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**Comparative effectiveness of non-reflective and reflective strategies to favor de-implementation of low-value prescribing for the primary prevention of cardiovascular disease in primary care: The DE-imFAR cluster randomized implementation trial**

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**Abstract****Background**

The DE-imFAR study aims to compare the effectiveness of several de-implementation strategies targeting clinicians' decision-making processes to reduce potentially inappropriate prescribing (PIP) of statins for cardiovascular disease (CVD) primary prevention.

**Methods**

A partially randomized, cluster implementation trial with an active comparator group, involving family physicians (FPs) with non-zero incidence rates of PIP of statins in 2021, was conducted in 13 integrated healthcare organizations (IHOs) in the Basque Health Service. All eligible FPs (n = 621) were exposed to (1) a non-reflective decision assistance (DA) strategy based on reminders. FPs from two IHOs were randomized to additionally receive one of two increasingly intensive reflective strategies: (2) a knowledge dissemination decision information (DI) strategy (n=59), or (3) a DI strategy plus audit and feedback (A&F) self-reflective decision (SRD) strategy (n=59). The main outcome was the change from baseline to 12 months after deployment in the likelihood of receiving new PIP of statins and advice on lifestyle modifications, estimated with generalized mixed effects models, in 45- to 74-year-old low cardiovascular risk patients with elevated cholesterol levels but no diagnosed CVD.

**Results**

After FPs' exposure to the corresponding strategies, rates of statin PIP decreased significantly in all groups ( $p < 0.001$ ). Concerning study's main observational comparisons between strategies, though the reduction obtained by the DI and SRD strategies were 33% (adjusted OR: 0.77; 95% CI: 0.58-1.01) and 6% (aOR: 0.94; 95% CI: 0.73-1.23) higher compared to the change from the DA, estimated differences did not reach statistical significance ( $p = 0.07$ ). When comparing the two reflective strategies together (DI + SRD) with the non-reflective (DA), a significant difference ( $p = 0.038$ ) was observed, being the odds of receiving PIP of statins 19% lower (aOR: 0.81; 95% CI: 0.66-0.99). In the experimental comparison between reflective strategies (SRD vs. DI), providing A&F to FPs showed no additional effect ( $p = 0.30$ ).

### Conclusions

De-implementation strategies that targeted clinical decision-making were effective in reducing PIP of statins for CVD primary prevention. Strategies that targeted reflective thinking and increased awareness of low-value prescribing showed a trend toward greater effectiveness. **Trial Registration:** ClinicalTrials.gov Identifier NCT04022850. Registered 17 July 2019.

**Keywords:** De-implementation, low-value care, cardiovascular disease prevention, primary care, potentially inappropriate prescribing

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**Contributions to the literature**

- The DE-imFAR study contributes to scientific knowledge on effectiveness of de-implementation strategies that target reflective and non-reflective clinical decision-making processes to reduce low-value statins prescribing for CVD primary prevention.
- To test the comparative effectiveness of three additive strategies in a real-world, primary care context, the study has a design that combines experimental and non-experimental comparisons and the RE-AIM framework for the evaluation of the results in terms of public health impact.

- The study suggests that strategies providing information that prompt cognitive engagement, raise consciousness and reflection upon prescribing behavior obtain better results than less-reflective strategies such as reminders and alerts.

## 1 Background

Low-value care refers to any healthcare service considered ineffective, unnecessary, or even harmful [1, 2]. The problem of low-value care and its adverse consequences in terms of quality, safety, and wider aspect of resources, have led to an increasing interest in identifying effective de-implementation strategies [3-5]. Yet de-implementation of low-value care remains challenging because there are many multilevel factors involved in the process of delivering low-value care, including misaligned financial incentives, defensive medical practice, deference to patient requests for testing or treatment, non-evidence-based clinical heuristics, and clinical practice cultures that encourage excessive care [6-8].

