non-randomized group for each of the
18
19 119 randomized FPs will be performed seeking to increase comparability and reduce
20
21 120 potential bias.
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122 INTRODUCTION

123 Reducing low-value healthcare, that is, clinical practices that have not been shown to be
124 efficient or effective, is becoming a global priority due to the widespread empirical
125 evidence of its high prevalence across healthcare systems, potential harm and its impact
126 on patient safety, resource use, and social inefficiency [1,2].
127

128 Nonetheless, reducing or eliminating low-value practices is a complex matter, as drivers
129 fostering or maintaining them seem to operate at multiple levels and be context specific.
130 Therefore, in order to design effective and efficient corrective measures, a careful
131 process of formal analysis of the determinants of the clinical behavior in question is
132 needed. In this context, behavior change theory has been extensively applied to
133 understand the factors that may influence clinical behavior, identify and design possible
134 techniques and interventions that could be used to change it, and explain the
135 mechanisms through which such interventions operate [3,4].
136

137 The DE-imFAR study (from the Spanish for de-implementation of low-value
138 pharmacological prescribing) is a two-phase project [5] that aims to apply behavioral

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2
3 139 science theory within a structured process involving the main stakeholders (health
4
5 140 professionals, patients, and researchers) in the design, deployment, and evaluation of
6
7 141 targeted de-implementation strategies for reducing potentially inappropriate prescribing
8
9 142 (PIP). Specifically, the targeted low-value practice of the DE-imFAR study is the
10
11 143 pharmacological prescription of statins in the primary prevention of cardiovascular
12
13 144 disease (CVD) in low-risk patients. In order to prevent CVD, one of the leading causes
14
15 145 of morbidity and death worldwide, there is general agreement on the indication of lipid-
16
17 146 lowering treatment, mainly with statins, in patients with a cardiovascular risk (CVR)
18
19 147 greater than 10% over 10 years or in secondary prevention [6-9]. Whereas, for primary
20
21 148 prevention in patients with low CVR (<10%), preventive activities should be focused on
22
23 149 the promotion of healthy lifestyles through optimizing diet, increasing physical activity,
24
25 150 and stopping smoking [6-9]. Moreover, international guidelines encourage discussion
26
27 151 with patients concerning the benefits of lifestyle modification for the prevention of CVD,
28
29 152 as well as other modifiable risk factors, before considering pharmacological treatment
30
31 153 [7-9].
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37 155 Within the Phase I of the DE-imFAR study, we first conducted a cross-sectional
38
39 156 observational study on the incidence of PIP of statins and provision of advice for
40
41 157 changing lifestyles in the Basque Health Service-Osakidetza in 2018. The results
42
43 158 showed that the prescription of statins had increased notably in the Basque Country
44
45 159 (Spain) with an estimated incidence of new PIP of 10.5 per 100,000 persons/year in
46
47 160 patients aged 40 to 75 years, without CVD, with moderately elevated cholesterol levels
48
49 161 but with a CVR <5% [10].
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54 163 Secondly, we applied two of the most successfully used behavior change theories in field
55
56 164 of Implementation Science, the Theoretical Domains Framework (TDF) [3,11,12] and
57
58 165 Behavior Change Wheel (BCW) [13], to a) understand and define the problem (low-value
59
60 166 practice) in behavioral terms and to select and specify the target behaviors; b) identify

1
2
3 167 the factors that may influence it; and c) map targeted de-implementation and
4
5 168 implementation strategies conducive to reducing the low-value practice in question.
6
7 169 Briefly, after having prioritized our specific target behavior (that is “clinician decision-
8
9 170 making on intervention/treatment to be provided based on objective clinical information
10
11 171 and subjective schemas and heuristics”), identified determinants (facilitators of the non-
12
13 172 desired behavior of PIP of statins and barriers to applying the recommended clinical
14
15 173 practice behavior of promoting healthy lifestyles), and mapped specific behavior change
16
17 174 techniques, three types of de-implementation strategies were selected based on being
18
19 175 the most potentially effective, feasible, and acceptable for influencing decision-making
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21 176 through different mechanisms [14]. Hence, the three strategies derived from the
22
23 177 systematic theory- and evidence-based intervention design process were: a) a non-
24
25 178 reflective decision assistance strategy based on providing evidence-based information
26
27 179 communication technology tools to help and guide decision-making; b) a decision
28
29 180 information strategy based on the dissemination of the evidence concerning CVD
30
31 181 primary prevention framed in a corporate campaign encouraging family physicians (FPs)
32
33 182 to move away from PIP; and c) a reflective decision structure strategy encouraging
34
35 183 reflection on actual performance based on an audit/feedback system [14].
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41 185 According to the literature review performed in Phase I of the DE-imFAR project [14]
42
43 186 regarding the evaluation of effective intervention strategies for the reduction of low-value
44
45 187 prescribing [15-24], multicomponent interventions—combining passive dissemination
46
47 188 interventions, based on training in or dissemination of clinical practice guidelines (CPGs),
48
49 189 with more proactive interventions incorporating decision-making aids or the sending of
50
51 190 audit/feedback— achieve the most positive results. Specifically, in the context of PIP of
52
53 191 statins, a positive impact has been observed on documentation of CVR and prescription
54
55 192 adequacy using a) multi-component dissemination strategies including informative web
56
57 193 pages, and implementation of electronic CPGs compared to routine practice and training
58
59 194 activities, and b) interventions based on sending clinical scenarios and cases, and
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3 195 audit/feedback to professionals, and decision support tools [19-23]. All these strategies
4
5 196 can be conceived and theoretically differentiated as a function of the way they may affect
6
7 197 clinicians' decision-making [25]. There is plenty of evidence demonstrating that it is
8
9 198 possible to de-implement inappropriate medical practices through the lens of clinician
10
11 199 cognition using audit/feedback, decision support tools, etc. [26-28]. In this context, the
12
13 200 growing field of choice architecture aims to explore how the structure and framing of
14
15 201 decision situations influence the choice of certain behaviors over alternative ones. On
16
17 202 the one hand, FPs' decision-making ability can be influenced by unconscious processes
18
19 203 that occur in response to environmental or emotive cues, that is, through type 1 (or non-
20
21 204 reflective) cognition. On the other, clinicians' conscious intention to change can be
22
23 205 promoted by engaging their reflective cognition to consciously evaluate and correct their
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25 206 inappropriate behavior, that is, using type 2 (or reflective) cognition [29]. However, further
26
27 207 research is needed to determine whether these evidence-based and barrier-specific
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29 208 strategies for de-implementation identified in DE-imFAR Phase I are also effective in our
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31 209 context.
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37 211 Thus, the goal of the present Phase II of the DE-imFAR study is to assess the potential
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39 212 effectiveness and feasibility of this set of de-implementation strategies to reduce the PIP
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41 213 of statins in the primary prevention of CVD (low-risk patients, REGICOR [30] CVR score
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43 214 <7.5%, with moderately elevated cholesterol levels, low-density lipoprotein (LDL)
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45 215 cholesterol levels between 70 and 189 mg/dL and/or total cholesterol (TC) between 200
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47 216 and 289 mg/dL, but without ischemic heart disease/CVD).
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51 218 Specifically, we aim to answer the following research questions:

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53 219 1. Observational comparison questions:

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55 220 As compared to a reference non-reflective decision assistance strategy based on
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57 221 reminders and decision support tools incorporated into the electronic health record
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59 222 (EHR) for helping clinical decision-making, what is the effect on the incidence of PIP of
60

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3 223 statins in CVD primary prevention and the rate of delivery of healthy lifestyle counseling
4
5 224 of a) a decision information strategy comprising a corporate “Stopping Low-Value
6
7 225 Prescribing” campaign and the dissemination of evidence-based CPGs for the primary
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9 226 prevention of CVD; b) a reflective decision structure strategy based on an audit/feedback
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11 227 system; and c) any intervention based on a reflective de-implementation strategy (a or
12
13 228 b)?
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17
18 230 2. Experimental comparison question:

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20 231 As compared to a decision information strategy comprising a corporate “Stopping Low-
21
22 232 Value Prescribing” campaign and the dissemination of evidence-based CPGs for the
23
24 233 primary prevention of CVD, together with the non-reflective decision assistance
25
26 234 intervention based on reminders and decision support tools incorporated into the EHR
27
28 235 for helping clinical decision-making, what is the effect on the incidence of PIP of statins
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30 236 in CVD primary prevention and the rate of delivery of healthy lifestyle counseling of
31
32 237 adding a reflective decision structure strategy based on an audit/feedback system?
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35 238

36 239 **METHODS AND ANALYSIS**

37 38 39 240 **Design**

40
41 241 A cluster randomized implementation trial with an additional control group will be
42
43 242 conducted for evaluating the potential effectiveness and feasibility of three de-
44
45 243 implementation strategies (Figure 1). A mixed methods evaluation will be undertaken:
46
47 244 quantitative for assessing the implementation results at the professional level
48
49 245 (effectiveness outcomes regarding changes in rates of PIP and healthy lifestyle
50
51 246 counseling) and qualitative for assessing the feasibility and perceived impact of the de-
52
53 247 implementation strategies from the FPs’ perspective and the experience and satisfaction
54
55 248 of patients concerning the clinical care received. The unit of randomization and
56
57 249 intervention will be the primary care FP, while observation and analysis will be performed
58
59 250 at professional and patient levels. The DE-imFAR research protocol was reviewed and
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3 251 approved by the Basque Country Clinical Research Ethics Committee (Reference:
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5 252 EOM2022018, approved on 30 March 2022) and was registered in the U.S. NLM
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7 253 ClinicalTrials.gov database (ClinicalTrials.gov Identifier NCT04022850, Registered 17
8
9 254 July 2019; Last update 31 January 2024).

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13 256 Osakidetza-Basque Health Service provides universal coverage and services are free at
14
15 257 the point of use, aside from co-payment for drugs, funded through regional general
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17 258 taxation. Primary, specialized, and social health-related service provision is organized
18
19 259 around 13 Integrated Healthcare Organizations (IHOs) that cover the 3 provinces of the
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21 260 region of the Basque Country: Araba, Bizkaia, and Gipuzkoa. Each resident is on the list
22
23 261 of one FP or pediatrician who offers comprehensive primary care and refers patients for
24
25 262 hospital and specialty services. Primary care professionals work in full-time teams,
26
27 263 including FPs, pediatricians, nurses, and administrative staff based at local centers
28
29 264 providing access to healthcare for users in a defined geographical area.

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31 265 We used the SPIRIT reporting guidelines and the SPIRIT checklist when writing the
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33 266 present study [31].

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36 37 268 **Participants**

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39 269 Eligibility criteria for the study will be:

- 40
41 270 1. Professionals: FPs belonging to any of the 13 IHOs of Osakidetza with a non-zero
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43 271 annual incidence rate of PIP of statins at baseline (2021) with a minimum cluster size of
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45 272 $n \geq 10$ patients
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47 273 2. Patients: All 40- to 74-year-old men and 45- to 74-year-old women with no history of
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49 274 statin use, LDL cholesterol levels between 70 and 189 mg/dL and/or TC between 200
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51 275 and 289 mg/dL but without ischemic heart disease/CVD, and an estimated CVR
52
53 276 REGICOR $< 7.5\%$ who attend at least one appointment at the participating FPs' practices
54
55 277 during the study period from May 2022 to May 2023, and followed until May 2024.

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57 278

279 **Clinical interventions**

280 The DE-imFAR study, with regard to the prescription of statins in primary prevention of
281 CVD, follows the clinical practice recommendations in Osakidetza-Basque Health
282 Service and the Spanish National Health System [6] as well as several international
283 guidelines [7-9]. Thus, these are the recommendations concerning when to initiate
284 treatment in primary prevention of CVD [6, 32]:

- 285 ▪ For individuals aged 40 to 75 years with an estimated 10-year CVR REGICOR
286 >10%, initiation of statin therapy is recommended.
- 287 ▪ In general, for individuals aged 40 to 75 years with CVR REGICOR <10% and
288 LDL cholesterol levels <190 mg/dL, it is recommended not to initiate statin
289 therapy, with the following considerations:
 - 290 ○ with CVR close to 10%, consider the presence of risk-enhancing factors
291 in decision-making.
 - 292 ○ with CVR <5%, it is recommended not to initiate statin therapy.
- 293 ▪ For patients with LDL cholesterol levels ≥ 190 mg/dL, it is recommended to assess
294 the presence of genetic dyslipidemia and potential cardiovascular risk-enhancing
295 factors. It is suggested to initiate statin therapy, together with healthy lifestyle
296 recommendations, regardless of cardiovascular risk.

297 In any case, the indication for treatment should be preceded and/or accompanied by
298 promotion of healthy lifestyles through healthful diet, regular physical activity and
299 smoking cessation. Moreover, it is recommended that the decision to initiate statin
300 therapy should consider individual baseline risk, absolute risk reduction and whether the
301 risk reduction justifies the potential harms and undesirable consequences of taking a
302 lifelong daily medication.

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304 **De-implementation strategies evaluated**

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3 305 Within the present Phase II of the DE-imFAR study, the three types of strategies that
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5 306 were derived from Phase I systematic theory- and evidence-based intervention design
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7 307 process will be set up (see Supplemental file 1 for a more detailed description):
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9 308 1) *A non-reflective decision assistance strategy*, that targets type 1 cognitive processes
10
11 309 through decision support systems that prompt and remind FPs about the recommended
12
13 310 practice in a simplified way, thereby reducing the cognitive burden. In short, pop-up
14
15 311 reminders and alerts with associated messages will be incorporated into the REGICOR
16
17 312 CVR calculator in OSABIDE (Osakidetza's EHR system) and within the prescription
18
19 313 pathway in PRESBIDE (the electronic drug prescribing component). The tools devised
20
21 314 include an interactive media-based algorithm stating the recommended practice for the
22
23 315 primary prevention of CVD in low-risk patients developed by an expert panel, and a
24
25 316 patient information sheet depicting and promoting evidence-based practice for
26
27 317 addressing cholesterol in the primary prevention of CVD in low-risk patients.
28
29

30 318 2) *A both reflective and non-reflective decision information strategy*, targeting both types
31
32 319 1 and 2 cognitive processes, based on the principle of knowledge dissemination and
33
34 320 consisting of a "Stopping Low-Value Prescribing" campaign run by the organization
35
36 321 (Osakidetza- Basque Health Service) that also eases access (decreasing the physical
37
38 322 effort required) to the evidence-based CPGs for the primary prevention of CVD in low-
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40 323 risk patients.
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43 324 3) *A reflective decision structure strategy*, that targets type 2 cognition through an
44
45 325 audit/feedback system reporting data with practice- and organizational-level
46
47 326 performance indicators regarding PIP of statins and healthy lifestyle promotion to prompt
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49 327 reflection about their own care practice, provided along with intention formation and goal-
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51 328 setting-focused messages.
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55 330 **Allocation of intervention units to compared groups**

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57 331 The DE-imFAR study is a cluster randomized implementation trial conducted under real
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59 332 world conditions of primary prevention of CVD in Primary Care (PC) where both clinical
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3 333 practices, i.e., inappropriate statin prescription and substandard promotion of healthy
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5 334 lifestyles, occur. The aforementioned de-implementation strategies will be cumulatively
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7 335 deployed in the routine conditions of health care service provision in Osakidetza to
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9 336 reduce the low-value practice and increase the recommended practice of PC healthcare
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11 337 professionals. Specifically, the decision support tools integrated in the EHR (non-
12
13 338 reflective decision assistance strategy) will be applied to all FPs from the 13 IHOs of
14
15 339 Osakidetza. Further, in addition to this first strategy, eligible FPs belonging to two IHOs
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17 340 (Barakaldo-Sestao and Ezkerraldea-Enkarterri-Cruces) will be randomly assigned to
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19 341 exposure to either the second (provision of decision information strategy) or second and
20
21 342 third (provision of decision information and reflective decision structure strategies). The
22
23 343 allocation sequence within these two groups will be generated using a specific restricted
24
25 344 randomization scheme by one member of the research team. The sequence will be
26
27 345 concealed at the coordinating center. In all cases, FPs will only be allocated to the study
28
29 346 groups after they have agreed to participate through an opt-out strategy. The data
30
31 347 analyst and the staff in charge of measurements will be blind to FP allocation to study
32
33 348 arms. Given that the audit/feedback strategy will involve regular reports sent privately to
34
35 349 individuals, participants in the experimental arms are also expected to be blind to group
36
37 350 allocation.
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43 352 **Outcome measures**

44
45 353 To evaluate the implementation of the de-implementation strategies compared in terms
46
47 354 of public health impact, we will use the following dimensions of the Reach, Effectiveness,
48
49 355 Adoption, Implementation, and Maintenance (RE-AIM) framework [33]:

51 356 *Reach*

52
53 357 Absolute number and percentage of patients in the target population who received the
54
55 358 recommended CVD primary prevention clinical intervention 12 months following FP's
56
57 359 exposure to the de-implementation strategies compared; and their representativeness.

59 360 *Effectiveness*

1
2
3 361 The study's main outcome will measure both the change in the incidence of the PIP of
4
5 362 statins and the change in the incidence of the provision of advice regarding healthy
6
7 363 lifestyles in patients of the target population eligible for CVD primary prevention, from
8
9 364 baseline to 12 months after exposure of target FPs to the de-implementation strategies.

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11 365

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13 366 As a secondary outcome, we will measure the change in the incidence of CVR
14
15 367 (REGICOR) documentation in the EHR, from baseline to 12 months after exposure of
16
17 368 FPs to the de-implementation strategies compared, in 40- to 74-year-old men and 45- to
18
19 369 74-year-old women without ischemic heart disease/CVD.

20
21
22 370 *Adoption*

23
24 371 Degree to which the recommended CVD primary prevention clinical intervention is
25
26 372 adopted by the FPs 12 months after exposure to the de-implementation strategies, that
27
28 373 will be measured by the percentage of FPs who reduce PIP of statins and/or increase
29
30 374 health promotion activities in the target population; and their representativeness.

31
32 375 *Implementation*

33
34 376 The fidelity of the delivery of each de-implementation strategy under study (i.e., the
35
36 377 degree to which they have been executed as planned) will be evaluated. To this end, a
37
38 378 complete record and subsequent description of the execution process, documentation of
39
40 379 adaptations made to the planned strategies, and process indicators of the delivery of and
41
42 380 exposure to the interventions (see Supplemental file 1 for specification of the exposure
43
44 381 to each strategy), will be used to assess the following components of fidelity: adherence,
45
46 382 dose, quality of delivery, professionals' responsiveness and program differentiation [34].

47
48 383 *Maintenance*

49
50 384 Change in the incidence of PIP of statins and provision of healthy lifestyle counseling in
51
52 385 eligible patients, 24 months after exposure of FPs to the de-implementation strategies
53
54 386 compared to levels observed at the 12-month assessment.

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58 388 *Other study covariates*

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3 389 In addition, and informed by the cross-sectional observational study performed in the
4
5 390 Phase I of the DE-imFAR study [10], potential confounders that may bias the estimated
6
7 391 effect of the de-implementation strategies on the change in PIP of statins will be
8
9 392 measured, both at a) health professional level: sociodemographic variables (age, sex),
10
11 393 baseline rate of PIP of statins; and b) patient level: socio-demographic variables (age,
12
13 394 sex, socioeconomic status) and clinical variables (baseline cholesterol level, presence
14
15 395 of hypertension, prescribed anti-hypertensive, tobacco use).
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18 396

397 **Feasibility Evaluation**

398 The professionals' perception of the feasibility of and satisfaction with the de-
399 implementation strategies to enhance the provision of the recommended CVD
400 prevention clinical practice will be assessed through key-informant semi-structured
401 individual interviews. Interviews will be carried out with at least 12 professionals until
402 data saturation is reached: at least six (three from each randomized arm) who reduced
403 their PIP and at least six who did not, as informed by the quantitative results. The
404 interview script will contain open-ended questions that will focus on the perceived value
405 of the de-implementation strategies and recommendations for their optimization.
406

407 Exposed patients' perception and experience regarding the quality of CVD prevention
408 care received will also be assessed through key-informant semi-structured interviews.
409 The interviews will be carried out with at least ten patients until data saturation is reached:
410 at least five with patients who have been clinically managed according to recommended
411 practice and five who have not. The interview script will contain open-ended questions
412 that will focus on the perceived CVD primary prevention care received.
413

414 Both professional and patient interviews will be conducted by two researchers with
415 experience in qualitative research methods, as well as knowledge of the clinical field and
416 the project. The interviews will be audio-recorded, with prior informed consent, and

1
2
3 417 transcribed verbatim. Regarding the analysis of the qualitative study, the responses will
4
5 418 be extracted from the transcript of the interviews. Several members of the research team
6
7 419 will participate in the analysis, promoting the exchange of perspectives and consensus,
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9 420 with the aim of triangulating the analysis. A deductive and an inductive perspective will
10
11 421 be combined. For the deductive perspective, the discourse of each professional and
12
13 422 patient interviewed will be associated with constructs derived from the behavior changes
14
15 423 theories (TDF, BCW, etc.) [3,11-13]. The inductive analysis will be based on the
16
17 424 postulates of grounded theory [35]. Researchers will use coding techniques, or line-by-
18
19 425 line analysis, looking for words and phrases that identify explanatory concepts.
20
21 426 Subsequently, thematic connections between the basic theoretical concepts and the
22
23 427 data will be developed.
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429 **Analysis**

430 Frequencies and proportions along with the corresponding 95% confidence intervals
431 (CIs) will be used to describe the prevalence and cumulative incidence of PIP of statins
432 and healthy lifestyle counseling in the primary prevention of CVD by FPs. The primary
433 effectiveness outcomes will be the changes in the cumulative incidence of PIP of statins
434 and healthy lifestyle counseling in patients from the target population (individuals with no
435 history of statin use, LDL cholesterol levels between 70 and 189 mg/dL and/or TC
436 between 200 and 289 mg/dL without past or current ischemic heart disease/CVD, and
437 an estimated CVR REGICOR <7.5% attending at least one clinical appointment with their
438 FP in the study period), from baseline to 12 months after exposure of FPs to the de-
439 implementation strategies. Therefore, to evaluate the impact of the three de-
440 implementation strategies, we will estimate the relative reduction in the risk of receiving
441 PIP of statins in patients from the target population assigned to the experimental
442 strategies over that in patients from the non-randomized group (non-reflective decision
443 assistance strategy group). With respect to this group and seeking to increase
444 comparability and reduce potential bias, in addition to evaluating the change in PIP of

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2
3 445 statins incidence in all eligible FPs, we will select two matched FP from this non-
4
5 446 randomized group for each of the randomized FPs taking into account both FP-related
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7 447 characteristics (e.g., baseline rate of PIP of statins, etc.) and characteristics of the
8
9 448 population of patients assigned to the FP (e.g., average socioeconomic status, etc.).
10
11 449 Change in PIP of statins incidence rates from baseline to those observed 12 and 24
12
13 450 months after FPs' exposure to the de-implementation strategies and the relative risk
14
15 451 reduction will be estimated with the corresponding 95% CIs. To adjust for potential
16
17 452 confounding factors, stratified statistical analyses and logistic models will be used. These
18
19 453 models will be extended to generalized mixed effects models to take into account the
20
21 454 hierarchical structure of data (patients nested in FPs and FPs in primary care teams),
22
23 455 with fixed effects (comparison group, effect of time on outcome indicators, and time-
24
25 456 group interactions) and random effects on the intercept and the time slope (for each
26
27 457 patient, FP, center, etc.). These models will be adjusted for potential confounders,
28
29 458 following a backward strategy, guided by the stratified analyses. A similar approach will
30
31 459 be taken to analyze the secondary outcomes. The analyses will be carried out with SAS
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33 460 (v. 9.2, SAS Institute, Cary, NC, USA), and R (R Development Core Team, 2014).
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39 462 Calculation of the required sample size for the most unfavorable scenario, this being the
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41 463 comparison between the two randomized de-implementation strategies, was based on:
42
43 464 i) a baseline incidence of statin PIP of 7.4% estimated among the patients of the target
44
45 465 population seen in 2021 by FPs with an incidence of PIP > 0% with a minimum cluster
46
47 466 size $n \geq 10$ patients, ii) an intra-class correlation coefficient of 0.01, iii) an average cluster
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49 467 size of 39 patients with a coefficient of variation of 0.63, iv) $\alpha = 0.05$ and statistical power
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51 468 of 80%, and v) hypothetical decreases in annual PIP rates of 20% in the decision
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53 469 information strategy group and 50% in the decision structure strategy group. With these
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55 470 assumptions, it was estimated that at least 58 FPs were required for each experimental
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57 471 arm.
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473 **Management, quality, and safety in data processing**

474 This study will be carried out in accordance with the international standards for
475 conducting epidemiological studies, included in the International Guidelines for Ethical
476 Review of Epidemiological Studies [36]. This is a prospective intervention study focused
477 mainly on the collection of information from data recorded by health professionals in the
478 Osakidetza EHR (OSABIDE) under routine clinical practice conditions. The process
479 indicators related to the clinical practice of the professionals (prescription of statins and
480 record in the EHR of provision of personalized healthy lifestyles advice concerning the
481 need to increase physical activity, eat a healthy diet and smoking cessation), patients'
482 sociodemographic and clinical characteristics (age, sex, CVR, active health problems
483 recorded in EHR, socioeconomic status, etc.) and clinical outcomes will be extracted
484 from OSABIDE through the corporate Oracle Business Intelligence platform. In
485 particular, for the provision of healthy lifestyles advice, OSABIDE includes a specific
486 electronic form to check that each single piece of advice (diet, exercise, tobacco quitting)
487 has/has not been provided. The Primary Care Research Unit of Bizkaia is formally
488 authorized to extract and use data from the EHR for research purposes by the Healthcare
489 Directorate of Osakidetza. On the other hand, it will be necessary to inform participants
490 about the study and obtain their written informed consent concerning the information
491 collected directly from the professionals and patients under study through the key-
492 informant semi-structured interviews (Supplemental File 2 and 3). All the information
493 regarding the study subjects, either extracted from EHRs or collected from the
494 participants expressly for this research, will be protected and treated confidentially for all
495 purposes, in accordance with the provisions of the Spanish Organic Law 3/2018, of 5
496 December, on Personal Data Protection and digital rights guarantee (LOPD-GDD) and
497 the provisions of Regulation (EU) 2016/679 of the European Parliament and of the
498 Council of 27 April 2016, on the protection of natural persons with regard to the
499 processing of personal data and on the free movement of such data (General Data
500 Protection Regulation, RGPD). Specifically, all data will be documented anonymously

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3 501 and de-identified, linked to a unique key that is meaningless outside the context of the
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5 502 system. The final resulting database will be exported to a formatted plain text file that will
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7 503 then be compressed and encrypted using a secure algorithm and subsequently be
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9 504 processed and included in a robust and secure database server.
10

11 505

12 506 **Patient and public involvement**

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14
15 507 Patients were involved in the DE-imFAR Phase I project as one of the main stakeholders
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17 508 (health professionals, patients, and researchers) in the formative process conducted to
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19 509 map and design de-implementation strategies to reduce PIP, which will be evaluated in
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21 510 the DE-imFAR Phase II project. Specifically, during the Phase I project, a focus group
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23 511 with six patients was conducted to ascertain patients' experience regarding the clinical
24
25 512 practice of statin prescription and triangulate physicians discourse [14].
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29 513 During the Phase II project, semi-structured interviews will be conducted with patients to
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31 514 assess their perception and experience of the clinical care received as a result of their
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33 515 healthcare professionals' exposure to the different de-implementation strategies. These
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35 516 interviews will help to better understand from the perspective of the study participants
36
37 517 the reasons why the strategies work (or do not work), to explain the variations in the
38
39 518 outcomes achieved and to identify the key components and those that need to be
40
41 519 optimized as well as triangulating the analysis.
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46 521 **ETHICS AND DISSEMINATION**

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49 522 The research protocol (version 1; 170221) has been approved by the Basque Country
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51 523 Clinical Research Ethics Committee (Reference: EOM2022018, approved on 30 March
52
53 524 2022) and was registered in the U.S. NLM ClinicalTrials.gov database (ClinicalTrials.gov
54
55 525 Identifier NCT04022850, Registered 17 July 2019; Last update 31 January 2024).The
56
57 526 Primary Care Research Unit of Bizkaia is explicitly authorized by the Healthcare
58
59 527 Directorate of Osakidetza - Basque Health Service to extract and use data from EHRs
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3 528 for research purposes. Since data supporting the present study will mostly concern
4
5 529 routine data retrieved from the EHR of the Basque Health Service-Osakidetza, it will be
6
7 530 only shared on justified request to the study guarantors. The results of this study will be
8
9 531 disseminated via publication in scientific peer-reviewed journals.
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11 532

13 533 **LIST OF ABBREVIATIONS**

14
15
16 534 EHR: Electronic health record

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18 535 BCW: Behavior Change Wheel

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20 536 CI: Confidence interval

21
22 537 CVD: Cardiovascular disease

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24 538 CVR: Cardiovascular risk

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26 539 CPG: Clinical practice guideline

27
28 540 FP: Family physician

29
30 541 IHO: Integrated Healthcare Organization

31
32 542 LDL: Low-density lipoprotein

33
34 543 PIP: Potentially inappropriate prescribing

35
36 544 PC: Primary care

37
38 545 RE-AIM: Reach, Effectiveness, Adoption, Implementation, and Maintenance

39
40 546 TC: Total cholesterol

41
42 547 TDF: Theoretical Domains Framework

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45 548

47 549 **FULL REFERENCES**

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689 **AUTHORS' CONTRIBUTIONS**

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3 690 AS, JIP, and GG conceived the idea and are the study guarantors. They are primarily
4
5 691 responsible for the study design and planning, obtained funding, will be responsible for
6
7 692 project coordination and supervision, analysis and interpretation of results, and were
8
9 693 responsible for manuscript preparation. RSR, IL, RSV, JAQ, RR, AE, CM, MMC, MM,
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11 694 CGR, RS, MOL, SC, NMI, ML, MGST, and AGA are co-investigators of the projects and
12
13 695 collaborated in the study design and/or manuscript preparation; and they will be
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15 696 responsible for study coordination and interpretation of results. AS, JIP, and AGA will be
16
17 697 responsible for the analysis of results. All authors read and approved the final version of
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19 698 the manuscript.
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708 The funding bodies have had no role in the design of the study, collection, analysis, or
709 interpretation of data or the writing of the manuscript.
710

711 **COMPETING INTERESTS STATEMENT**

712 The authors declare that they have no competing interests.
713

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9 720 Health Organization.

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13 **722 WORD COUNT**

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15 723 4353 words excluding title page, abstract, strengths and limitations of this study, list of
16
17 724 abbreviations, full references, authors' contributions, funding statement, competing
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19 725 interests statement and acknowledgements.
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726 **FIGURES**

727 **Figure 1. Study design diagram. (PDF format)**

728 Note: FP: Family Physician; IHO: Integrated Healthcare Organization; R: Randomization.

For peer review only

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3 729 **SUPPLEMENTAL FILES**
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5 730 **Supplemental File 1 [DE-imFAR de-implementation strategies] (PDF format)**
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732 **Supplemental File 2 [DE-imFAR Phase II - Informed Consent Form for Family**
733 **Physicians (Spanish)] (PDF format)**

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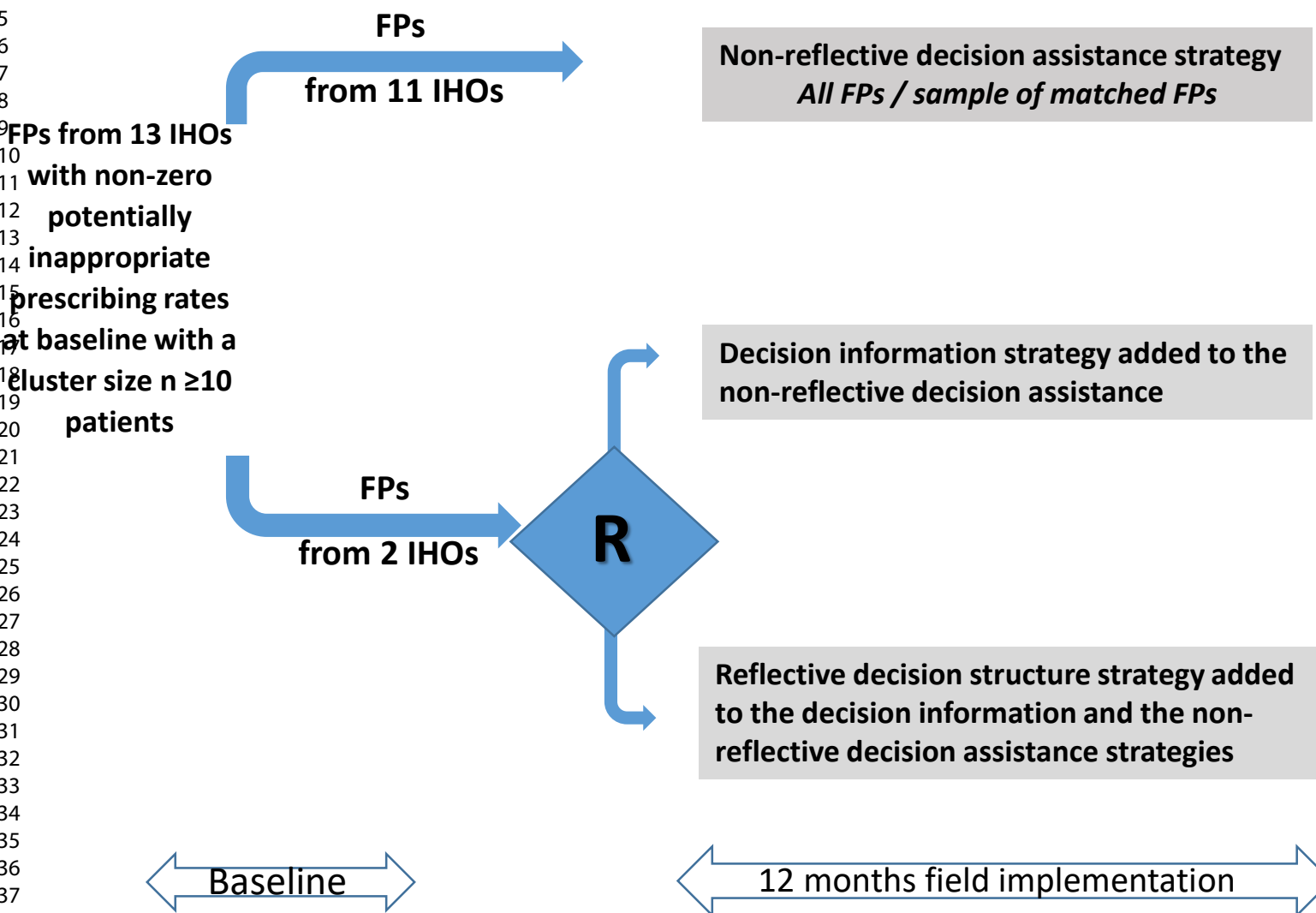
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3 735 **Supplemental File 3 [DE-imFAR Phase II - Informed Consent Form for Patients**
4 **(Spanish)] (PDF format)**
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Experimental implementation trial with an additional control group

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Change in the incidence of potentially inappropriate prescriptions and provision of lifestyle advice from baseline to 12 months after exposure of physicians to the compared strategies, in 40- to 74-year-old men and 45- to 74-year-old women with no history of statin use, with LDL-cholesterol levels between 70 and 189 mg/dl and/or Total Cholesterol between 200 and 289 mg/dl but without ischemic heart/cardiovascular disease and with an estimated cardiovascular risk <7.5% attending during the field-work period

Outcome

The DE-imFAR de-implementation strategies

1. Strategy - *Non-reflective decision assistance strategy*

Support for clinical decision-making on the primary prevention of cardiovascular disease (CVD) in low cardiovascular risk (CVR) patients integrated into the electronic health record (EHR) of the Basque Health Service (Osakidetza), based on pop-up reminders and alerts, together with an interactive media-based algorithm stating the recommended practice and a patient information sheet.

1.1. Target audience

This strategy targets all family physicians (FPs) from all 13 Integrated Healthcare Organizations (IHOs) of the Basque Health Service (Osakidetza), both in primary and specialist or hospital care.

1.2. Active components (actions) of the intervention

- “Lighthouse” guiding alert in the REGICOR CVR calculator. Reminders of recommended clinical practice in the primary prevention of CVD that pop-up in the REGICOR CVR calculator when the CVR is estimated in patients aged between 35 and 74 years old. The alert varies depending on the CVR score (<10% or ≥10%).

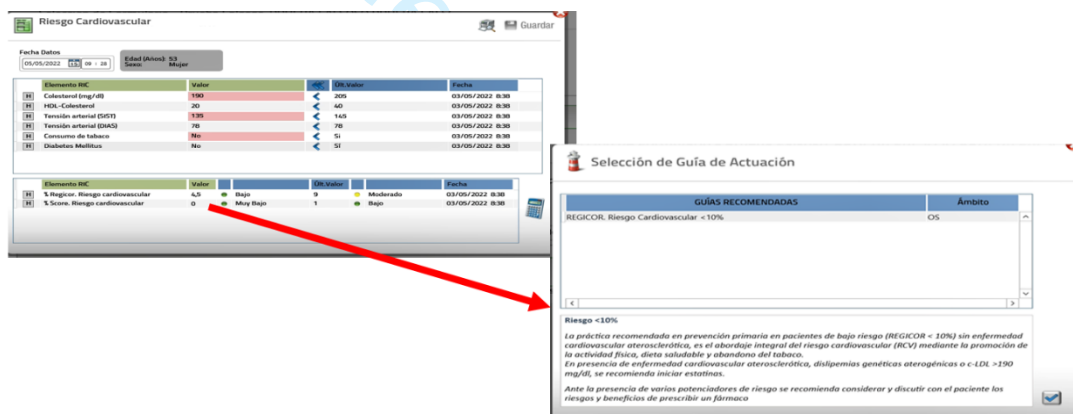


Figure 1. Pop-up reminder (“Lighthouse” guiding alert) in the REGICOR cardiovascular risk calculator when estimated cardiovascular risk score is <10%.

- Alerts in PRESBIDE. Pop-up reminders that appear when the PRESBIDE software is used to prescribe statins. There are three types of alerts depending on the patient’s age group (<35, 35-74, and ≥75 years old). Further, links are provided to a decision-making algorithm and a patient information sheet (i-botika).
- Decision-making algorithm: “Management of cholesterol as a risk factor in primary prevention of cardiovascular disease”. Clinical decision tree presenting potential courses of action based on clinical practice guidelines (CPGs), specifically for reducing cholesterol for the primary prevention of CVD in patients of different age groups and levels of CVR. Interactive decision-making support tool, developed by researchers collaborating in the DE-imFAR project, that also includes links for downloading two further documents: one providing information on CVD risk factors and the other on the 5As “Ask, Assess, Advise, Assist, Arrange” clinical intervention, recommended for promoting healthy lifestyles.

- Patient information sheet on cholesterol levels (i-botika: “Cholesterol levels are not the only thing”, developed in the framework of this project, providing information on high cholesterol levels and their role together with other risk factors associated with CVD)

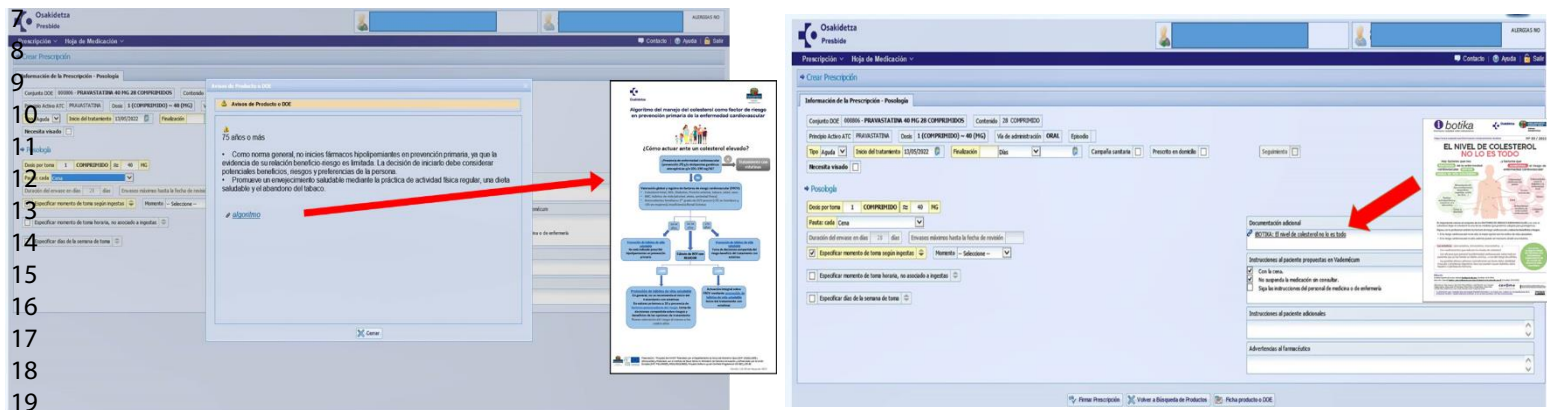


Figure 2. a). Pop-up reminder in the PRESBIDE software with recommendations on the prescribing of statins in people ≥ 75 years old that includes a link to the “Management of cholesterol as a risk factor in primary prevention of cardiovascular disease” algorithm, b) PRESBIDE form for prescribing statins, with a link to the patient information sheet (i-botika).

1.3. Objectives: *Determinant - What needs to change*

Pop-up alerts, reminders, and an algorithm

Cognitive and interpersonal skills:

- ✓ Enhance skills to enable appropriate prescribing of statins based on clinical practice recommendations

Attention, memory, and decision-making processes:

- ✓ Promote recall of recommended clinical practice in the primary prevention of CVD, reducing the impact of therapeutic inertia

Context and resources:

- ✓ Develop support systems in the EHR as reminders of and to promote the practices recommended in CPGs for the primary prevention of CVD (avoiding statins and encouraging healthy lifestyles)
- ✓ Restrict or impede inappropriate prescribing of statins due to clinical prescribing behavior driven by simplicity and speed

Emotion/Reinforcement:

- ✓ Reduce the likelihood of inappropriate prescribing due to habit, routine, or inertia (to “treat” cholesterol), through the experiencing of negative emotions when going against the recommended practice and this is made evident by alerts

Patient information sheet

Social influence (patient involvement):

- ✓ Increase patient awareness of the problems associated with the inappropriate prescribing of statins: risks vs benefits
- ✓ Increase patient knowledge of the criteria and courses of action recommended in CPGs (concerning cholesterol, CVD, and CVR)

1.4. Choice architecture techniques

A. Decision Information

A1. Translate information: change the format or presentation of information but not the content.

Reframe: present the (same) information in several ways, e.g., Presenting the contents of CPGs in several different ways (i.e., text within alerts, in the form of an algorithm, etc.).

Simplify: reduce the burden of cognitive effort necessary to process the information available and increase its usefulness in the decision-making process, e.g., algorithm.

A2. Make information visible: make necessary information readily accessible.

Make external information visible: make decision-relevant information visible, e.g., text within alerts recalling the CPGs.

B. Decision structure

B1. Change choice defaults

Prompted choice: avoid the status quo bias or default effects because of inertia or assumed recommendations, e.g., pop-up alerts.

B2. Change option-related effort: change physical effort.

Increase physical effort: e.g., pop-up alerts.

C. Decision assistance

C1. Provide reminders: provide positive reminders that heighten the salience of a desired option and/or diminish the salience of an undesired option, e.g., Pop-up alerts with the recommendation to not prescribe statins.

1.5. Exposure

- “Lighthouse” guiding alert in the REGICOR CVR calculator: by clicking to “save” the result after estimating CVR
- Alerts in PRESBIDE: by starting to prescribe statins or clicking on the links to the algorithm or the patient information sheet

2. Strategy - Reflective/non-reflective decision information strategy

Corporate campaign entitled “Stopping low-value prescribing” (in Spanish: “*Abandono de prescripciones farmacológicas de escaso valor*”), promoted through a knowledge dissemination strategy based on circulars and notifications (e.g., mass mailing and internal newsletters) concerning content, informative material and documents on recommended clinical practice and improving the appropriateness and/or optimization in prescribing drug treatments, including that of statins for the primary prevention of CVD, made available to FPs on the corporate intranets of the Ezkerraldea-Enkarterri-Cruces (EEC) and Barakaldo-Sestao (BS) IHOs, part of the Basque Health Service (Osakidetza).

2.1. Target audience

This strategy targets all FPs from the EEC and BS IHOs, who will also be exposed to the first strategy, namely, non-reflective decision assistance.

2.2. Active components (actions) of the intervention

- Adherence to and implementation of best practice pages on the EEC and BS IHO intranets which have dedicated sections focused on improving the appropriateness of the use of statins providing easy access to the CPGs and recommended practice for the primary prevention of CVD.



Figure 3. Main page of the adherence to and implementation of best practice (“*Adecuación e Implementación de Buenas Prácticas*”) section on the Ezkerraldea-Enkarterri-Cruces Integrated Healthcare Organization intranet and main page of the dedicated “Stopping inappropriate prescribing of statins for the primary prevention of cardiovascular disease” section. Equivalent pages were also created on the Barakaldo-Sestao Integrated Healthcare Organization intranet.

- Corporate dissemination campaign: activities aimed at attracting FPs to the pages created on the EEC and BS IHO intranets, in order that they access the information and documents available
 - News story on the launch of the campaign with links to the pages on the corporate intranets, e.g.,

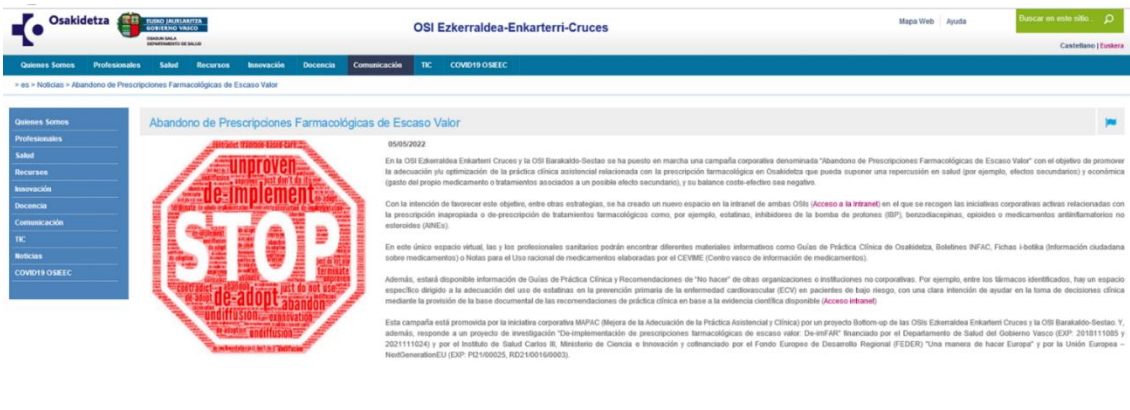


Figure 4. News story published on the Ezkerraldea-Enkarterri-Cruces Integrated Healthcare Organization intranet to announce the launch of the corporate “Stopping low-value prescribing” campaign and the development of pages on its intranet and that of the Barakaldo-Sestao Integrated Healthcare Organization, on May 5, 2022. The story was also published on the Barakaldo-Sestao Integrated Healthcare Organization intranet.

- **Monthly newsletter:** reporting of the launch of the campaign in the monthly newsletter circulated by the BS IHO to all its employees
- **Mass mailing** on the launch of the campaign with links to the pages on the corporate intranets
- **Revitalization of the corporate campaign:** periodic publication of news stories on the EEC and BS IHO intranets with content related to the campaign informing FPs of the updating of content/informative materials (for example, any changes in the recommendations in CPGs and INFAC [pharmacotherapy information] newsletters) on the dedicated pages on the intranets of both IHOs, aimed at improving the appropriateness of the use of statins in primary prevention of CVD, including links to these pages.
- **Justification email** from the Healthcare Management of the Basque Health Service, telling all FPs about the initiatives being put in place to improve the approach to the prevention of CVD, improving the appropriateness of statin prescribing, and encouraging the provision of healthy lifestyle advice, among other components.

2.3. Objectives: Determinant - *What needs to change*

Knowledge:

- ✓ Increase awareness of the problem of the inappropriate prescribing of statins
- ✓ Increase knowledge of the CPGs on the primary prevention of CVD, in particular, the appropriate or recommended care as a function of the estimated CVR
- ✓ Provide evidence-based standardized and up-to-date clinical guidelines

Behavior regulation:

- ✓ Encourage reflection on practice/performance in relation to inappropriate prescribing of statins in the primary prevention of CVD

Beliefs about capabilities:

- ✓ Strengthen the belief that the prescribing of statins is not as straightforward and safe as might be thought
- ✓ Strengthen the belief that statin treatment is not easy for patients (dosage)

Beliefs about consequences:

- ✓ Strengthen the belief that not prescribing statins for the primary prevention of CVD is not the same as “not treating”.
- ✓ Strengthen the belief that statins are not more effective in reducing cardiovascular events than healthy lifestyle promotion in the primary prevention of CVD
- ✓ Strengthen the belief that statins, in the primary prevention of CVD, may have adverse effects and are not risk-free.

Professional/social role and identity:

- ✓ Foster the belief that appropriate primary prevention of CVD is considered important at the organizational level and among peers.
- ✓ Strengthen understanding that the role of FPs goes beyond that of prescribing drugs.

Social influence:

- ✓ Increase awareness of the organizational goals for reducing inappropriate prescribing of statins in the primary prevention of CVD.
- ✓ Increase patient awareness of the problems associated with the inappropriate prescribing of statins: risks vs benefits
- ✓ Increase patient knowledge of the criteria and recommended courses of action (concerning cholesterol, CVD, and CVR)

Emotion/reinforcement:

- ✓ Reduce the likelihood of inappropriate prescribing due to habit, routine, or inertia (to “treat” cholesterol), through the experiencing of negative emotions when going against the recommended clinical practice and this is made evident by alerts.

Cognitive and interpersonal skills:

- ✓ Enhance skills to enable the appropriate prescribing of statins based on CPGs.

2.4. Choice architecture techniques**A. Decision Information**

A1. Translate Information: change the format or presentation of information but not the content.

Reframe: present the (same) information in several ways, e.g., clinical guidelines, algorithm, patient information leaflet.

Simplify: reduce the burden of cognitive effort necessary to process the information available and increase its usefulness in the decision-making process, e.g., algorithm.

A2. Make information visible: make necessary information readily accessible.

Make external information visible: make decision-relevant information visible, e.g., Links about inappropriate statin prescription in the Basque Health Service (Osakidetza), adverse effects of statins and cholesterol treatment, and promotion of the campaign through emails and news.

A3. Provide social reference point: influence decision-making through other’s behavior.

Refer to descriptive norm: depict the observable behavior of other people to impact on the decision-making process, e.g., links about inappropriate statin prescription in the Basque Health Service (Osakidetza).

Refer to opinion leader: use them as information disseminators to improve the impact of the campaign, e.g., Setting of goals in an email sent by an opinion leader, using the source as much as the content of the message to improve the impact of the campaign.

B. Decision structure

B2. Change option-related effort: modify the physical or financial effort involved in the decision-making process.

Change physical effort, e.g., decreasing physical effort by making all theme-related information accessible on the same website and including links to the website in the text of emails and news stories.

C. Decision assistance

C1. Provide reminders: provide positive reminders that heighten the salience of a desired option and/or diminish the salience of an undesired option, e.g., links to clinical guidelines with recommended practice about CVD primary prevention, and information about adverse effects of statins.

2.5. Exposure

- By accessing the pages of the EEC and BS IHO corporate intranet and clicking on the links to the CPGs, INFAC newsletters, i-botika patient information sheets, recommendations, etc. available in the dedicated “Stopping inappropriate prescribing of statins for the primary prevention of cardiovascular disease” section
- By accessing the news section on the dedicated pages on the intranets of EEC and BS IHOs

3. Strategy - Reflective decision structure strategy

Sending of regular personalized *Audit & Feedback (A&F)* reports with practice- and organizational-level performance indicators of the FPs regarding inappropriate prescribing of statins and healthy lifestyle promotion in the primary prevention of CVD in low-risk patients in the Basque Health Service

3.1. Target audience

This strategy targets a randomly selected set of FPs from the EEC and BS IHOs, who will also be exposed to the previously described interventions, namely, *non-reflective decision assistance and decision information*.

3.2. Active components (actions) of the intervention

- Informative email concerning the sending of A&F reports, including the possibility to opt out: email with information for primary care FPs of the EEC and BS IHOs on the sending of regular personalized A&F reports, in the framework of the corporate campaign, with the goal of encouraging adherence to recommendations and stopping inappropriate prescribing of statins
- A&F reports mailing: periodic A&F reports with indicators describing global performance across the Basque Health Service: a) rate of new potentially inappropriate prescribing of statins to people without CVD and with REGICOR CVR scores <7.5% and practice in the promotion of healthy habits in these patients; b) rate of documentation of CVR (in the 2 years before the prescription date) in all 40- to 75-year-olds with no clinical history of CVR who are newly prescribed statins. Future A&F reports are expected to contain a link to a short voluntary exercise on goal setting for improving the appropriateness of statin prescribing for the primary prevention of CVD

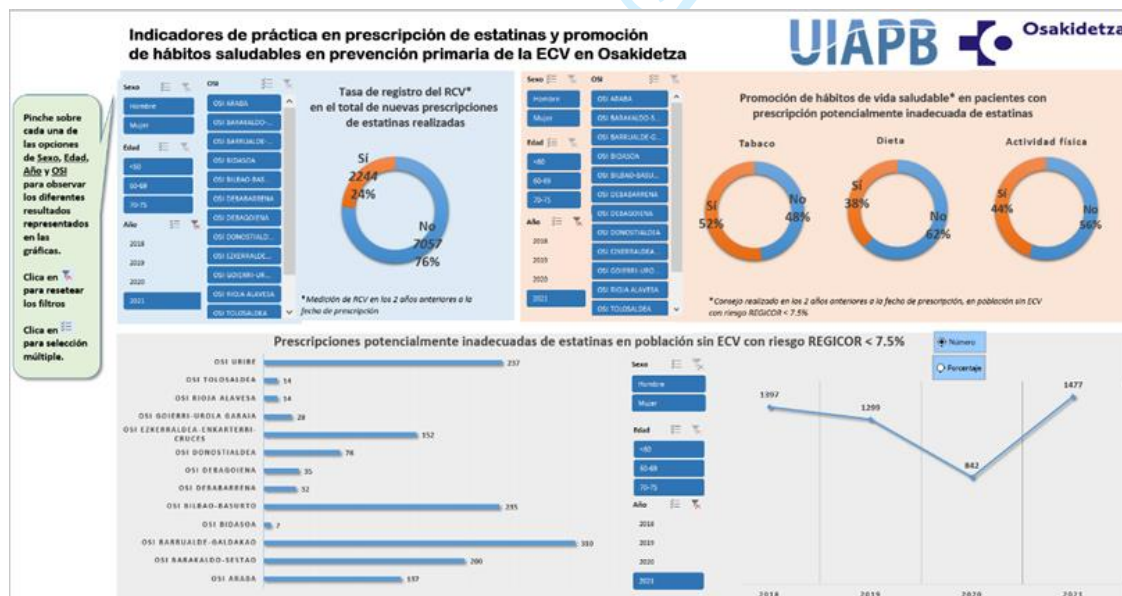


Figure 5. Draft of the Audit & Feedback report with practice- and organizational-level performance indicators of the family physicians regarding inappropriate prescribing of statins and healthy lifestyle promotion in the primary prevention of cardiovascular disease in low-risk patients in the Basque Health Service

3.3. Objectives: Determinant - What needs to change

Knowledge:

- ✓ Increase awareness of the problem of the inappropriate prescribing of statins

Behavior regulation:

- ✓ Make data available on inappropriate prescribing of statins for the primary prevention of CVD
- ✓ Provide tools for the setting of clear specific goals, at personal and organizational levels, regarding the reduction of inappropriate prescribing of statins for the primary prevention of CVD

Active reflection on personal practice:

- ✓ Encourage further reflection on practice/performance in relation to inappropriate prescribing of statins for the primary prevention of CVD

Intentions:

- ✓ Reduce the intention to prescribe statins inappropriately and increase the intention to promote healthy lifestyles for the primary prevention of CVD

Goals:

- ✓ Encourage commitment to practice in the primary prevention of CVD that is in accordance with recommendations
- ✓ Increase the motivation to promote healthy lifestyles in the primary prevention of CVD

Beliefs about capabilities:

- ✓ Strengthen self-efficacy and enhance the skills required for promoting healthy lifestyles

Emotion:

- ✓ Strengthen self-confidence about not prescribing statins for the primary prevention of CVD
- ✓ Foster belief in the safety of and trust in the courses of action recommended in the guidelines
- ✓ Experience a negative emotion after inappropriate prescribing

Professional/social role and identity:

- ✓ Foster the belief that appropriate primary prevention of CVD is considered important at the organizational level and among peers
- ✓ Strengthen understanding that the role of FPs goes beyond prescribing drugs

Reinforcement:

- ✓ Generate positive/negative reinforcement related to good/poor performance in the primary prevention of CVD.

3.4. Choice architecture techniques

A. Decision Information

A1. Translate Information: change the format or presentation of information but not the content.

Simplify: reduce the burden of cognitive effort necessary to process the information available and increase its usefulness in the decision-making process, e.g., presenting prescription rate data in a simple, user-friendly way, namely, on a dashboard.

A2. Make information visible: make necessary information readily accessible.

Make own behavior visible: feedback.

Make external information visible: make decision-relevant information visible, e.g., showing the prescription rates of other FPs and other IHOs.

A3. Provide social reference point: influence decision-making through the behavior of others.

Refer to descriptive norm: depict the observable behavior of other people to impact on the decision-making process, e.g., showing other FPs' prescribing behavior.

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4 **B. Decision structure**

5 **B2. Change opinion-related effort:** modify the physical or financial effort involved in the
6 decision-making process.

7 **Decrease physical effort:** collect all prescribing data in one file, e.g., dashboard.
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10 **C. Decision assistance**

11 **C2. Facilitate commitment:** overcome constrained self-control and bridge the intention-
12 behavior gap.

13 **Support self-commitment:** arrange with the aim of helping fulfill a plan, e.g., self-commitment
14 questionnaire
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17 **3.5. Exposure**

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Annex I. GLOSSARY OF TERMS

1. De-implementation: De-implementation is defined as the process of reducing or abandoning the use of guidelines practices, interventions or policies that are found to be ineffective, are not proven to be effective, do not have adequate scientific support, are less effective or less cost-effective than an alternative one, are potentially harmful to patients, or that represent low-value care.

2. Implementation: Implementation (commonly defined as “to do”), in the context of Implementation Science refers to the actively designed process of putting into practice or integrating evidence-based interventions (e.g., practice, program, policy,...) within a specific real-world setting.

3. Theoretical Domains Framework (TDF): The Theoretical Domains Framework (TDF) is an integrative framework developed from a synthesis of psychological theories as a vehicle to help apply theoretical approaches to interventions aimed at behavior change. The TDF comprises of 14 domains and 84 constructs that allows synthesis of a multitude of coherent behavior change theories into a single framework that allows assessment and explanation of behavioral problems and associated barriers and enablers, and inform the design of appropriately targeted interventions.

References:

1. Michie S, Johnston M, Abraham C, et al. Making psychological theory useful for implementing evidence based practice: a consensus approach. *Qual Saf Health Care*. 2005;14(1):26-33. doi:10.1136/qshc.2004.011155.
2. Cane J, O'Connor D, Michie S. Validation of the theoretical domains framework for use in behaviour change and implementation research. *Implement Sci*. 2012;7:37. doi:10.1186/1748-5908-7-37.
3. Atkins L, Francis J, Islam R, et al. A guide to using the Theoretical Domains Framework of behaviour change to investigate implementation problems. *Implement Sci*. 2017;12(1):77. doi: 10.1186/s13012-017-0605-9.

4. Behavior Change Wheel (BCW): The Behavior Change Wheel (BCW) is a theory- and evidence-based tool that provides a process for designing or refining behavior change interventions and policies. Its purpose is to promote a systematic and comprehensive analysis of behavior in its context to guide change. It can be used to identify the interventions and policies likely to be effective in changing behavior.

Reference:

1. Michie S, van Stralen MM, West R. The behaviour change wheel: a new method for characterising and designing behaviour change interventions. *Implement Sci*. 2011 23;6:42. Published 2011 Apr 23. doi:10.1186/1748-5908-6-42.

5. Statin: Statins, also known as HMG-CoA reductase inhibitors, are a class of lipid-lowering medications that are used to lower blood low-density lipoprotein (LDL) cholesterol levels.

6. Non-reflective: Non-reflective processes, such as habits and routines, are defined as those factors that bypass conscious deliberation and so generate actions fast, effortlessly, automatically and with little deliberation and awareness.

7. Reflective: Reflective processes involves conscious deliberation over situational demands, available options and/or outcome expectancies; and therefore generate slow and effortful actions or behaviors via reasoned intentions.

8. Decision assistance strategy. Decision information strategy. Decision structure strategy

According to the taxonomy suggested by Münscher et al., there are three broad categories of choice architecture intervention techniques: decision information, decision structure, and decision assistance (Münscher et al., 2016).

- i) **Decision information** interventions aim to facilitate access to decision-relevant information without altering the options themselves by increasing its availability, comprehensibility, and/or personal relevance to the decision maker. There are several ways of achieving it, such as (re)arranging existing information or changing its presentation/format, providing social reference point, etc.
- ii) **Decision structure** interventions target the way in which the choice options are organized and structured through the arrangement of choice alternatives and the format of decision making, which includes setting default options, rearranging their composition, and changing option-related efforts or consequences of selecting it.
- iii) **Decision assistance** interventions aim to bridge the intention–behavior gap by reinforcing self-regulation by providing decision makers with further assistance to help them follow through with their intentions. To do so, examples of decision assistance interventions techniques include provision of reminders of the desirable behavioral option as well as facilitating deliberate commitment to beneficial actions.

References:

1. Münscher R, Vetter M, Scheuerle T. A review and taxonomy of choice architecture techniques. *J Behav Decis Mak.* 2016;29(5):511-24. doi.org/10.1002/bdm.1897.
2. Mertens S, Herberz M, Hahnel UJJ, Brosch T. The effectiveness of nudging: A meta-analysis of choice architecture interventions across behavioral domains. *Proc Natl Acad Sci USA.* 2022;119(1):e2107346118. doi: 10.1073/pnas.2107346118. Erratum in: *Proc Natl Acad Sci USA.* 2022;119(19):e2204059119.

9. Audit & feedback (A&F): Audit and feedback is a strategy that aims to encourage individuals to change their practice and improve their performance. In the audit process, an individual's professional practice or performance is assessed and monitored based on specific, pre-defined criteria or standards. Then, the results of the comparison is fed back to the individual in a structured manner.



Hoja de Información al Profesional de la salud y Consentimiento Informado

Título: Efectividad de estrategias de de-implementación para favorecer el abandono de prescripciones farmacológicas de bajo valor en prevención primaria de la ECV: proyecto De-imFAR Fase II

Investigador Principal: Álvaro Sánchez Pérez

Servicio/Centro: Subdirección para la coordinación de atención primaria/Unidad de investigación atención primaria-IIS Biocruces Bizkaia

Entidad financiadora: Instituto de salud Carlos III

Apreciado Sr./a,

Osakidetza-Servicio Vasco de Salud, con el propósito de mejorar la calidad en la prestación de servicios de salud hacia la ciudadanía, le invita a participar en el estudio “Efectividad de estrategias de de-implementación para favorecer el abandono de prescripciones farmacológicas de bajo valor en prevención primaria de la ECV: proyecto De-imFAR Fase II”.

Antes de decidir si desea participar, es importante que entienda los objetivos, la importancia de su participación y en qué consistirá, además de qué uso se dará a los datos recogidos y los posibles beneficios y riesgos.

Léalo atentamente y consulte cualquier duda con los miembros del equipo de investigación.



1. OBJETO DEL GRUPO DE DISCUSIÓN

El objetivo de los grupos de discusión del Proyecto De-ImFAR es generar conocimiento –a través de las percepciones de los/las profesionales de medicina de atención primaria- sobre la práctica clínica en prevención primaria de eventos cardiovasculares en pacientes de bajo riesgo. A través de una serie de preguntas abiertas se analizarán diferentes aspectos relacionados con el manejo del riesgo cardiovascular en estos pacientes, tratando de conocer la opinión de todos los integrantes del grupo sobre este tema.

No existen respuestas buenas o malas. Cualquier integrante del grupo está invitado a expresar libremente su opinión y a respetar la de los otros integrantes, aunque sea diferente de la suya.

2. PARTICIPACIÓN Y RETIRADA DEL ESTUDIO

Este estudio está aprobado por el Comité de Ética de la Investigación con Medicamentos de Euskadi (CEIm-E). Su participación en el mismo es voluntaria y en cualquier momento puede decidir abandonarlo, aunque haya proporcionado el consentimiento y el estudio esté en pleno desarrollo. Además, usted tiene derecho a solicitar al equipo investigador del estudio, en cualquier momento, y sin necesidad de especificar el motivo, la eliminación de sus datos.

3. DESARROLLO DEL ESTUDIO

Se realizará una sola entrevista llevada a cabo por dos investigadores con experiencia en métodos de investigación cualitativa, así como en el campo clínico y el proyecto. En dicha entrevista se le harán preguntas sobre su percepción y adaptación a las intervenciones implantadas. La discusión grupal será grabada (en formato audio) con el fin de transcribirla íntegramente. Esto permite a los miembros del equipo participar en la discusión sin necesidad de tomar notas, evitándose así el riesgo de no reflejar fidedignamente las opiniones expresadas por los miembros del grupo.



4. USO Y CONFIDENCIALIDAD DE LOS DATOS

Los datos que se obtengan en el grupo de discusión se utilizarán únicamente con fines de investigación y solamente por parte del equipo de investigación de la Unidad de Investigación de Atención Primaria de Bizkaia (UIAPB). Todas las opiniones expresadas por los/las participantes serán tratadas de manera anónima y confidencial. Se le informa de que no se va a recoger ningún dato de carácter personal.

El estudio cumple lo establecido en el REGLAMENTO (UE) 2016/679 DEL PARLAMENTO EUROPEO Y DEL CONSEJO de 27 de abril de 2016 relativo a la protección de las personas físicas en lo que respecta al tratamiento de datos personales y a la libre circulación de estos datos. Se le solicita también su consentimiento para la realización de este proyecto de investigación conforme a las exigencias del Reglamento Europeo 2016/679 de Protección de Datos y a la Ley Orgánica 3/2018, de 5 de diciembre, de Protección de Datos Personales y garantía de los derechos digitales que deroga la Ley Orgánica 15/1999, de 5 de diciembre, de protección de datos personales. No se cederán datos a terceros, salvo obligación legal.

Para contactar con los responsables del estudio puede dirigirse a:

Nombre: Álvaro Sánchez Pérez

Teléfono: 946006673

e-mail: alvaro.sanchezperez@osakidetza.eus

Dirección: Edificio Biocruces 3, Plaza Cruces 12, 48903



5. DECLARACION DEL CONSENTIMIENTO INFORMADO

Título: Efectividad de estrategias de de-implementación para favorecer el abandono de prescripciones farmacológicas de bajo valor en prevención primaria de la ECV: proyecto De-imFAR Fase II

Investigador Principal: Álvaro Sánchez Pérez

Servicio/Centro: Subdirección para la coordinación de atención primaria/Unidad de investigación atención primaria-IIS Biocruces Bizkaia

Yo, Don/Doña....., Médico/a de Atención Primaria del Centro de Salud....., he leído este documento, he comprendido las explicaciones en él facilitadas acerca de la grabación del grupo de discusión y he podido resolver todas las preguntas que he planteado al respecto. Comprendo que mi participación en este ensayo es voluntaria y que puedo retirarme en cualquier momento.

También he sido informado/a de que mis datos personales serán protegidos y serán utilizados únicamente con fines de investigación por el equipo de investigadores de la Unidad de Investigación de Atención Primaria de Bizkaia (UIAPB).

Tomando todo ello en consideración y en tales condiciones, CONSIENTO participar en el grupo de discusión, en la grabación del mismo y en que los datos que se deriven de mi participación sean utilizados para cubrir los objetivos especificados en el documento.

EN CONSECUENCIA, DOY MI CONSENTIMIENTO PARA PARTICIPAR EN ESTE PROYECTO DE INVESTIGACIÓN.

..... Firma del/la médico Firma del/la responsable del proyecto

..... Nombre y apellidos Nombre y apellidos

Fecha/...../20..... Fecha/...../20.....



Hoja de Información al Paciente y Consentimiento Informado

Título: Efectividad de estrategias de de-implementación para favorecer el abandono de prescripciones farmacológicas de bajo valor en prevención primaria de la ECV: proyecto De-imFAR Fase II

Investigador Principal: Álvaro Sánchez Pérez

Servicio/Centro: Subdirección para la coordinación de atención primaria/Unidad de investigación atención primaria-IIS Biocruces Bizkaia

Entidad financiadora: Instituto de salud Carlos III

Apreciado Sr./a,

Osakidetza-Servicio Vasco de Salud, con el propósito de mejorar la calidad en la prestación de servicios de salud hacia la ciudadanía, le invita a participar en el estudio “Efectividad de estrategias de de-implementación para favorecer el abandono de prescripciones farmacológicas de bajo valor en prevención primaria de la ECV: proyecto De-imFAR Fase II”.

Antes de decidir si desea participar, es importante que entienda los objetivos, la importancia de su participación y en qué consistirá, además de qué uso se dará a los datos recogidos y los posibles beneficios y riesgos.

Léalo atentamente y consulte cualquier duda con los miembros del equipo de investigación.



1. OBJETO DEL GRUPO DE DISCUSIÓN

El objetivo de los grupos de discusión del Proyecto De-ImFAR es generar conocimiento –a través de las percepciones de los/las pacientes de atención primaria- sobre la práctica clínica en prevención primaria de eventos cardiovasculares en pacientes de bajo riesgo. A través de una serie de preguntas abiertas se analizarán diferentes aspectos relacionados con la experiencia percibida por los/las pacientes con la atención recibida, tratando de conocer la opinión de todos los integrantes del grupo sobre este tema.

No existen respuestas buenas o malas. Cualquier integrante del grupo está invitado a expresar libremente su opinión y a respetar la de los otros integrantes, aunque sea diferente de la suya.

2. PARTICIPACIÓN Y RETIRADA DEL ESTUDIO

Este estudio está aprobado por el Comité de Ética de la Investigación con Medicamentos de Euskadi (CEIm-E). Su participación en el mismo es voluntaria y en cualquier momento puede decidir abandonarlo, aunque haya proporcionado el consentimiento y el estudio esté en pleno desarrollo. Su decisión no afectará la atención sanitaria que reciba posteriormente. Además, usted tiene derecho a solicitar al equipo investigador del estudio, en cualquier momento, y sin necesidad de especificar el motivo, la eliminación de sus datos. Su participación en este estudio no supondrá para usted ningún coste económico, así como tampoco será recompensado económicamente por ello.

3. DESARROLLO DEL ESTUDIO

Se realizará una sola entrevista llevada a cabo por dos investigadores con experiencia en métodos de investigación cualitativa, así como en el campo clínico y el proyecto. En dicha entrevista se le harán preguntas sobre su experiencia y satisfacción con el servicio recibido en prevención primaria de eventos cardiovasculares.

La discusión grupal será grabada (en formato audio) con el fin de transcribirla íntegramente. Esto permite a los miembros del equipo participar en la discusión sin necesidad de tomar notas, evitándose así el riesgo de no reflejar fidedignamente las opiniones expresada por los miembros del grupo.



4. USO Y CONFIDENCIALIDAD DE LOS DATOS

Los datos que se obtengan en el grupo de discusión se utilizarán únicamente con fines de investigación y solamente por parte del equipo de investigación de la Unidad de Investigación de Atención Primaria de Bizkaia (UIAPB). Todas las opiniones expresadas por los/las participantes serán tratadas de manera anónima y confidencial. Se le informa de que no se va a recoger ningún dato de carácter personal.

El estudio cumple lo establecido en el REGLAMENTO (UE) 2016/679 DEL PARLAMENTO EUROPEO Y DEL CONSEJO de 27 de abril de 2016 relativo a la protección de las personas físicas en lo que respecta al tratamiento de datos personales y a la libre circulación de estos datos. Se le solicita también su consentimiento para la realización de este proyecto de investigación conforme a las exigencias del Reglamento Europeo 2016/679 de Protección de Datos y a la Ley Orgánica 3/2018, de 5 de diciembre, de Protección de Datos Personales y garantía de los derechos digitales que deroga la Ley Orgánica 15/1999, de 5 de diciembre, de protección de datos personales. No se cederán datos a terceros, salvo obligación legal.

Si usted tiene alguna duda o requiere cualquier tipo de información no dude en contactar con el/la médico que le informa, Dr./a _____, cuyo lugar de trabajo es el Servicio de _____ del Hospital Universitario _____; teléfono: _____ (extensión _____).

Usted también puede contactar con el Investigador Principal responsable:

Nombre: Álvaro Sánchez Pérez

Teléfono: 946006673

e-mail: alvaro.sanchezperez@osakidetza.eus

Dirección: Edificio Biocruces 3, Plaza Cruces 12, 48903



5. DECLARACION DEL CONSENTIMIENTO INFORMADO

Título: Efectividad de estrategias de de-implementación para favorecer el abandono de prescripciones farmacológicas de bajo valor en prevención primaria de la ECV: proyecto De-imFAR Fase II

Investigador Principal: Álvaro Sánchez Pérez

Investigador/a médico/a:.....

Servicio/Centro: Subdirección para la coordinación de atención primaria/Unidad de investigación atención primaria-IIS Biocruces Bizkaia

Yo, Don/Doña.....(nombre y apellidos del paciente),

he leído este documento, he comprendido las explicaciones en él facilitadas acerca de la grabación del grupo de discusión y he podido resolver todas las preguntas que he planteado al respecto. Comprendo que mi participación en este ensayo es voluntaria y que puedo retirarme en cualquier momento.

También he sido informado/a de que mis datos personales serán protegidos y serán utilizados únicamente con fines de investigación por el equipo de investigadores de la Unidad de Investigación de Atención Primaria de Bizkaia (UIAPB).

Tomando todo ello en consideración y en tales condiciones, CONSIENTO participar en el grupo de discusión, en la grabación del mismo y en que los datos que se deriven de mi participación sean utilizados para cubrir los objetivos especificados en el documento.

EN CONSECUENCIA, DOY MI CONSENTIMIENTO PARA PARTICIPAR EN ESTE PROYECTO DE INVESTIGACIÓN.

.....

Firma del/la paciente

.....

Firma del/la médico responsable

.....

Nombre y apellidos

.....

Nombre y apellidos

Fecha/...../20.....

Fecha/...../20.....



SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description	Addressed on page number
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	4
	2b	All items from the World Health Organization Trial Registration Data Set	N/A
Protocol version	3	Date and version identifier	19
Funding	4	Sources and types of financial, material, and other support	24
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	1-2
	5b	Name and contact information for the trial sponsor	2
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	24
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	N/A
Introduction			
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	5-7
	6b	Explanation for choice of comparators	7-8
Objectives	7	Specific objectives or hypotheses	8-9
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	9, 12-13

Methods: Participants, interventions, and outcomes

Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	10
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	10
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	12
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	N/A
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	N/A
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	N/A
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	13-15
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	N/A
Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	17
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	N/A

Methods: Assignment of interventions (for controlled trials)

Allocation:

Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	13
---------------------	-----	--	----

1	Allocation		Mechanism of implementing the allocation sequence (eg, central	
2	concealment	16b	telephone; sequentially numbered, opaque, sealed envelopes),	13
3	mechanism		describing any steps to conceal the sequence until interventions are	
4			assigned	
5				
6	Implementati	16c	Who will generate the allocation sequence, who will enrol	13
7	on		participants, and who will assign participants to interventions	
8				
9	Blinding		Who will be blinded after assignment to interventions (eg, trial	
10	(masking)	17a	participants, care providers, outcome assessors, data analysts), and	13
11			how	
12				
13				
14		17b	If blinded, circumstances under which unblinding is permissible, and	
15			procedure for revealing a participant's allocated intervention during	N/A
16			the trial	
17				
18				
19	Methods: Data collection, management, and analysis			
20				
21	Data collection		Plans for assessment and collection of outcome, baseline, and	
22	methods	18a	other trial data, including any related processes to promote data	18
23			quality (eg, duplicate measurements, training of assessors) and a	
24			description of study instruments (eg, questionnaires, laboratory	
25			tests) along with their reliability and validity, if known. Reference to	
26			where data collection forms can be found, if not in the protocol	
27				
28				
29		18b	Plans to promote participant retention and complete follow-up,	N/A
30			including list of any outcome data to be collected for participants	
31			who discontinue or deviate from intervention protocols	
32				
33	Data		Plans for data entry, coding, security, and storage, including any	
34	management	19	related processes to promote data quality (eg, double data entry;	18
35			range checks for data values). Reference to where details of data	
36			management procedures can be found, if not in the protocol	
37				
38				
39	Statistical		Statistical methods for analysing primary and secondary outcomes.	
40	methods	20a	Reference to where other details of the statistical analysis plan can	16-17
41			be found, if not in the protocol	
42				
43		20b	Methods for any additional analyses (eg, subgroup and adjusted	17
44			analyses)	
45				
46				
47		20c	Definition of analysis population relating to protocol non-adherence	
48			(eg, as randomised analysis), and any statistical methods to handle	N/A
49			missing data (eg, multiple imputation)	
50				
51				
52	Methods: Monitoring			
53				
54	Data monitoring		Composition of data monitoring committee (DMC); summary of its	
55		21a	role and reporting structure; statement of whether it is independent	N/A
56			from the sponsor and competing interests; and reference to where	
57			further details about its charter can be found, if not in the protocol.	
58			Alternatively, an explanation of why a DMC is not needed	
59				
60				

1		Description of any interim analyses and stopping guidelines,	
2	21b	including who will have access to these interim results and make	N/A
3		the final decision to terminate the trial	
4			
5	Harms	Plans for collecting, assessing, reporting, and managing solicited	
6	22	and spontaneously reported adverse events and other unintended	N/A
7		effects of trial interventions or trial conduct	
8			
9	Auditing	Frequency and procedures for auditing trial conduct, if any, and	
10	23	whether the process will be independent from investigators and the	N/A
11		sponsor	
12			
13			
14			
15	Ethics and dissemination		
16	Research ethics	Plans for seeking research ethics committee/institutional review	
17	approval	board (REC/IRB) approval	19
18			
19	Protocol	Plans for communicating important protocol modifications (eg,	
20	amendments	changes to eligibility criteria, outcomes, analyses) to relevant parties	
21	25	(eg, investigators, REC/IRBs, trial participants, trial registries,	N/A
22		journals, regulators)	
23			
24			
25	Consent or	Who will obtain informed consent or assent from potential trial	
26	assent	participants or authorised surrogates, and how (see Item 32)	15,18
27	26a		
28			
29	26b	Additional consent provisions for collection and use of participant	N/A
30		data and biological specimens in ancillary studies, if applicable	
31			
32	Confidentiality	How personal information about potential and enrolled participants	
33	27	will be collected, shared, and maintained in order to protect	18
34		confidentiality before, during, and after the trial	
35			
36	Declaration of	Financial and other competing interests for principal investigators	
37	interests	for the overall trial and each study site	24
38			
39	Access to data	Statement of who will have access to the final trial dataset, and	
40	29	disclosure of contractual agreements that limit such access for	19-20
41		investigators	
42			
43			
44	Ancillary and	Provisions, if any, for ancillary and post-trial care, and for	
45	post-trial care	compensation to those who suffer harm from trial participation	N/A
46			
47	Dissemination	Plans for investigators and sponsor to communicate trial results to	
48	policy	participants, healthcare professionals, the public, and other relevant	
49	31a	groups (eg, via publication, reporting in results databases, or other	20
50		data sharing arrangements), including any publication restrictions	
51			
52			
53	31b	Authorship eligibility guidelines and any intended use of	N/A
54		professional writers	
55			
56	31c	Plans, if any, for granting public access to the full protocol,	18
57		participant-level dataset, and statistical code	
58			
59			
60	Appendices		19-20

1	Informed		Model consent form and other related documentation given to	
2	consent	32	participants and authorised surrogates	28,29
3	materials			
4				
5	Biological		Plans for collection, laboratory evaluation, and storage of biological	
6	specimens	33	specimens for genetic or molecular analysis in the current trial and	N/A
7			for future use in ancillary studies, if applicable	
8				

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "[Attribution-NonCommercial-NoDerivs 3.0 Unported](#)" license.

Reference: Chan A-W, Tetzlaff JM, Altman DG, et al. SPIRIT 2013 Statement: Defining standard protocol items for clinical trials. *Ann Intern Med.* 2013 Feb 5;158(3):200-207. doi: 10.7326/0003-4819-158-3-201302050-00583.

BMJ Open

The De-imFAR Phase II Project: A study protocol for a cluster randomized implementation trial to evaluate the effectiveness of de-implementation strategies to reduce low-value statin prescribing in the primary prevention of Cardiovascular Disease.

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	<p>Research on Chronicity, Primary Care, and Health Promotion (RICAPPS) Gonzalez Saenz de Tejada, Marta; Biocruces Bizkaia Health Research Institute, Network for Research on Chronicity, Primary Care, and Health Promotion (RICAPPS)</p> <p>García-Alvarez, Arturo; Osakidetza-Basque Health Service, Primary Care Research Unit of Bizkaia. Deputy Directorate of Healthcare Assistance; Biocruces Bizkaia Health Research Institute</p> <p>Grandes, Gonzalo; Osakidetza-Basque Health Service, Primary Care Research Unit of Bizkaia. Deputy Directorate of Healthcare Assistance; Biocruces Bizkaia Health Research Institute</p>
Primary Subject Heading:	Evidence based practice
Secondary Subject Heading:	General practice / Family practice, Health services research, Cardiovascular medicine, Research methods
Keywords:	Primary Care < Primary Health Care, Clinical Decision-Making, Clinical Trial, PREVENTIVE MEDICINE, Implementation Science, Cardiovascular Disease

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TITLE PAGE

Title

The De-imFAR Phase II Project: A study protocol for a cluster randomized implementation trial to evaluate the effectiveness of de-implementation strategies to reduce low-value statin prescribing in the primary prevention of Cardiovascular Disease.

Author's details Alvaro Sanchez^{1*}, Jose I. Pijoan², Rita Sainz de Rozas³, Itxasne Lekue³, Ricardo San Vicente⁴, Jose Antonio Quindimil⁵, Rafael Rotaecche⁶, Arritxu Etxeberria⁷, Carmela Mozo⁷, Monica Martinez-Cengotitabengoa⁸, Monica Monge⁹, Cristina Gómez-Ramírez¹⁰, Ricardo Samper¹¹, Mikel Ogueta Lana¹², Sara Celorrio¹³, Nerea Merino-Inda¹⁴, Marta Llarena¹⁵, Marta Gonzalez Saenz de Tejada¹⁵, Arturo Garcia-Alvarez¹, and Gonzalo Grandes¹

¹ Primary Care Research Unit of Bizkaia, Deputy Directorate of Healthcare Assistance, Biobizkaia Health Research Institute, Basque Health Service - Osakidetza, Network for Research on Chronicity, Primary Care, and Health Promotion (RICAPPS), Barakaldo, Bizkaia, Spain.

² Clinical Epidemiology Unit, Biobizkaia Health Research Institute, Basque Health Service - Osakidetza, Barakaldo, Bizkaia, Spain. CIBER de Epidemiología y Salud Pública (CIBERESP), Instituto de Salud Carlos III, Spain.

³ Primary Care Pharmacy Unit, Ezkerraldea-Enkarterri-Cruces Integrated Health Organization, Basque Health Service – Osakidetza, Biobizkaia Health Research Institute, Barakaldo, Bizkaia, Spain.

⁴ Zumarraga Health Center, Goierri-Alto Urola Integrated Health Organization, Basque Health Service – Osakidetza, Zumárraga, Gipuzkoa, Spain.

⁵ Sestao Health Center, Barakaldo-Sestao Integrated Health Organization, Basque Health Service – Osakidetza, Sestao, Bizkaia, Spain.

1
2
3 29 ⁶ Primary Care Research Unit of Gipuzkoa, Organization of Integrated Health Services
4
5 30 of Gipuzkoa, Biogipuzkoa Health Research Institute, Donostia-San Sebastian,
6
7 31 Gipuzkoa, Spain

8
9 32 ⁷ Primary Care Pharmacy, Donostialdea Integrated Health Organization, Hernani,
10
11 33 Gipuzkoa, Spain

12
13 34 ⁸ School of Pharmacy, University of the Basque Country UPV/EHU, Vitoria-Gasteiz,
14
15 35 Spain. Psychology Clinic of East Anglia, Norwich, UK. Osakidetza Basque Health
16
17 36 Service, Barakaldo, Spain.

18
19
20 37 ⁹ Corporate Pharmacy Service, Directorate of Healthcare Assistance, Osakidetza-
21
22 38 Basque Health Service Central Services, Vitoria-Gasteiz, Spain

23
24 39 ¹⁰ Cardiology Department, Cruces University Hospital, Ezkerraldea-Enkarterri-Cruces
25
26 40 Integrated Health Organization, Basque Health Service – Osakidetza, Barakaldo,
27
28 41 Bizkaia, Spain.

29
30 42 ¹¹ Corporate Pharmacy Service, Directorate of Healthcare Assistance, Osakidetza-
31
32 43 Basque Health Service Central Services, Vitoria-Gasteiz, Spain

33
34 44 ¹² Subdirectorate of Quality and Health Information Systems, Osakidetza-Basque Health
35
36 45 Service Central Services, Vitoria-Gasteiz, Spain

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38
39 46 ¹³ Barakaldo-Sestao Integrated Health Organization, Basque Health Service –
40
41 47 Osakidetza, Barakaldo, Spain

42
43 48 ¹⁴ Biobizkaia Health Research Institute, Barakaldo, Bizkaia, Spain.

44
45 49 ¹⁵ Biobizkaia Health Research Institute, Network for Research on Chronicity, Primary
46
47 50 Care, and Health Promotion (RICAPPS), Barakaldo, Bizkaia, Spain.

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51
52 52 *** Corresponding author:**

53
54 53 Alvaro Sánchez

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56 54 E-mail: Alvaro.sanchezperez@osakidetza.eus

57
58 55 Primary Care Research Unit of Bizkaia, Deputy Directorate of Healthcare Assistance,

59
60 56 Biobizkaia Health Research Institute, Basque Health Service – Osakidetza, Network for

1
2
3 57 Research on Chronicity, Primary Care, and Health Promotion (RICAPPS). Plaza Cruces
4
5 58 s/n, E-48903 Barakaldo, Bizkaia, Spain.
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60 **ABSTRACT**

61 **Introduction**

62 This study aims to reduce potentially inappropriate prescribing (PIP) of statins and foster
63 healthy lifestyle promotion in cardiovascular disease (CVD) primary prevention in low-
64 risk patients. To this end, we will compare the effectiveness and feasibility of several de-
65 implementation strategies developed following the structured design process of the
66 Behavior Change Wheel targeting key determinants of clinical decision-making process
67 in CVD prevention.

68 **Methods and analysis**

69 A cluster randomized implementation trial, with an additional control group, will be
70 launched, involving family physicians (FPs) from 13 Integrated Healthcare Organizations
71 (IHOs) of Osakidetza-Basque Health Service with non-zero incidence rates of PIP of
72 statins in 2021. All FPs will be exposed to a non-reflective decision assistance strategy
73 based on reminders and decision support tools. Additionally, FPs from two of the IHOs
74 will be randomly assigned to one of two increasingly intensive de-implementation
75 strategies: adding a decision information strategy based on knowledge dissemination,
76 and a reflective decision structure strategy through audit/feedback. The target population
77 comprises 45- to 74-year-old women and 40- to 74-year-old men with moderately
78 elevated cholesterol levels but no diagnosed CVD and low cardiovascular risk
79 (REGICOR <7.5%), who attend at least one appointment with any of the participating
80 FPs (May 2022-May 2023), and will be followed until May 2024. We use the Reach,
81 Effectiveness, Adoption, Implementation and Maintenance (RE-AIM) framework to
82 evaluate outcomes. The main outcome will be the change in the incidence rate of PIP of
83 statins and healthy lifestyle counseling in the study population 12 and 24 months after

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3 84 FPs' exposure to the strategies. Moreover, FPs' perception of their feasibility and
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5 85 acceptability, and patient experience regarding quality of care received will be evaluated.
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7 86 **Ethics and dissemination**
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9 87 The study was approved by the Basque Country Clinical Research Ethics Committee
10
11 88 and was registered in ClinicalTrials.gov (NCT04022850). Results will be disseminated in
12
13 89 scientific peer-reviewed journals.
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16 90 **Keywords:** Inappropriate Prescribing, Cardiovascular Diseases / prevention & control,
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18 91 Hypercholesterolemia / drug therapy, Implementation Science, Research Design,
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20 92 Primary care.
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25 94 **STRENGTHS AND LIMITATIONS OF THIS STUDY**
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- 27 95 • A strength of the DE-imFAR study is that it involves an efficient design that
28
29 96 combines experimental and non-experimental comparisons through two randomly
30
31 97 assigned intervention arms and one non-randomized control arm to test the
32
33 98 comparative effectiveness on reducing potentially inappropriate prescribing (PIP)
34
35 99 of statins and increasing healthy lifestyle promotion of several de-implementation
36
37 100 strategies deployed in real-world settings.
38
39 101 • Counting with one non-randomized control arm is a strength because it allows
40
41 102 capturing the effect of temporal trends, regression to the mean, and the learning
42
43 103 curve due to the reference/background strategy to which all targeted family
44
45 104 physicians (FPs) are exposed, when comparing this reference strategy with the
46
47 105 two experimental de-implementation strategies.
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49 106 • Another strength is the use of qualitative methods to better understand, from the
50
51 107 perspective of the study participants, the reasons why (why not) the strategies
52
53 108 work, to explain the variations in the results achieved and to identify the essential
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55 109 components of the strategy and those that will require to be optimized.
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3 110 • To the best of our knowledge, the DE-imFAR study is one of the firsts of its kind
4
5 111 that specifically uses the RE-AIM framework for the evaluation of the study results
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7 112 in terms of public health impacts.
8
9 113 • The main limitation lies in the planned comparisons of the randomized groups with
10
11 114 respect to the control arm, likely to differ to some extent at baseline because of
12
13 115 the non-random process of generation. To tackle this limitation, in addition to
14
15 116 evaluating the change in PIP incidence in all eligible FPs, a matching strategy with
16
17 117 the selection of one matched FP from this non-randomized group for each of the
18
19 118 randomized FPs will be performed in order to increase comparability and reduce
20
21 119 potential bias.
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26 121 INTRODUCTION

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28 122 Reducing low-value healthcare, that is, clinical practices that have not been shown to be
29
30 123 efficient or effective, is becoming a global priority due to the widespread empirical
31
32 124 evidence of its high prevalence across healthcare systems, potential harm and its impact
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34 125 on patient safety, resource use, and social inefficiency [1,2].
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39 127 Nonetheless, reducing or eliminating low-value practices is a complex matter, since
40
41 128 drivers that foster or maintain them seem to operate at multiple levels and be context
42
43 129 specific. Therefore, in order to design effective and efficient corrective measures, a
44
45 130 careful process of formal analysis of the determinants of the clinical behavior in question
46
47 131 is needed. In this context, behavior change theory has been extensively applied to
48
49 132 understand the factors that may influence clinical behavior, identify and design possible
50
51 133 techniques and interventions that could be used to change it, and explain the
52
53 134 mechanisms through which such interventions operate [3,4].
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58 136 The DE-imFAR study (“De-implementation of low-value pharmacological prescribing” in
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60 137 Spanish) is a two-phase project [5] that aims to apply behavioral science theory within a

1
2
3 138 structured process involving the main stakeholders (health professionals, patients, and
4
5 139 researchers) in the design, deployment, and evaluation of targeted de-implementation
6
7 140 strategies to reduce potentially inappropriate prescribing (PIP). Specifically, in the DE-
8
9 141 imFAR study the target low-value practice is the pharmacological prescription of statins
10
11 142 in the primary prevention of cardiovascular disease (CVD) in low-risk patients. In order
12
13 143 to prevent CVD, one of the leading causes of morbidity and death worldwide, there is
14
15 144 general agreement on the indication of lipid-lowering treatment, mainly with statins, for
16
17 145 patients with a 10-year cardiovascular risk (CVR) greater than 10% or in the secondary
18
19 146 prevention [6-9]. Whereas, in the primary prevention for patients with low CVR (<10%),
20
21 147 preventive activities should be focused on the promotion of healthy lifestyles through
22
23 148 optimizing diet, increasing physical activity, and stopping smoking [6-9]. Moreover,
24
25 149 international guidelines encourage discussion with patients about the benefits of lifestyle
26
27 150 modification for the prevention of CVD, as well as other modifiable risk factors, before
28
29 151 considering pharmacological treatment [7-9].
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35 153 Within the Phase I of the DE-imFAR study, we first conducted a cross-sectional
36
37 154 observational study on the incidence of PIP of statins and provision of advice on lifestyle
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39 155 modification in the Basque Health Service-Osakidetza in 2018. The results showed that
40
41 156 the prescription of statins had notably increased in the Basque Country (Spain) with an
42
43 157 estimated incidence of new PIP of 10.5 per 100,000 persons/year in patients aged 40 to
44
45 158 75 years, without CVD, with moderately elevated cholesterol levels but with a CVR <5%
46
47 159 [10].
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51 161 Secondly, we applied two of the most successfully used behavior change theories in the
52
53 162 field of Implementation Science, the Theoretical Domains Framework (TDF) [3,11,12]
54
55 163 and Behavior Change Wheel (BCW) [13], to a) understand and define the problem (low-
56
57 164 value practice) in behavioral terms and select and specify the target behaviors; b) identify
58
59 165 the factors that may influence it; and c) map targeted de-implementation and
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3 166 implementation strategies conducive to reducing the low-value practice in question.
4
5 167 Briefly, after having prioritized our specific target behavior (that is “clinician decision-
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7 168 making on intervention/treatment to be provided based on objective clinical information
8
9 169 and subjective schemas and heuristics”), identified the determinants (facilitators of the
10
11 170 non-desired behavior of PIP of statins and barriers to apply the recommended clinical
12
13 171 practice behavior of promoting healthy lifestyles), and mapped specific behavior change
14
15 172 techniques, three types of de-implementation strategies were selected based on being
16
17 173 the most potentially effective, feasible, and acceptable to influence decision-making
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19 174 through different mechanisms [14]. Hence, the three strategies derived from the
20
21 175 systematic theory- and evidence-based intervention design process were: a) a non-
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23 176 reflective decision assistance strategy based on providing family physicians (FP) with
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25 177 evidence-based information communication technology tools to help and guide decision-
26
27 178 making; b) a decision information strategy based on the dissemination of CVD primary
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29 179 prevention evidence framed in a corporate campaign encouraging FPs to abandon PIP;
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31 180 and c) a reflective decision structure strategy encouraging reflection on actual
32
33 181 performance based on an audit/feedback system [14].
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39 183 According to the literature review performed within the Phase I of the DE-imFAR project
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41 184 [14] regarding the evaluation of effective intervention strategies for the reduction of low-
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43 185 value prescribing [15-24], multicomponent interventions—combining passive
44
45 186 dissemination interventions, based on training in or dissemination of clinical practice
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47 187 guidelines (CPGs), with more proactive interventions incorporating decision-making aids
48
49 188 or sending audit/feedback—achieve the most positive results. Specifically, in the context
50
51 189 of PIP of statins, a positive impact was observed on recording of CVR and prescription
52
53 190 adequacy using a) multicomponent dissemination strategies including informational
54
55 191 websites and implementation of electronic CPGs compared to routine practice and
56
57 192 training activities, and b) interventions based on sending clinical scenarios/cases and
58
59 193 audit/feedback to professionals as well as decision support tools [19-23]. All these

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3 194 strategies can be conceived and theoretically differentiated in terms of how they may
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5 195 affect clinicians' decision-making [25]. There is plenty of evidence to support de-
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7 196 implementation of inappropriate medical practices through the lens of clinician cognition
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9 197 using audit/feedback, decision support tools, etc. [26-28]. In this context, the growing
10
11 198 field of choice architecture aims to explore how the structure and framing of decision
12
13 199 situations influence the choice of certain behaviors over alternative ones. On the one
14
15 200 hand, FPs' decision-making ability can be influenced by unconscious processes that
16
17 201 occur in response to environmental or emotive cues, that is, through Type 1 (or
18
19 202 automatic) cognition. On the other, clinicians' conscious intention to change can be
20
21 203 promoted by engaging their reflective cognition to consciously evaluate and correct their
22
23 204 inappropriate behavior, that is, using Type 2 (or reflective) cognition [29]. However,
24
25 205 further research is needed to determine whether these evidence-based and barrier-
26
27 206 specific de-implementation strategies identified in the DE-imFAR Phase I are also
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29 207 effective in our context.
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35 209 Thus, the goal of the present Phase II of the DE-imFAR study is to assess the potential
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37 210 effectiveness and feasibility of this set of de-implementation strategies to reduce the PIP
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39 211 of statins in the primary prevention of CVD (low-risk patients, REGICOR [30] CVR score
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41 212 <7.5%, with moderately elevated cholesterol levels, low-density lipoprotein (LDL)
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43 213 cholesterol levels between 70 and 189 mg/dL and/or total cholesterol (TC) between 200
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45 214 and 289 mg/dL, but without ischemic heart disease/CVD).
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50 216 Specifically, we aim to answer the following research questions:

51 217 1. Observational comparison questions:

52
53 218 Compared to a reference non-reflective decision assistance strategy based on reminders
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55 219 and decision support tools integrated into the electronic health record (EHR) to help
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57 220 clinical decision-making, what is the effect on the incidence of PIP of statins and of
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59 221 delivery of healthy lifestyle counseling in CVD primary prevention of a) a decision
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3 222 information strategy comprising a corporate “Stopping Low-Value Prescribing” campaign
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5 223 and the dissemination of evidence-based CPGs for the primary prevention of CVD; b) a
6
7 224 reflective decision structure strategy based on an audit/feedback system; and c) any
8
9 225 intervention based on a reflective de-implementation strategy (a or b)?
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11 226

12
13 227 2. Experimental comparison question:

14
15 228 Compared to a decision information strategy comprising a corporate “Stopping Low-
16
17 229 Value Prescribing” campaign and the dissemination of evidence-based CPGs for the
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19 230 primary prevention of CVD, together with the non-reflective decision assistance
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21 231 intervention based on reminders and decision support tools integrated into the EHR to
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23 232 help clinical decision-making, what is the effect on the incidence of PIP of statins and of
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25 233 delivery of healthy lifestyle counseling in CVD primary prevention of adding a reflective
26
27 234 decision structure strategy based on an audit/feedback system?
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31 32 236 **METHODS AND ANALYSIS**

33 34 237 **Design**

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36 238 A cluster randomized implementation trial with an additional control group will be
37
38 239 conducted to evaluate the potential effectiveness and feasibility of three de-
39
40 240 implementation strategies (Figure 1). A mixed methods evaluation will be undertaken:
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42 241 quantitative in order to assess the implementation results at professional level
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44 242 (effectiveness outcomes regarding changes in the incidence rates of PIP of statins and
45
46 243 provision of healthy lifestyle counseling) and qualitative to assess the feasibility and
47
48 244 perceived impact of the de-implementation strategies from the FPs’ perspective and
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50 245 patients’ experience and satisfaction with the clinical care received. The unit of
51
52 246 randomization and intervention will be the primary care FP, while observation and
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54 247 analysis will be performed at professional and patient levels. The DE-imFAR research
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56 248 protocol was reviewed and approved by the Basque Country Clinical Research Ethics
57
58 249 Committee (Reference: EOM2022018, approved on 30 March 2022) and was registered
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2
3 250 in the U.S. NLM ClinicalTrials.gov database (ClinicalTrials.gov Identifier NCT04022850,
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5 251 Registered 17 July 2019; Last update 5 February 2024).

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9 253 Osakidetza-Basque Health Service provides universal coverage and services are free at
10
11 254 the point of use, aside from drug copayment, funded through regional general taxation.

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13 255 Primary, specialized, and social health-related service provision is organized around 13

14
15 256 Integrated Healthcare Organizations (IHOs) that cover the 3 provinces of the region of

16
17 257 the Basque Country: Araba, Bizkaia, and Gipuzkoa. Each resident is on the list of one

18
19 258 FP or pediatrician who provides comprehensive primary care and refers patients to

20
21 259 hospital and specialized services. Primary care professionals work in full-time teams,

22
23 260 which include FPs, pediatricians, nurses and administrative staff, based at local centers

24
25 261 that provide users with access to healthcare in a defined geographical area.

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27 262 We used the SPIRIT reporting guidelines and the SPIRIT checklist when writing the

28
29 263 present study [31].

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32 33 265 **Participants**

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35 266 Eligibility criteria for the study will be:

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37 267 1. Professionals: FPs belonging to any of the 13 IHOs of Osakidetza with a non-zero

38
39 268 annual incidence rate of PIP of statins at baseline (2021) with a minimum cluster size of

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41 269 $n \geq 10$ patients

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43 270 2. Patients: All 40- to 74-year-old men and 45- to 74-year-old women with no history of

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45 271 statin use, LDL cholesterol levels between 70 and 189 mg/dL and/or TC between 200

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47 272 and 289 mg/dL but without ischemic heart disease/CVD, and an estimated CVR

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49 273 REGICOR $< 7.5\%$ who attend at least one appointment with any of the participating FP

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51 274 during the study period (from May 2022 to May 2023).

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54 55 276 **Clinical interventions**

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3 277 The DE-imFAR study, with regard to the prescription of statins in the primary prevention
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5 278 of CVD, follows the clinical practice recommendations in Osakidetza-Basque Health
6
7 279 Service and the Spanish National Health System [6] as well as several international
8
9 280 guidelines [7-9]. Thus, these are the recommendations concerning when to initiate
10
11 281 treatment in the primary prevention of CVD [6, 32]:

- 12
13 282 ▪ For individuals aged 40 to 75 years with an estimated 10-year CVR REGICOR
14
15 283 >10%, initiation of statin therapy is recommended.
- 16
17 284 ▪ In general, for individuals aged 40 to 75 years with CVR REGICOR <10% and
18
19 285 LDL cholesterol levels <190 mg/dL, it is recommended not to initiate statin
20
21 286 therapy, with the following considerations:
- 22
23 ○ with CVR close to 10%, consider the presence of risk-enhancing factors
24
25 287 in decision-making.
- 26
27 288 ○ with CVR <5%, it is recommended not to initiate statin therapy.
- 28
29 289 ▪ For patients with LDL cholesterol levels \geq 190 mg/dL, it is recommended to assess
30
31 290 the presence of genetic dyslipidemia and potential cardiovascular risk-enhancing
32
33 291 factors. It is suggested to initiate statin therapy, together with healthy lifestyle
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35 292 recommendations, regardless of cardiovascular risk.
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39 294 In any case, the indication for treatment should be preceded and/or accompanied by
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41 295 promotion of healthy lifestyles through healthful diet, regular physical activity and
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43 296 smoking cessation. Moreover, it is recommended that the decision to initiate statin
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45 297 therapy should consider individual baseline risk, absolute risk reduction and whether the
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47 298 risk reduction justifies the potential harms and undesirable consequences of taking a
48
49 299 lifelong daily medication.

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51 300

52 53 301 **De-implementation strategies evaluated**

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55 302 Within the present Phase II of the DE-imFAR study, the three types of strategies that
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57 303 were derived from the Phase I systematic theory- and evidence-based intervention
58
59 304 design process will be set up (see Supplemental file 1 for a more detailed description):

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3 305 1) *A non-reflective decision assistance strategy* that targets Type 1 cognitive processes
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5 306 through decision support systems that prompt and remind FPs about the recommended
6
7 307 practice in a simplified way, thereby reducing the cognitive burden. In short, pop-up
8
9 308 reminders and alerts with associated messages will be integrated into OSABIDE's
10
11 309 (Osakidetza's EHR system) REGICOR CVR calculator and PRESBIDE (the electronic
12
13 310 drug prescribing component). The tools devised include an interactive media-based
14
15 311 algorithm with the recommended practice for the primary prevention of CVD in low-risk
16
17 312 patients developed by an expert panel, and a patient information sheet that depicts and
18
19 313 promotes evidence-based practice to address cholesterol in the primary prevention of
20
21 314 CVD in low-risk patients.

22
23
24 315 2) *A both reflective and non-reflective decision information strategy* that targets both
25
26 316 Type 1 and 2 cognitive processes, based on the principle of knowledge dissemination
27
28 317 and consisting of a "Stopping Low-Value Prescribing" campaign run by the organization
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30 318 (Osakidetza- Basque Health Service) that also eases access (decreasing the physical
31
32 319 effort required) to the evidence-based CPGs for the primary prevention of CVD in low-
33
34 320 risk patients.

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37 321 3) *A reflective decision structure strategy* that targets Type 2 cognition through an
38
39 322 audit/feedback system that reports data about individual's and organizational
40
41 323 performance indicators with regard to PIP of statins and healthy lifestyle promotion to
42
43 324 prompt reflection on their own clinical practice, provided along with intention formation
44
45 325 and goal-setting-focused messages.

46
47 326

327 **Allocation of intervention units to compared groups**

328 The DE-imFAR study is a cluster randomized implementation trial conducted under real
329 world conditions in the primary prevention of CVD in Primary Care (PC) where both
330 clinical practices, i.e., inappropriate statin prescription and substandard promotion of
331 healthy lifestyles, occur. The aforementioned de-implementation strategies will be
332 cumulatively deployed under routine conditions of healthcare service provision in

1
2
3 333 Osakidetza to reduce the low-value practice and increase the recommended practice by
4
5 334 PC healthcare professionals. Specifically, the decision support tools integrated into the
6
7 335 EHR (non-reflective decision assistance strategy) will be applied to all FPs from the 13
8
9 336 IHOs of Osakidetza. Further, in addition to this first strategy, eligible FPs belonging to
10
11 337 two IHOs (Barakaldo-Sestao and Ezkerraldea-Enkarterri-Cruces) will be randomly
12
13 338 assigned to the exposure to either the second (provision of decision information strategy)
14
15 339 or the second and third (provision of decision information and reflective decision structure
16
17 340 strategies). The allocation sequence within these two groups will be generated using a
18
19 341 specific restricted randomization scheme by one member of the research team. The
20
21 342 sequence will be concealed at the coordinating center. In all cases, FPs will be only
22
23 343 allocated to the study groups after they have agreed to participate through an opt-out
24
25 344 strategy. The data analyst and the staff in charge of measurements will be blind to FP
26
27 345 allocation to study arms. Given that the audit/feedback strategy will involve regular
28
29 346 reports privately sent to individuals, the participants in the experimental arms are also
30
31 347 expected to be blind to group allocation.
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349 **Outcome measures**

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39 350 To evaluate the implementation of the de-implementation strategies in terms of public
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41 351 health impact, we will use the following dimensions of the Reach, Effectiveness,
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43 352 Adoption, Implementation, and Maintenance (RE-AIM) framework [33]:
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45 353 *Reach*

46
47 354 Absolute number and percentage of patients in the target population who received the
48
49 355 recommended CVD primary prevention clinical intervention 12 months after FP's
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51 356 exposure to the de-implementation strategies compared; and their representativeness.
52

53 357 *Effectiveness*

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55 358 The study's main outcome will measure both the change in the incidence of the PIP of
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57 359 statins and the change in the incidence of the provision of healthy lifestyle advice in
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3 360 patients in the target population eligible for CVD primary prevention, from baseline to 12
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5 361 months after exposure of target FPs to the de-implementation strategies.
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7 362
8
9 363 As a secondary outcome, we will compare the change in the incidence of CVR
10
11 364 (REGICOR) recording in the EHR, from baseline to 12 months after exposure of FPs to
12
13 365 the de-implementation strategies compared, in 40- to 74-year-old men and 45- to 74-
14
15 366 year-old women without ischemic heart disease/CVD.
16

17 367 *Adoption*

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20 368 Degree to which the recommended CVD primary prevention clinical intervention is
21
22 369 adopted by the FPs 12 months after their exposure to the de-implementation strategies,
23
24 370 that will be measured by the percentage of FPs who reduce PIP of statins and/or increase
25
26 371 health promotion activities in the target population; and their representativeness.
27

28 372 *Implementation*

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30 373 The fidelity of the delivery of each de-implementation strategy under study (i.e., the
31
32 374 degree to which they were executed as planned) will be evaluated. To this end, a
33
34 375 complete record and subsequent description of the execution process, documentation of
35
36 376 adaptations made to the planned strategies, and process indicators of the delivery of and
37
38 377 exposure to the interventions (see Supplemental file 1 for specification of the exposure
39
40 378 to each strategy), will be used to assess the following components of fidelity: adherence,
41
42 379 dose, quality of delivery, professionals' responsiveness and program differentiation [34].
43
44

45 380 *Maintenance*

46
47 381 Change in the incidence of PIP of statins and provision of healthy lifestyle counseling in
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49 382 eligible patients, 24 months after exposure of FPs to the de-implementation strategies
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51 383 compared to the levels observed at the 12-month assessment.
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55 385 *Other study covariates*

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57 386 In addition, and informed by the cross-sectional observational study performed in the
58
59 387 Phase I of the DE-imFAR study [10], potential confounders that may bias the estimated
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3 388 effect of the de-implementation strategies on the change in PIP of statins will be
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5 389 measured, both at a) health professional level: sociodemographic variables (age, sex),
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7 390 baseline incidence rate of PIP of statins; and b) patient level: sociodemographic variables
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9 391 (age, sex, socioeconomic status) and clinical variables (baseline cholesterol level,
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11 392 presence of hypertension, prescribed antihypertensives, tobacco use).
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14 393

15 394 **Feasibility Evaluation**

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17 395 Professionals' perception of the feasibility and acceptability of the de-implementation
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19 396 strategies to enhance the provision of the recommended CVD primary prevention clinical
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21 397 practice will be assessed through key informant semi-structured individual interviews.
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23 398 The interviews will be carried out with at least 12 professionals until data saturation is
24
25 399 reached: at least six (three from each randomized arm) who reduced their PIP of statins
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27 400 and at least six who did not, as informed by the quantitative results. The interview script
28
29 401 will contain open-ended questions that will focus on the perceived value of the de-
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31 402 implementation strategies and recommendations for their optimization.
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37 404 Patients' experience and perception of the quality of CVD prevention care received will
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39 405 be also assessed through key informant semi-structured interviews. The interviews will
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41 406 be carried out with at least ten patients until data saturation is reached: at least five
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43 407 patients who were clinically managed according to the recommended practice and five
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45 408 who did not. The interview script will contain open-ended questions that will focus on the
46
47 409 perceived care received.
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52 411 Both professional and patient interviews will be conducted by two researchers with
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54 412 experience in qualitative research methods, as well as knowledge of the clinical field and
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56 413 the project. The interviews will be audio recorded, with prior informed consent, and
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58 414 verbatim transcribed. Regarding the analysis of the qualitative study, the responses will
59
60 415 be extracted from the interview transcripts. Several members of the research team will

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2
3 416 participate in the analysis, promoting the exchange of perspectives and consensus, with
4
5 417 the aim of triangulating the analysis. Deductive and inductive approaches will be
6
7 418 combined. For the deductive approach, the discourse of each professional and patient
8
9 419 interviewed will be associated with constructs derived from the behavior change theories
10
11 420 (TDF, BCW, etc.) [3,11-13]. The inductive analysis will be based on the postulates of
12
13 421 grounded theory [35]. Researchers will use coding techniques, or line-by-line analysis,
14
15 422 looking for words and phrases that identify explanatory concepts. Subsequently,
16
17 423 thematic connections between the basic theoretical concepts and the data will be
18
19 424 developed.
20
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22 425

23 24 426 **Analysis**

25
26 427 Frequencies and proportions along with the corresponding 95% confidence intervals
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28 428 (CIs) will be used to describe the prevalence and cumulative incidence of PIP of statins
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30 429 and healthy lifestyle counseling in the primary prevention of CVD by FPs. The primary
31
32 430 effectiveness outcomes will be the changes in the cumulative incidence of PIP of statins
33
34 431 and healthy lifestyle counseling in patients from the target population (individuals with no
35
36 432 history of statin use, LDL cholesterol levels between 70 and 189 mg/dL and/or TC
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38 433 between 200 and 289 mg/dL, without past or current ischemic heart disease/CVD, and
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40 434 an estimated CVR REGICOR <7.5% who attend at least one medical appointment with
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42 435 their FP during the study period), from baseline to 12 months after exposure of FPs to
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44 436 the de-implementation strategies. Therefore, to evaluate the impact of the three de-
45
46 437 implementation strategies, we will estimate the relative risk reduction of receiving PIP of
47
48 438 statins in patients from the target population whose FPs were assigned to the
49
50 439 experimental strategies over that in patients from the non-randomized group (non-
51
52 440 reflective decision assistance strategy group). With respect to this group and in order to
53
54 441 increase comparability and reduce potential bias, in addition to evaluating the change in
55
56 442 the incidence rate of PIP of statins in patients from all eligible FPs, we will select two
57
58 443 matched FPs from this non-randomized group for each of the randomized FP taking into
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3 444 account both FP' characteristics (e.g., baseline incidence rate of PIP of statins, etc.) and
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5 445 characteristics of the patients assigned to the FP (e.g., average socioeconomic status,
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7 446 etc.). Change in the incidence rates of PIP of statins from baseline to 12 and 24 months
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9 447 after FPs' exposure to the de-implementation strategies and the relative risk reduction
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11 448 will be estimated with the corresponding 95% CIs. To adjust for potential confounding
12
13 449 factors, stratified statistical analyses and logistic models will be used. These models will
14
15 450 be extended to generalized mixed effects models to take into account the hierarchical
16
17 451 structure of data (patients nested within FPs and FPs within primary care teams), with
18
19 452 fixed effects (comparison group, effect of time on outcome indicators, and time-group
20
21 453 interactions) and random effects on the intercept and the time slope (for each patient,
22
23 454 FP, center, etc.). These models will be adjusted for potential confounders, following a
24
25 455 backward strategy, guided by the stratified analyses. A similar approach will be taken to
26
27 456 analyze the secondary outcomes. The analysis will be carried out using SAS (v. 9.2, SAS
28
29 457 Institute, Cary, NC, USA) and R (R Development Core Team, 2014).
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34
35 459 Calculation of the required sample size in the worst-case scenario, i.e. the comparison
36
37 460 between the two randomized de-implementation strategies, was based on: i) a baseline
38
39 461 incidence rate of statin PIP of 7.4% estimated among the patients from the target
40
41 462 population seen in 2021 by FPs with an incidence rate of statin PIP > 0% with a minimum
42
43 463 cluster size $n \geq 10$ patients, ii) an intra-class correlation coefficient of 0.01, iii) an average
44
45 464 cluster size of 39 patients with a coefficient of variation of 0.63, iv) $\alpha = 0.05$ and statistical
46
47 465 power of 80%, and v) hypothetical decreases in annual PIP incidence rates of 20% in
48
49 466 the decision information strategy group and 50% in the decision structure strategy group.
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51 467 With these assumptions, it was estimated that at least 58 FPs were required for each
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53 468 experimental arm.
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57 470 **Management, quality, and safety in data processing**

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3 471 This study will be carried out in accordance with international standards for the conduct
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5 472 of epidemiological studies, included in the International Guidelines for Ethical Review of
6
7 473 Epidemiological Studies [36]. This is a prospective intervention study mainly focused on
8
9 474 the collection of information from data recorded by health professionals in the Osakidetza
10
11 475 EHR (OSABIDE) under routine clinical practice conditions. The process indicators
12
13 476 related to the professionals' clinical practice (prescription of statins and record in the
14
15 477 EHR of provision of personalized healthy lifestyle advice on the need to increase physical
16
17 478 activity, follow a healthy diet and smoking cessation), patients' sociodemographic and
18
19 479 clinical characteristics (age, sex, CVR, active health problems recorded in the EHR,
20
21 480 socioeconomic status, etc.) and clinical outcomes will be extracted from OSABIDE
22
23 481 through the corporate Oracle Business Intelligence platform. In particular, for the
24
25 482 provision of healthy lifestyle advice, OSABIDE includes a specific electronic form to
26
27 483 check that each single piece of advice (diet, exercise, tobacco quitting) was or was not
28
29 484 provided. The Primary Care Research Unit of Bizkaia is formally authorized to extract
30
31 485 and use data from the EHR for research purposes by the Healthcare Directorate of
32
33 486 Osakidetza. On the other hand, it will be necessary to inform participants (professionals
34
35 487 and patients) about the study and obtain their written informed consent concerning the
36
37 488 information directly collected from them through the key informant semi-structured
38
39 489 interviews (Supplemental File 2 and 3). All the information regarding the study subjects,
40
41 490 either expressly extracted for this research from EHRs or collected from the participants,
42
43 491 will be protected and treated confidentially for all purposes, in accordance with the
44
45 492 provisions of the Spanish Organic Law 3/2018, of 5 December, on Personal Data
46
47 493 Protection and digital rights guarantee (LOPD-GDD) and the provisions of Regulation
48
49 494 (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016, on the
50
51 495 protection of natural persons with regard to the processing of personal data and on the
52
53 496 free movement of such data (General Data Protection Regulation, RGPD). Specifically,
54
55 497 all data will be anonymously documented and de-identified, linked to a unique code that
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57 498 is meaningless without the context of the system. The final resulting database will be
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3 499 exported to a formatted plain text file that then will be compressed and encrypted using
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5 500 a secure algorithm and subsequently will be processed and included in a robust and
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7 501 secure database server.
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11 503 **Patient and public involvement**

13 504 Patients were involved in the DE-imFAR Phase I project as one of the main stakeholders
14
15 505 (health professionals, patients, and researchers) in the formative process conducted to
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17 506 map and design de-implementation strategies to reduce PIP, which will be evaluated in
18
19 507 the DE-imFAR Phase II project. Specifically, during the Phase I project, a focus group
20
21 508 with six patients was conducted to ascertain patients' experience with the clinical practice
22
23 509 of statin prescription and triangulate physicians discourse [14].
24
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26
27 510 During the Phase II project, semi-structured interviews will be conducted with patients to
28
29 511 assess their experience and perception of the clinical care received as a result of their
30
31 512 healthcare professionals' exposure to the different de-implementation strategies. These
32
33 513 interviews will help to better understand from the perspective of the study participants
34
35 514 the reasons why the strategies work (or do not), to explain the variations in the outcomes
36
37 515 and to identify the key strategy components and those that need to be optimized as well
38
39 516 as triangulating the analysis.
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43 518 **DISCUSSION**

45
46 519 The goal of the present study is to improve CVD primary prevention clinical practice in a
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48 520 real world setting in primary care by putting into practice procedures and methods for the
49
50 521 design, deployment, and evaluation of implementation/de-implementation strategies
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52 522 informed by behavioral and implementation sciences. Specifically, the Phase II of the
53
54 523 DE-imFAR study focuses on reducing PIP of statins in CVD primary prevention in
55
56 524 patients with moderate hypercholesterolemia and low CVR and fostering healthy lifestyle
57
58 525 promotion as the recommended treatment option. To do so, the study will deploy several
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3 526 de-implementation strategies derived from the Phase I formative study that targets key
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5 527 determinants of the decision-making process involved in the provision of CVD primary
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7 528 prevention by FPs. If the results are successful, policymakers and health managers and
8
9 529 professionals will have valid and robust, locally relevant evidence that will support the
10
11 530 need to introduce these innovations in methods and procedures informed by
12
13 531 implementation science to tackle the hard task of reducing the burden of low-value
14
15 532 pharmacological prescription in clinical care services.
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18 533

20 534 **ETHICS AND DISSEMINATION**

22 535 The research protocol (version 1; 170221) was approved by the Basque Country Clinical
23
24 536 Research Ethics Committee (Reference: EOM2022018, approved on 30 March 2022)
25
26 537 and was registered in the U.S. NLM ClinicalTrials.gov database (ClinicalTrials.gov
27
28 538 Identifier NCT04022850, Registered 17 July 2019; Last update 5 February 2024).The
29
30 539 Primary Care Research Unit of Bizkaia is explicitly authorized by the Healthcare
31
32 540 Directorate of Osakidetza - Basque Health Service to extract and use data from EHRs
33
34 541 for research purposes. Since data supporting the present study will mostly concern
35
36 542 routine data retrieved from the EHR of the Basque Health Service-Osakidetza, it will be
37
38 543 only shared upon justified request to the study guarantors. The results of this study will
39
40 544 be disseminated via publication in scientific peer-reviewed journals.
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44 545

46 546 **LIST OF ABBREVIATIONS**

48 547 EHR: Electronic health record
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50 548 BCW: Behavior Change Wheel
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52 549 CI: Confidence interval
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54 550 CVD: Cardiovascular disease
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56 551 CVR: Cardiovascular risk
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58 552 CPG: Clinical practice guideline
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3 553 FP: Family physician
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5 554 IHO: Integrated Healthcare Organization
6
7 555 LDL: Low-density lipoprotein
8
9 556 PIP: Potentially inappropriate prescribing
10
11 557 PC: Primary care
12
13 558 RE-AIM: Reach, Effectiveness, Adoption, Implementation, and Maintenance
14
15 559 TC: Total cholesterol
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17 560 TDF: Theoretical Domains Framework
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30 701

702 **AUTHORS' CONTRIBUTIONS**

703 AS, JIP, and GG conceived the idea and are the study guarantors. They are primarily
704 responsible for the study design and planning, obtained funding, will be responsible for
705 project coordination and supervision, analysis and interpretation of results, and were
706 responsible for manuscript preparation. RSR, IL, RSV, JAQ, RR, AE, CM, MMC, MM,
707 CGR, RS, MOL, SC, NMI, ML, MGST, and AGA are co-investigators of the projects and
708 collaborated in the study design and/or manuscript preparation; and they will be
709 responsible for study coordination and interpretation of results. AS, JIP, and AGA will be
710 responsible for the analysis of results. All authors read and approved the final version of
711 the manuscript.

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1
2
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4
5 717 Union – NextGenerationEU funds, that finance the actions of the Recovery and
6
7 718 Resilience Facility (Mecanismo para la Recuperación y la Resiliencia -MRR), through
8
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10
11 720 the Basque Government (funded projects 2018111085 and 2021111024). The funding
12
13 721 bodies have had no role in the design of the study, collection, analysis, or interpretation
14
15 722 of data or the writing of the manuscript.
16
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18 723

724 **COMPETING INTERESTS STATEMENT**

725 The authors declare that they have no competing interests.
726

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730 Integration) and Nagore Zarraonandia Ayo (Directorate of Care Integration) at
731 Ezkerraldea-Enkarterri-Cruces Integrated Health Organization, Lourdes Vivanco
732 (Medical Directorate) and Vanesa Martín (Quality Unit) at Barakaldo-Sestao Integrated
733 Health Organization.
734

735 **WORD COUNT**

736 4515 words excluding title page, abstract, strengths and limitations of this study, list of
737 abbreviations, full references, authors' contributions, funding statement, competing
738 interests statement and acknowledgements.

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739 **FIGURES**

740 **Figure 1. Study design diagram. (PDF format)**

741 Note: FP: Family Physician; IHO: Integrated Healthcare Organization; R: Randomization.

For peer review only

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3 742 **SUPPLEMENTAL FILES**
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5 743 **Supplemental File 1 [DE-imFAR de-implementation strategies] (PDF format)**
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745 **Supplemental File 2 [DE-imFAR Phase II - Informed Consent Form for Family**
746 **Physicians (Spanish)] (PDF format)**

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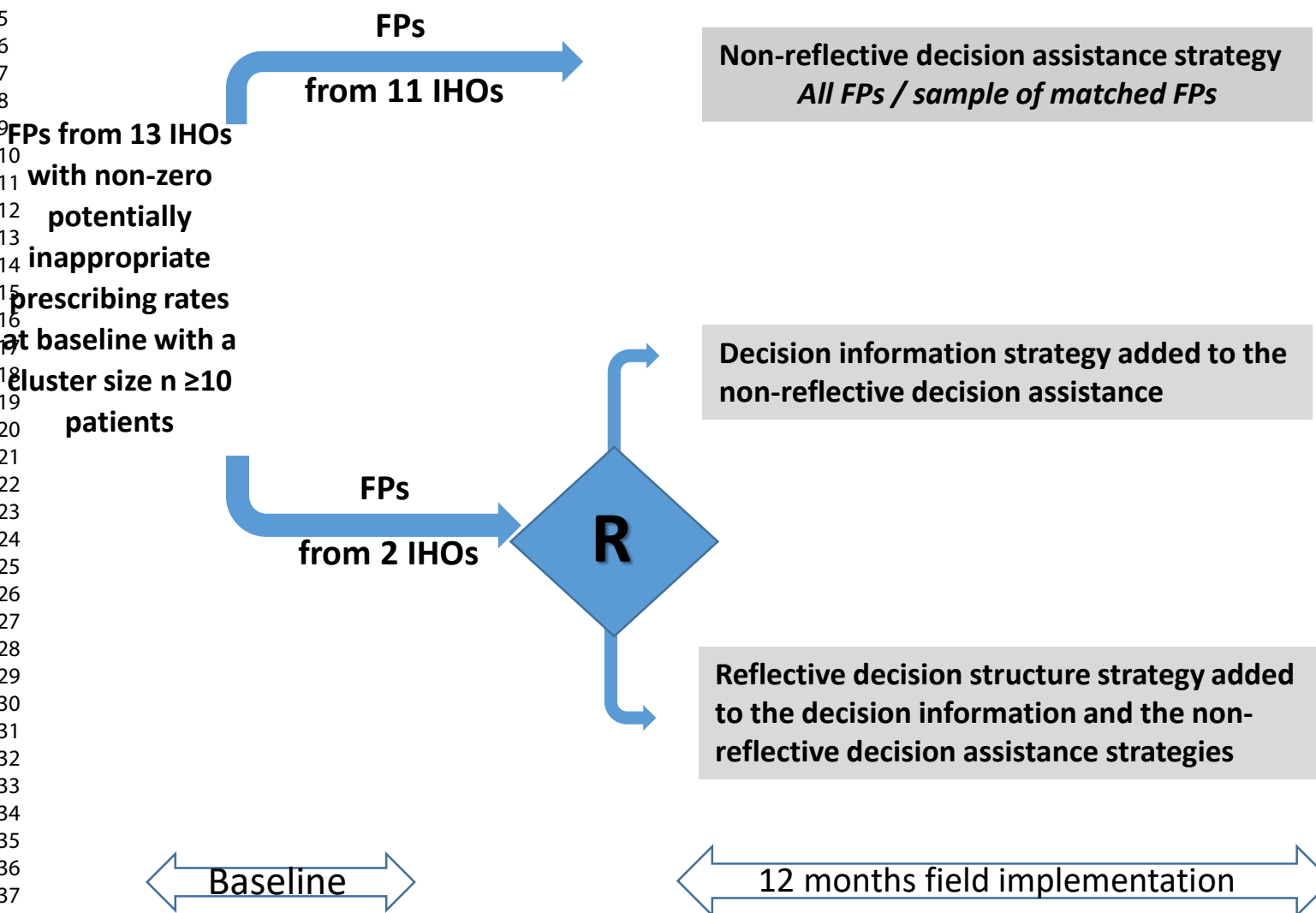
For peer review only

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3 748 **Supplemental File 3 [DE-imFAR Phase II - Informed Consent Form for Patients**
4 **(Spanish)] (PDF format)**
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Experimental implementation trial with an additional control group

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Change in the incidence of potentially inappropriate prescriptions and provision of lifestyle advice from baseline to 12 months after exposure of physicians to the compared strategies, in 40- to 74-year-old men and 45- to 74-year-old women with no history of statin use, with LDL-cholesterol levels between 70 and 189 mg/dl and/or Total Cholesterol between 200 and 289 mg/dl but without ischemic heart/cardiovascular disease and with an estimated cardiovascular risk $<7.5\%$ attending during the field-work period

Outcome

The DE-imFAR de-implementation strategies

1. Strategy - Non-reflective decision assistance strategy

Support for clinical decision-making on the primary prevention of cardiovascular disease (CVD) in low cardiovascular risk (CVR) patients integrated into the electronic health record (EHR) of the Basque Health Service (Osakidetza), based on pop-up reminders and alerts, together with an interactive media-based algorithm stating the recommended practice and a patient information sheet.

1.1. Target audience

This strategy targets all family physicians (FPs) from all 13 Integrated Healthcare Organizations (IHOs) of the Basque Health Service (Osakidetza), both in primary and specialist or hospital care.

1.2. Active components (actions) of the intervention

- “Lighthouse” guiding alert in the REGICOR CVR calculator. Reminders of recommended clinical practice in the primary prevention of CVD that pop-up in the REGICOR CVR calculator when the CVR is estimated in patients aged between 35 and 74 years old. The alert varies depending on the CVR score (<10% or ≥10%).

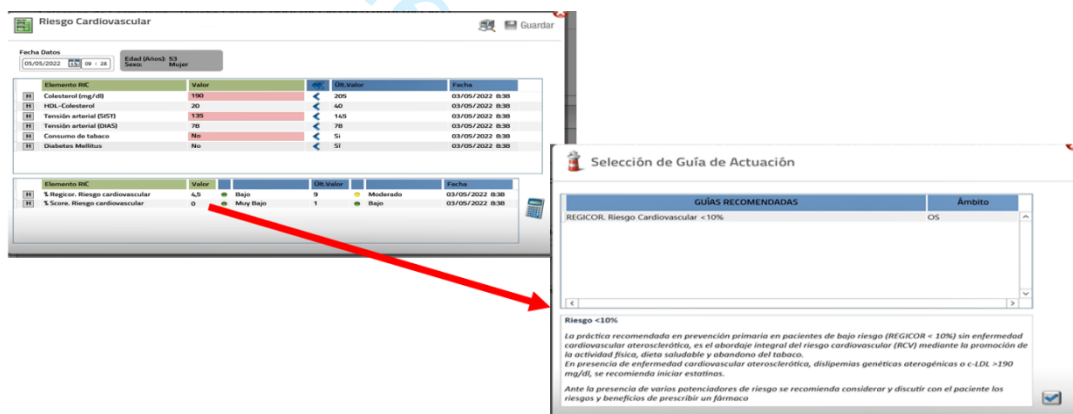


Figure 1. Pop-up reminder (“Lighthouse” guiding alert) in the REGICOR cardiovascular risk calculator when estimated cardiovascular risk score is <10%.

- Alerts in PRESBIDE. Pop-up reminders that appear when the PRESBIDE software is used to prescribe statins. There are three types of alerts depending on the patient’s age group (<35, 35-74, and ≥75 years old). Further, links are provided to a decision-making algorithm and a patient information sheet (i-botika).
- Decision-making algorithm: “Management of cholesterol as a risk factor in primary prevention of cardiovascular disease”. Clinical decision tree presenting potential courses of action based on clinical practice guidelines (CPGs), specifically for reducing cholesterol for the primary prevention of CVD in patients of different age groups and levels of CVR. Interactive decision-making support tool, developed by researchers collaborating in the DE-imFAR project, that also includes links for downloading two further documents: one providing information on CVD risk factors and the other on the 5As “Ask, Assess, Advise, Assist, Arrange” clinical intervention, recommended for promoting healthy lifestyles.

- Patient information sheet on cholesterol levels (i-botika: “Cholesterol levels are not the only thing”, developed in the framework of this project, providing information on high cholesterol levels and their role together with other risk factors associated with CVD)

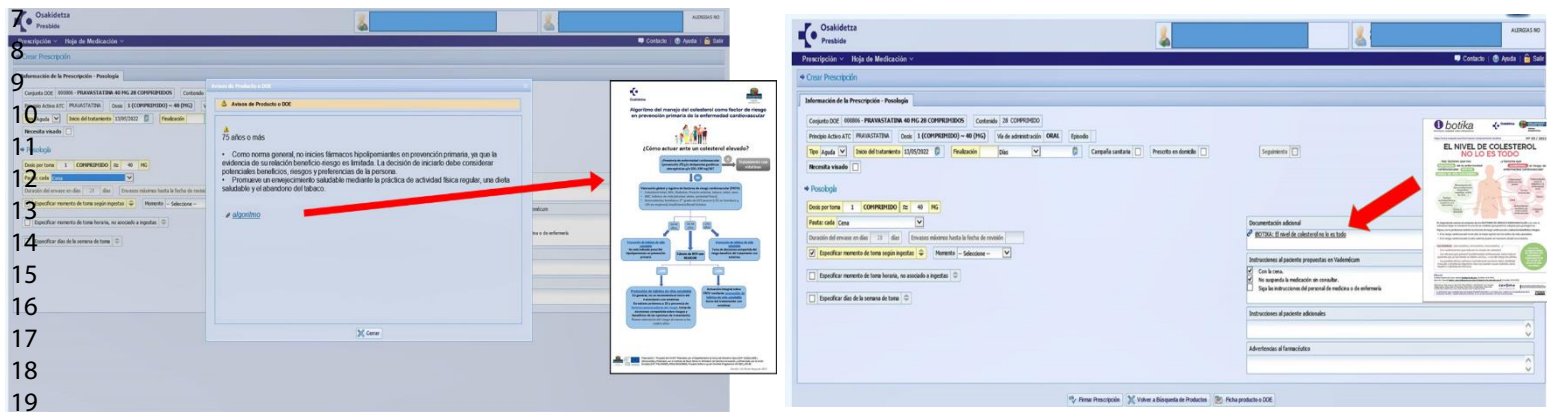


Figure 2. a). Pop-up reminder in the PRESBIDE software with recommendations on the prescribing of statins in people ≥ 75 years old that includes a link to the “Management of cholesterol as a risk factor in primary prevention of cardiovascular disease” algorithm, b) PRESBIDE form for prescribing statins, with a link to the patient information sheet (i-botika).

1.3. Objectives: *Determinant - What needs to change*

Pop-up alerts, reminders, and an algorithm

Cognitive and interpersonal skills:

- ✓ Enhance skills to enable appropriate prescribing of statins based on clinical practice recommendations

Attention, memory, and decision-making processes:

- ✓ Promote recall of recommended clinical practice in the primary prevention of CVD, reducing the impact of therapeutic inertia

Context and resources:

- ✓ Develop support systems in the EHR as reminders of and to promote the practices recommended in CPGs for the primary prevention of CVD (avoiding statins and encouraging healthy lifestyles)
- ✓ Restrict or impede inappropriate prescribing of statins due to clinical prescribing behavior driven by simplicity and speed

Emotion/Reinforcement:

- ✓ Reduce the likelihood of inappropriate prescribing due to habit, routine, or inertia (to “treat” cholesterol), through the experiencing of negative emotions when going against the recommended practice and this is made evident by alerts

Patient information sheet

Social influence (patient involvement):

- ✓ Increase patient awareness of the problems associated with the inappropriate prescribing of statins: risks vs benefits
- ✓ Increase patient knowledge of the criteria and courses of action recommended in CPGs (concerning cholesterol, CVD, and CVR)

1.4. Choice architecture techniques

A. Decision Information

A1. Translate information: change the format or presentation of information but not the content.

Reframe: present the (same) information in several ways, e.g., Presenting the contents of CPGs in several different ways (i.e., text within alerts, in the form of an algorithm, etc.).

Simplify: reduce the burden of cognitive effort necessary to process the information available and increase its usefulness in the decision-making process, e.g., algorithm.

A2. Make information visible: make necessary information readily accessible.

Make external information visible: make decision-relevant information visible, e.g., text within alerts recalling the CPGs.

B. Decision structure

B1. Change choice defaults

Prompted choice: avoid the status quo bias or default effects because of inertia or assumed recommendations, e.g., pop-up alerts.

B2. Change option-related effort: change physical effort.

Increase physical effort: e.g., pop-up alerts.

C. Decision assistance

C1. Provide reminders: provide positive reminders that heighten the salience of a desired option and/or diminish the salience of an undesired option, e.g., Pop-up alerts with the recommendation to not prescribe statins.

1.5. Exposure

- “Lighthouse” guiding alert in the REGICOR CVR calculator: by clicking to “save” the result after estimating CVR
- Alerts in PRESBIDE: by starting to prescribe statins or clicking on the links to the algorithm or the patient information sheet

2. Strategy - Reflective/non-reflective decision information strategy

Corporate campaign entitled “Stopping low-value prescribing” (in Spanish: “*Abandono de prescripciones farmacológicas de escaso valor*”), promoted through a knowledge dissemination strategy based on circulars and notifications (e.g., mass mailing and internal newsletters) concerning content, informative material and documents on recommended clinical practice and improving the appropriateness and/or optimization in prescribing drug treatments, including that of statins for the primary prevention of CVD, made available to FPs on the corporate intranets of the Ezkerraldea-Enkarterri-Cruces (EEC) and Barakaldo-Sestao (BS) IHOs, part of the Basque Health Service (Osakidetza).

2.1. Target audience

This strategy targets all FPs from the EEC and BS IHOs, who will also be exposed to the first strategy, namely, non-reflective decision assistance.

2.2. Active components (actions) of the intervention

- Adherence to and implementation of best practice pages on the EEC and BS IHO intranets which have dedicated sections focused on improving the appropriateness of the use of statins providing easy access to the CPGs and recommended practice for the primary prevention of CVD.



Figure 3. Main page of the adherence to and implementation of best practice (“*Adecuación e Implementación de Buenas Prácticas*”) section on the Ezkerraldea-Enkarterri-Cruces Integrated Healthcare Organization intranet and main page of the dedicated “Stopping inappropriate prescribing of statins for the primary prevention of cardiovascular disease” section. Equivalent pages were also created on the Barakaldo-Sestao Integrated Healthcare Organization intranet.

- Corporate dissemination campaign: activities aimed at attracting FPs to the pages created on the EEC and BS IHO intranets, in order that they access the information and documents available
 - News story on the launch of the campaign with links to the pages on the corporate intranets, e.g.,

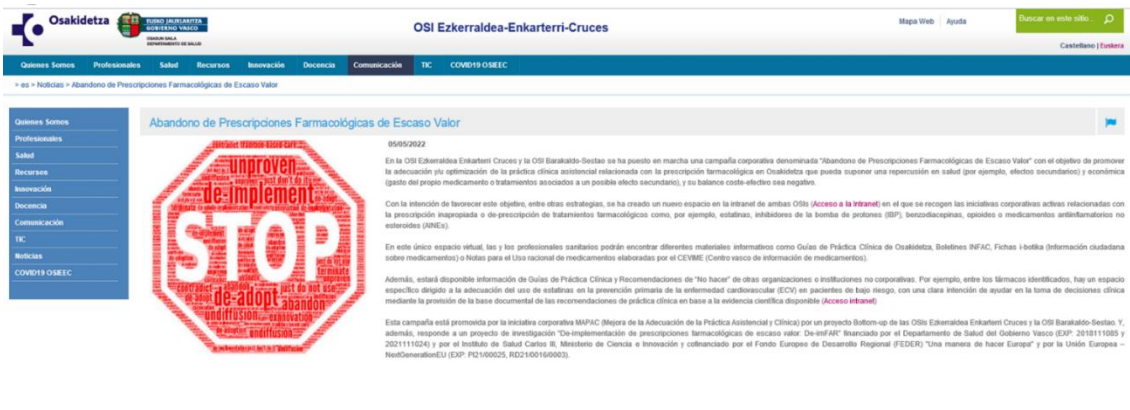


Figure 4. News story published on the Ezkerraldea-Enkarterri-Cruces Integrated Healthcare Organization intranet to announce the launch of the corporate “Stopping low-value prescribing” campaign and the development of pages on its intranet and that of the Barakaldo-Sestao Integrated Healthcare Organization, on May 5, 2022. The story was also published on the Barakaldo-Sestao Integrated Healthcare Organization intranet.

- **Monthly newsletter:** reporting of the launch of the campaign in the monthly newsletter circulated by the BS IHO to all its employees
- **Mass mailing** on the launch of the campaign with links to the pages on the corporate intranets
- **Revitalization of the corporate campaign:** periodic publication of news stories on the EEC and BS IHO intranets with content related to the campaign informing FPs of the updating of content/informative materials (for example, any changes in the recommendations in CPGs and INFAC [pharmacotherapy information] newsletters) on the dedicated pages on the intranets of both IHOs, aimed at improving the appropriateness of the use of statins in primary prevention of CVD, including links to these pages.
- **Justification email** from the Healthcare Management of the Basque Health Service, telling all FPs about the initiatives being put in place to improve the approach to the prevention of CVD, improving the appropriateness of statin prescribing, and encouraging the provision of healthy lifestyle advice, among other components.

2.3. Objectives: Determinant - *What needs to change*

Knowledge:

- ✓ Increase awareness of the problem of the inappropriate prescribing of statins
- ✓ Increase knowledge of the CPGs on the primary prevention of CVD, in particular, the appropriate or recommended care as a function of the estimated CVR
- ✓ Provide evidence-based standardized and up-to-date clinical guidelines

Behavior regulation:

- ✓ Encourage reflection on practice/performance in relation to inappropriate prescribing of statins in the primary prevention of CVD

Beliefs about capabilities:

- ✓ Strengthen the belief that the prescribing of statins is not as straightforward and safe as might be thought
- ✓ Strengthen the belief that statin treatment is not easy for patients (dosage)

Beliefs about consequences:

- ✓ Strengthen the belief that not prescribing statins for the primary prevention of CVD is not the same as “not treating”.
- ✓ Strengthen the belief that statins are not more effective in reducing cardiovascular events than healthy lifestyle promotion in the primary prevention of CVD
- ✓ Strengthen the belief that statins, in the primary prevention of CVD, may have adverse effects and are not risk-free.

Professional/social role and identity:

- ✓ Foster the belief that appropriate primary prevention of CVD is considered important at the organizational level and among peers.
- ✓ Strengthen understanding that the role of FPs goes beyond that of prescribing drugs.

Social influence:

- ✓ Increase awareness of the organizational goals for reducing inappropriate prescribing of statins in the primary prevention of CVD.
- ✓ Increase patient awareness of the problems associated with the inappropriate prescribing of statins: risks vs benefits
- ✓ Increase patient knowledge of the criteria and recommended courses of action (concerning cholesterol, CVD, and CVR)

Emotion/reinforcement:

- ✓ Reduce the likelihood of inappropriate prescribing due to habit, routine, or inertia (to “treat” cholesterol), through the experiencing of negative emotions when going against the recommended clinical practice and this is made evident by alerts.

Cognitive and interpersonal skills:

- ✓ Enhance skills to enable the appropriate prescribing of statins based on CPGs.

2.4. Choice architecture techniques**A. Decision Information**

A1. Translate Information: change the format or presentation of information but not the content.

Reframe: present the (same) information in several ways, e.g., clinical guidelines, algorithm, patient information leaflet.

Simplify: reduce the burden of cognitive effort necessary to process the information available and increase its usefulness in the decision-making process, e.g., algorithm.

A2. Make information visible: make necessary information readily accessible.

Make external information visible: make decision-relevant information visible, e.g., Links about inappropriate statin prescription in the Basque Health Service (Osakidetza), adverse effects of statins and cholesterol treatment, and promotion of the campaign through emails and news.

A3. Provide social reference point: influence decision-making through other’s behavior.

Refer to descriptive norm: depict the observable behavior of other people to impact on the decision-making process, e.g., links about inappropriate statin prescription in the Basque Health Service (Osakidetza).

Refer to opinion leader: use them as information disseminators to improve the impact of the campaign, e.g., Setting of goals in an email sent by an opinion leader, using the source as much as the content of the message to improve the impact of the campaign.

B. Decision structure

B2. Change option-related effort: modify the physical or financial effort involved in the decision-making process.

Change physical effort, e.g., decreasing physical effort by making all theme-related information accessible on the same website and including links to the website in the text of emails and news stories.

C. Decision assistance

C1. Provide reminders: provide positive reminders that heighten the salience of a desired option and/or diminish the salience of an undesired option, e.g., links to clinical guidelines with recommended practice about CVD primary prevention, and information about adverse effects of statins.

2.5. Exposure

- By accessing the pages of the EEC and BS IHO corporate intranet and clicking on the links to the CPGs, INFAC newsletters, i-botika patient information sheets, recommendations, etc. available in the dedicated “Stopping inappropriate prescribing of statins for the primary prevention of cardiovascular disease” section
- By accessing the news section on the dedicated pages on the intranets of EEC and BS IHOs

3. Strategy - Reflective decision structure strategy

Sending of regular personalized *Audit & Feedback (A&F)* reports with practice- and organizational-level performance indicators of the FPs regarding inappropriate prescribing of statins and healthy lifestyle promotion in the primary prevention of CVD in low-risk patients in the Basque Health Service

3.1. Target audience

This strategy targets a randomly selected set of FPs from the EEC and BS IHOs, who will also be exposed to the previously described interventions, namely, *non-reflective decision assistance and decision information*.

3.2. Active components (actions) of the intervention

- Informative email concerning the sending of A&F reports, including the possibility to opt out: email with information for primary care FPs of the EEC and BS IHOs on the sending of regular personalized A&F reports, in the framework of the corporate campaign, with the goal of encouraging adherence to recommendations and stopping inappropriate prescribing of statins
- A&F reports mailing: periodic A&F reports with indicators describing global performance across the Basque Health Service: a) rate of new potentially inappropriate prescribing of statins to people without CVD and with REGICOR CVR scores <7.5% and practice in the promotion of healthy habits in these patients; b) rate of documentation of CVR (in the 2 years before the prescription date) in all 40- to 75-year-olds with no clinical history of CVR who are newly prescribed statins. Future A&F reports are expected to contain a link to a short voluntary exercise on goal setting for improving the appropriateness of statin prescribing for the primary prevention of CVD

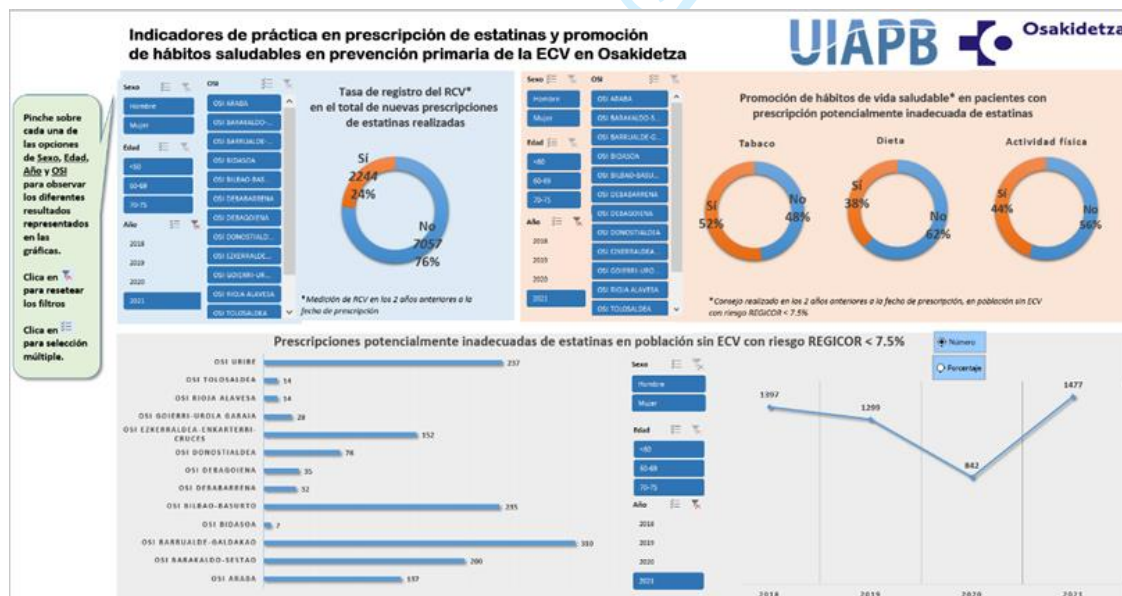


Figure 5. Draft of the Audit & Feedback report with practice- and organizational-level performance indicators of the family physicians regarding inappropriate prescribing of statins and healthy lifestyle promotion in the primary prevention of cardiovascular disease in low-risk patients in the Basque Health Service

3.3. Objectives: Determinant - What needs to change

Knowledge:

- ✓ Increase awareness of the problem of the inappropriate prescribing of statins

Behavior regulation:

- ✓ Make data available on inappropriate prescribing of statins for the primary prevention of CVD
- ✓ Provide tools for the setting of clear specific goals, at personal and organizational levels, regarding the reduction of inappropriate prescribing of statins for the primary prevention of CVD

Active reflection on personal practice:

- ✓ Encourage further reflection on practice/performance in relation to inappropriate prescribing of statins for the primary prevention of CVD

Intentions:

- ✓ Reduce the intention to prescribe statins inappropriately and increase the intention to promote healthy lifestyles for the primary prevention of CVD

Goals:

- ✓ Encourage commitment to practice in the primary prevention of CVD that is in accordance with recommendations
- ✓ Increase the motivation to promote healthy lifestyles in the primary prevention of CVD

Beliefs about capabilities:

- ✓ Strengthen self-efficacy and enhance the skills required for promoting healthy lifestyles

Emotion:

- ✓ Strengthen self-confidence about not prescribing statins for the primary prevention of CVD
- ✓ Foster belief in the safety of and trust in the courses of action recommended in the guidelines
- ✓ Experience a negative emotion after inappropriate prescribing

Professional/social role and identity:

- ✓ Foster the belief that appropriate primary prevention of CVD is considered important at the organizational level and among peers
- ✓ Strengthen understanding that the role of FPs goes beyond prescribing drugs

Reinforcement:

- ✓ Generate positive/negative reinforcement related to good/poor performance in the primary prevention of CVD.

3.4. Choice architecture techniques

A. Decision Information

A1. Translate Information: change the format or presentation of information but not the content.

Simplify: reduce the burden of cognitive effort necessary to process the information available and increase its usefulness in the decision-making process, e.g., presenting prescription rate data in a simple, user-friendly way, namely, on a dashboard.

A2. Make information visible: make necessary information readily accessible.

Make own behavior visible: feedback.

Make external information visible: make decision-relevant information visible, e.g., showing the prescription rates of other FPs and other IHOs.

A3. Provide social reference point: influence decision-making through the behavior of others.

Refer to descriptive norm: depict the observable behavior of other people to impact on the decision-making process, e.g., showing other FPs' prescribing behavior.

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4 **B. Decision structure**

5 **B2. Change opinion-related effort:** modify the physical or financial effort involved in the
6 decision-making process.

7 **Decrease physical effort:** collect all prescribing data in one file, e.g., dashboard.
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10 **C. Decision assistance**

11 **C2. Facilitate commitment:** overcome constrained self-control and bridge the intention-
12 behavior gap.

13 **Support self-commitment:** arrange with the aim of helping fulfill a plan, e.g., self-commitment
14 questionnaire
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17 **3.5. Exposure**

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Annex I. GLOSSARY OF TERMS

1. De-implementation: De-implementation is defined as the process of reducing or abandoning the use of guidelines practices, interventions or policies that are found to be ineffective, are not proven to be effective, do not have adequate scientific support, are less effective or less cost-effective than an alternative one, are potentially harmful to patients, or that represent low-value care.

2. Implementation: Implementation (commonly defined as “to do”), in the context of Implementation Science refers to the actively designed process of putting into practice or integrating evidence-based interventions (e.g., practice, program, policy,...) within a specific real-world setting.

3. Theoretical Domains Framework (TDF): The Theoretical Domains Framework (TDF) is an integrative framework developed from a synthesis of psychological theories as a vehicle to help apply theoretical approaches to interventions aimed at behavior change. The TDF comprises of 14 domains and 84 constructs that allows synthesis of a multitude of coherent behavior change theories into a single framework that allows assessment and explanation of behavioral problems and associated barriers and enablers, and inform the design of appropriately targeted interventions.

References:

1. Michie S, Johnston M, Abraham C, et al. Making psychological theory useful for implementing evidence based practice: a consensus approach. *Qual Saf Health Care*. 2005;14(1):26-33. doi:10.1136/qshc.2004.011155.
2. Cane J, O'Connor D, Michie S. Validation of the theoretical domains framework for use in behaviour change and implementation research. *Implement Sci*. 2012;7:37. doi:10.1186/1748-5908-7-37.
3. Atkins L, Francis J, Islam R, et al. A guide to using the Theoretical Domains Framework of behaviour change to investigate implementation problems. *Implement Sci*. 2017;12(1):77. doi: 10.1186/s13012-017-0605-9.

4. Behavior Change Wheel (BCW): The Behavior Change Wheel (BCW) is a theory- and evidence-based tool that provides a process for designing or refining behavior change interventions and policies. Its purpose is to promote a systematic and comprehensive analysis of behavior in its context to guide change. It can be used to identify the interventions and policies likely to be effective in changing behavior.

Reference:

1. Michie S, van Stralen MM, West R. The behaviour change wheel: a new method for characterising and designing behaviour change interventions. *Implement Sci*. 2011 23;6:42. Published 2011 Apr 23. doi:10.1186/1748-5908-6-42.

5. Statin: Statins, also known as HMG-CoA reductase inhibitors, are a class of lipid-lowering medications that are used to lower blood low-density lipoprotein (LDL) cholesterol levels.

6. Non-reflective: Non-reflective processes, such as habits and routines, are defined as those factors that bypass conscious deliberation and so generate actions fast, effortlessly, automatically and with little deliberation and awareness.

7. Reflective: Reflective processes involves conscious deliberation over situational demands, available options and/or outcome expectancies; and therefore generate slow and effortful actions or behaviors via reasoned intentions.

8. Decision assistance strategy. Decision information strategy. Decision structure strategy

According to the taxonomy suggested by Münscher et al., there are three broad categories of choice architecture intervention techniques: decision information, decision structure, and decision assistance (Münscher et al., 2016).

- i) **Decision information** interventions aim to facilitate access to decision-relevant information without altering the options themselves by increasing its availability, comprehensibility, and/or personal relevance to the decision maker. There are several ways of achieving it, such as (re)arranging existing information or changing its presentation/format, providing social reference point, etc.
- ii) **Decision structure** interventions target the way in which the choice options are organized and structured through the arrangement of choice alternatives and the format of decision making, which includes setting default options, rearranging their composition, and changing option-related efforts or consequences of selecting it.
- iii) **Decision assistance** interventions aim to bridge the intention–behavior gap by reinforcing self-regulation by providing decision makers with further assistance to help them follow through with their intentions. To do so, examples of decision assistance interventions techniques include provision of reminders of the desirable behavioral option as well as facilitating deliberate commitment to beneficial actions.

References:

1. Münscher R, Vetter M, Scheuerle T. A review and taxonomy of choice architecture techniques. *J Behav Decis Mak.* 2016;29(5):511-24. doi.org/10.1002/bdm.1897.
2. Mertens S, Herberz M, Hahnel UJJ, Brosch T. The effectiveness of nudging: A meta-analysis of choice architecture interventions across behavioral domains. *Proc Natl Acad Sci USA.* 2022;119(1):e2107346118. doi: 10.1073/pnas.2107346118. Erratum in: *Proc Natl Acad Sci USA.* 2022;119(19):e2204059119.

9. Audit & feedback (A&F): Audit and feedback is a strategy that aims to encourage individuals to change their practice and improve their performance. In the audit process, an individual's professional practice or performance is assessed and monitored based on specific, pre-defined criteria or standards. Then, the results of the comparison is fed back to the individual in a structured manner.



Hoja de Información al Profesional de la salud y Consentimiento Informado

Título: Efectividad de estrategias de de-implementación para favorecer el abandono de prescripciones farmacológicas de bajo valor en prevención primaria de la ECV: proyecto De-imFAR Fase II

Investigador Principal: Álvaro Sánchez Pérez

Servicio/Centro: Subdirección para la coordinación de atención primaria/Unidad de investigación atención primaria-IIS Biocruces Bizkaia

Entidad financiadora: Instituto de salud Carlos III

Apreciado Sr./a,

Osakidetza-Servicio Vasco de Salud, con el propósito de mejorar la calidad en la prestación de servicios de salud hacia la ciudadanía, le invita a participar en el estudio “Efectividad de estrategias de de-implementación para favorecer el abandono de prescripciones farmacológicas de bajo valor en prevención primaria de la ECV: proyecto De-imFAR Fase II”.

Antes de decidir si desea participar, es importante que entienda los objetivos, la importancia de su participación y en qué consistirá, además de qué uso se dará a los datos recogidos y los posibles beneficios y riesgos.

Léalo atentamente y consulte cualquier duda con los miembros del equipo de investigación.



1. OBJETO DEL GRUPO DE DISCUSIÓN

El objetivo de los grupos de discusión del Proyecto De-ImFAR es generar conocimiento –a través de las percepciones de los/las profesionales de medicina de atención primaria- sobre la práctica clínica en prevención primaria de eventos cardiovasculares en pacientes de bajo riesgo. A través de una serie de preguntas abiertas se analizarán diferentes aspectos relacionados con el manejo del riesgo cardiovascular en estos pacientes, tratando de conocer la opinión de todos los integrantes del grupo sobre este tema.

No existen respuestas buenas o malas. Cualquier integrante del grupo está invitado a expresar libremente su opinión y a respetar la de los otros integrantes, aunque sea diferente de la suya.

2. PARTICIPACIÓN Y RETIRADA DEL ESTUDIO

Este estudio está aprobado por el Comité de Ética de la Investigación con Medicamentos de Euskadi (CEIm-E). Su participación en el mismo es voluntaria y en cualquier momento puede decidir abandonarlo, aunque haya proporcionado el consentimiento y el estudio esté en pleno desarrollo. Además, usted tiene derecho a solicitar al equipo investigador del estudio, en cualquier momento, y sin necesidad de especificar el motivo, la eliminación de sus datos.

3. DESARROLLO DEL ESTUDIO

Se realizará una sola entrevista llevada a cabo por dos investigadores con experiencia en métodos de investigación cualitativa, así como en el campo clínico y el proyecto. En dicha entrevista se le harán preguntas sobre su percepción y adaptación a las intervenciones implantadas. La discusión grupal será grabada (en formato audio) con el fin de transcribirla íntegramente. Esto permite a los miembros del equipo participar en la discusión sin necesidad de tomar notas, evitándose así el riesgo de no reflejar fidedignamente las opiniones expresadas por los miembros del grupo.



4. USO Y CONFIDENCIALIDAD DE LOS DATOS

Los datos que se obtengan en el grupo de discusión se utilizarán únicamente con fines de investigación y solamente por parte del equipo de investigación de la Unidad de Investigación de Atención Primaria de Bizkaia (UIAPB). Todas las opiniones expresadas por los/las participantes serán tratadas de manera anónima y confidencial. Se le informa de que no se va a recoger ningún dato de carácter personal.

El estudio cumple lo establecido en el REGLAMENTO (UE) 2016/679 DEL PARLAMENTO EUROPEO Y DEL CONSEJO de 27 de abril de 2016 relativo a la protección de las personas físicas en lo que respecta al tratamiento de datos personales y a la libre circulación de estos datos. Se le solicita también su consentimiento para la realización de este proyecto de investigación conforme a las exigencias del Reglamento Europeo 2016/679 de Protección de Datos y a la Ley Orgánica 3/2018, de 5 de diciembre, de Protección de Datos Personales y garantía de los derechos digitales que deroga la Ley Orgánica 15/1999, de 5 de diciembre, de protección de datos personales. No se cederán datos a terceros, salvo obligación legal.

Para contactar con los responsables del estudio puede dirigirse a:

Nombre: Álvaro Sánchez Pérez

Teléfono: 946006673

e-mail: alvaro.sanchezperez@osakidetza.eus

Dirección: Edificio Biocruces 3, Plaza Cruces 12, 48903



5. DECLARACION DEL CONSENTIMIENTO INFORMADO

Título: Efectividad de estrategias de de-implementación para favorecer el abandono de prescripciones farmacológicas de bajo valor en prevención primaria de la ECV: proyecto De-imFAR Fase II

Investigador Principal: Álvaro Sánchez Pérez

Servicio/Centro: Subdirección para la coordinación de atención primaria/Unidad de investigación atención primaria-IIS Biocruces Bizkaia

Yo, Don/Doña....., Médico/a de Atención Primaria del Centro de Salud....., he leído este documento, he comprendido las explicaciones en él facilitadas acerca de la grabación del grupo de discusión y he podido resolver todas las preguntas que he planteado al respecto. Comprendo que mi participación en este ensayo es voluntaria y que puedo retirarme en cualquier momento.

También he sido informado/a de que mis datos personales serán protegidos y serán utilizados únicamente con fines de investigación por el equipo de investigadores de la Unidad de Investigación de Atención Primaria de Bizkaia (UIAPB).

Tomando todo ello en consideración y en tales condiciones, CONSIENTO participar en el grupo de discusión, en la grabación del mismo y en que los datos que se deriven de mi participación sean utilizados para cubrir los objetivos especificados en el documento.

EN CONSECUENCIA, DOY MI CONSENTIMIENTO PARA PARTICIPAR EN ESTE PROYECTO DE INVESTIGACIÓN.

..... Firma del/la médico Firma del/la responsable del proyecto

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Hoja de Información al Paciente y Consentimiento Informado

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Antes de decidir si desea participar, es importante que entienda los objetivos, la importancia de su participación y en qué consistirá, además de qué uso se dará a los datos recogidos y los posibles beneficios y riesgos.

Léalo atentamente y consulte cualquier duda con los miembros del equipo de investigación.



1. OBJETO DEL GRUPO DE DISCUSIÓN

El objetivo de los grupos de discusión del Proyecto De-ImFAR es generar conocimiento –a través de las percepciones de los/las pacientes de atención primaria- sobre la práctica clínica en prevención primaria de eventos cardiovasculares en pacientes de bajo riesgo. A través de una serie de preguntas abiertas se analizarán diferentes aspectos relacionados con la experiencia percibida por los/las pacientes con la atención recibida, tratando de conocer la opinión de todos los integrantes del grupo sobre este tema.

No existen respuestas buenas o malas. Cualquier integrante del grupo está invitado a expresar libremente su opinión y a respetar la de los otros integrantes, aunque sea diferente de la suya.

2. PARTICIPACIÓN Y RETIRADA DEL ESTUDIO

Este estudio está aprobado por el Comité de Ética de la Investigación con Medicamentos de Euskadi (CEIm-E). Su participación en el mismo es voluntaria y en cualquier momento puede decidir abandonarlo, aunque haya proporcionado el consentimiento y el estudio esté en pleno desarrollo. Su decisión no afectará la atención sanitaria que reciba posteriormente. Además, usted tiene derecho a solicitar al equipo investigador del estudio, en cualquier momento, y sin necesidad de especificar el motivo, la eliminación de sus datos. Su participación en este estudio no supondrá para usted ningún coste económico, así como tampoco será recompensado económicamente por ello.

3. DESARROLLO DEL ESTUDIO

Se realizará una sola entrevista llevada a cabo por dos investigadores con experiencia en métodos de investigación cualitativa, así como en el campo clínico y el proyecto. En dicha entrevista se le harán preguntas sobre su experiencia y satisfacción con el servicio recibido en prevención primaria de eventos cardiovasculares.

La discusión grupal será grabada (en formato audio) con el fin de transcribirla íntegramente. Esto permite a los miembros del equipo participar en la discusión sin necesidad de tomar notas, evitándose así el riesgo de no reflejar fidedignamente las opiniones expresada por los miembros del grupo.



4. USO Y CONFIDENCIALIDAD DE LOS DATOS

Los datos que se obtengan en el grupo de discusión se utilizarán únicamente con fines de investigación y solamente por parte del equipo de investigación de la Unidad de Investigación de Atención Primaria de Bizkaia (UIAPB). Todas las opiniones expresadas por los/las participantes serán tratadas de manera anónima y confidencial. Se le informa de que no se va a recoger ningún dato de carácter personal.

El estudio cumple lo establecido en el REGLAMENTO (UE) 2016/679 DEL PARLAMENTO EUROPEO Y DEL CONSEJO de 27 de abril de 2016 relativo a la protección de las personas físicas en lo que respecta al tratamiento de datos personales y a la libre circulación de estos datos. Se le solicita también su consentimiento para la realización de este proyecto de investigación conforme a las exigencias del Reglamento Europeo 2016/679 de Protección de Datos y a la Ley Orgánica 3/2018, de 5 de diciembre, de Protección de Datos Personales y garantía de los derechos digitales que deroga la Ley Orgánica 15/1999, de 5 de diciembre, de protección de datos personales. No se cederán datos a terceros, salvo obligación legal.

Si usted tiene alguna duda o requiere cualquier tipo de información no dude en contactar con el/la médico que le informa, Dr./a _____, cuyo lugar de trabajo es el Servicio de _____ del Hospital Universitario _____; teléfono: _____ (extensión _____).

Usted también puede contactar con el Investigador Principal responsable:

Nombre: Álvaro Sánchez Pérez

Teléfono: 946006673

e-mail: alvaro.sanchezperez@osakidetza.eus

Dirección: Edificio Biocruces 3, Plaza Cruces 12, 48903



5. DECLARACION DEL CONSENTIMIENTO INFORMADO

Título: Efectividad de estrategias de de-implementación para favorecer el abandono de prescripciones farmacológicas de bajo valor en prevención primaria de la ECV: proyecto De-imFAR Fase II

Investigador Principal: Álvaro Sánchez Pérez

Investigador/a médico/a:.....

Servicio/Centro: Subdirección para la coordinación de atención primaria/Unidad de investigación atención primaria-IIS Biocruces Bizkaia

Yo, Don/Doña.....(nombre y apellidos del paciente),

he leído este documento, he comprendido las explicaciones en él facilitadas acerca de la grabación del grupo de discusión y he podido resolver todas las preguntas que he planteado al respecto. Comprendo que mi participación en este ensayo es voluntaria y que puedo retirarme en cualquier momento.

También he sido informado/a de que mis datos personales serán protegidos y serán utilizados únicamente con fines de investigación por el equipo de investigadores de la Unidad de Investigación de Atención Primaria de Bizkaia (UIAPB).

Tomando todo ello en consideración y en tales condiciones, CONSIENTO participar en el grupo de discusión, en la grabación del mismo y en que los datos que se deriven de mi participación sean utilizados para cubrir los objetivos especificados en el documento.

EN CONSECUENCIA, DOY MI CONSENTIMIENTO PARA PARTICIPAR EN ESTE PROYECTO DE INVESTIGACIÓN.

.....

.....

Firma del/la paciente

Firma del/la médico responsable

.....

.....

Nombre y apellidos

Nombre y apellidos

Fecha/...../20.....

Fecha/...../20.....



SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description	Addressed on page number
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	4
	2b	All items from the World Health Organization Trial Registration Data Set	N/A
Protocol version	3	Date and version identifier	19
Funding	4	Sources and types of financial, material, and other support	24
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	1-2
	5b	Name and contact information for the trial sponsor	2
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	25
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	N/A
Introduction			
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	5-7
	6b	Explanation for choice of comparators	7-8
Objectives	7	Specific objectives or hypotheses	8-9
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	9, 12-13

Methods: Participants, interventions, and outcomes

Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	10
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	10
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	12
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	N/A
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	N/A
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	N/A
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	13-15
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	N/A
Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	17
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	N/A

Methods: Assignment of interventions (for controlled trials)

Allocation:

Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	13
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1	Allocation		Mechanism of implementing the allocation sequence (eg, central	
2	concealment	16b	telephone; sequentially numbered, opaque, sealed envelopes),	13
3	mechanism		describing any steps to conceal the sequence until interventions are	
4			assigned	
5				
6	Implementati	16c	Who will generate the allocation sequence, who will enrol	13
7	on		participants, and who will assign participants to interventions	
8				
9	Blinding		Who will be blinded after assignment to interventions (eg, trial	
10	(masking)	17a	participants, care providers, outcome assessors, data analysts), and	13
11			how	
12				
13				
14		17b	If blinded, circumstances under which unblinding is permissible, and	
15			procedure for revealing a participant's allocated intervention during	N/A
16			the trial	
17				
18				

19 **Methods: Data collection, management, and analysis**

21	Data collection		Plans for assessment and collection of outcome, baseline, and	
22	methods	18a	other trial data, including any related processes to promote data	18
23			quality (eg, duplicate measurements, training of assessors) and a	
24			description of study instruments (eg, questionnaires, laboratory	
25			tests) along with their reliability and validity, if known. Reference to	
26			where data collection forms can be found, if not in the protocol	
27				
28				
29		18b	Plans to promote participant retention and complete follow-up,	N/A
30			including list of any outcome data to be collected for participants	
31			who discontinue or deviate from intervention protocols	
32				
33	Data		Plans for data entry, coding, security, and storage, including any	
34	management	19	related processes to promote data quality (eg, double data entry;	18
35			range checks for data values). Reference to where details of data	
36			management procedures can be found, if not in the protocol	
37				
38				
39	Statistical		Statistical methods for analysing primary and secondary outcomes.	
40	methods	20a	Reference to where other details of the statistical analysis plan can	16-17
41			be found, if not in the protocol	
42				
43		20b	Methods for any additional analyses (eg, subgroup and adjusted	17
44			analyses)	
45				
46				
47		20c	Definition of analysis population relating to protocol non-adherence	
48			(eg, as randomised analysis), and any statistical methods to handle	N/A
49			missing data (eg, multiple imputation)	
50				
51				

52 **Methods: Monitoring**

54	Data monitoring		Composition of data monitoring committee (DMC); summary of its	
55		21a	role and reporting structure; statement of whether it is independent	N/A
56			from the sponsor and competing interests; and reference to where	
57			further details about its charter can be found, if not in the protocol.	
58			Alternatively, an explanation of why a DMC is not needed	
59				
60				

1		Description of any interim analyses and stopping guidelines,	
2	21b	including who will have access to these interim results and make	N/A
3		the final decision to terminate the trial	
4			
5	Harms	Plans for collecting, assessing, reporting, and managing solicited	
6		and spontaneously reported adverse events and other unintended	N/A
7	22	effects of trial interventions or trial conduct	
8			
9	Auditing	Frequency and procedures for auditing trial conduct, if any, and	
10		whether the process will be independent from investigators and the	N/A
11	23	sponsor	
12			
13			
14			
15	Ethics and dissemination		
16	Research ethics	Plans for seeking research ethics committee/institutional review	
17	approval	board (REC/IRB) approval	19
18			
19	Protocol	Plans for communicating important protocol modifications (eg,	
20	amendments	changes to eligibility criteria, outcomes, analyses) to relevant parties	
21		(eg, investigators, REC/IRBs, trial participants, trial registries,	N/A
22	25	journals, regulators)	
23			
24			
25	Consent or	Who will obtain informed consent or assent from potential trial	
26	assent	participants or authorised surrogates, and how (see Item 32)	15,18
27			
28			
29	26b	Additional consent provisions for collection and use of participant	N/A
30		data and biological specimens in ancillary studies, if applicable	
31			
32	Confidentiality	How personal information about potential and enrolled participants	
33		will be collected, shared, and maintained in order to protect	18
34	27	confidentiality before, during, and after the trial	
35			
36	Declaration of	Financial and other competing interests for principal investigators	
37	interests	for the overall trial and each study site	25
38			
39	Access to data	Statement of who will have access to the final trial dataset, and	
40		disclosure of contractual agreements that limit such access for	19-20
41	29	investigators	
42			
43			
44	Ancillary and	Provisions, if any, for ancillary and post-trial care, and for	
45	post-trial care	compensation to those who suffer harm from trial participation	N/A
46			
47	Dissemination	Plans for investigators and sponsor to communicate trial results to	
48	policy	participants, healthcare professionals, the public, and other relevant	
49	31a	groups (eg, via publication, reporting in results databases, or other	20
50		data sharing arrangements), including any publication restrictions	
51			
52			
53	31b	Authorship eligibility guidelines and any intended use of	N/A
54		professional writers	
55			
56	31c	Plans, if any, for granting public access to the full protocol,	18
57		participant-level dataset, and statistical code	
58			
59			
60	Appendices		

1	Informed		Model consent form and other related documentation given to	
2	consent	32	participants and authorised surrogates	28,29
3	materials			
4				
5	Biological		Plans for collection, laboratory evaluation, and storage of biological	
6	specimens	33	specimens for genetic or molecular analysis in the current trial and	N/A
7			for future use in ancillary studies, if applicable	
8				

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "[Attribution-NonCommercial-NoDerivs 3.0 Unported](#)" license.

Reference: Chan A-W, Tetzlaff JM, Altman DG, et al. SPIRIT 2013 Statement: Defining standard protocol items for clinical trials. *Ann Intern Med.* 2013 Feb 5;158(3):200-207. doi: 10.7326/0003-4819-158-3-201302050-00583.