Healthcare professionals face stressful conditions on a daily basis (e.g., time constraints, and work overload) under which they are required to make efficient clinical decisions related to tests, treatments, procedures, and referrals. Models and theories focused on understanding how practitioners make decisions and behave when managing low-value procedures suggest that clinical decision-making is the result of two distinct modes of cognitive processing: 1) intuitive cognition or system type 1, which is a set of largely unconscious processes in response to environmental or emotional cues and are based on previously learned, ingrained heuristics; and 2) reflective cognition or system type 2, which is a conscious process of evaluating options based on a combination of utility, risk, capabilities, and social influences [9]. It is important to understand how these ways of thinking influence behavior and clinical decisions to design effective de-implementation strategies.

Historically, reducing low-value care at physician level has been addressed with variable success through interventions that have mostly targeted rational clinical decision-making (educational based interventions, audit and feedback [A&F], etc.). On the other hand, emerging strategies to reduce low-value care using behavioral science to facilitate high-value clinical decision-making have shown promising results [7]. One promising field of research on influencing decision-making combines implementation science with behavioral economics to identify and leverage cognitive heuristics, and thereby, maximize the likelihood of desired behavior and identify ways to structure the environment to facilitate the adoption of evidence-based practices by clinicians [10, 11].

The two-phased DE-imFAR project (“De-implementation of low-value pharmacological prescribing” in Spanish) aims to design, deploy, and evaluate targeted de-implementation strategies informed by behavioral science theory to reduce low-value care in the primary prevention of cardiovascular disease (CVD). Specifically, the target low-value practice is the prescribing of statins for CVD primary prevention in low-risk patients [12]. Based on practice guidelines and recommendations [13-16], there is insufficient evidence to support statin therapy in CVD primary prevention for individuals with low cardiovascular risk (CVR), and especially in the absence of risk-enhancing factors it can be considered a potentially inappropriate prescribing (PIP). Further, for the primary prevention of CVD, the promotion of healthy lifestyles by encouraging a healthful diet, regular physical activity, and smoking cessation should be the preferred practice [13-16].

Within the DE-imFAR phase I study, representatives of the main stakeholders (health professionals, patients and researchers), following a systematic process informed by the Behavior Change Wheel [17]: a) identified the determinants of the low-value practice, b) identified targets or areas for

improvement, and c) mapped behavior change interventions and de-implementation strategies that target clinical decision-making when dealing with the primary prevention of CVD in low-risk patients in primary care (PC) [18]. The designed de-implementation strategies may be categorized as influencing decision-making through three different approaches: 1) decision assistance (i.e., to help clinical decision-making through alerts and reminder systems), 2) decision information (i.e., to facilitate decision-making by providing information and increasing knowledge through a corporate campaign encouraging the abandonment of low-value prescribing), and 3) self-reflective decisions (e.g., stimulate reflection by providing relevant information on behavior using an A&F system to enhance self-regulation in decision-making) [19].

The DE-imFAR phase II study aims to compare the effectiveness of these three de-implementation strategies that target clinicians' reflective and non-reflective decision-making processes to reduce low-value care in the primary prevention of CVD. Specifically the goal of the study is to evaluate their effectiveness in reducing the PIP of statins and in increasing the corresponding recommended practice, namely, healthy lifestyle promotion, within the context of CVD primary prevention in low-risk patients seen in PC under routine conditions of healthcare service provision.

## **2 Methods**

### **2.1 Design**

This was a partially randomized, cluster implementation trial with an active comparator group, conducted under real-world conditions in the primary prevention of CVD in PC that involved family physicians (FPs) from 13 integrated healthcare organizations (IHOs) in Basque Health Service – Osakidetza

(Figure 1). The unit of randomization and intervention was the FP, while observation and analysis were performed at physician and patient levels. This study adopted a design that combines experimental and non-experimental comparisons.

**Figure 1** CONSORT flow diagram. (PDF format). Note: FP: family physician; IHO: integrated healthcare organization; BS: Barakaldo-Sestao; EEC: Ezkerraldea-Enkarterri-Cruces; PIP: potentially inappropriate prescribing; N: number of patients; R: randomization; DA: decision assistance; DI: decision information; SRD: self-reflective decision.

The quantitative evaluation to assess the effectiveness results of the de-implementation strategies at physician and patient levels was carried out considering the year 2021 rate of new PIP of statins and healthy lifestyle advice as the baseline period measurement and a post-intervention measurement 12 months after the deployment of the strategies for the field implementation period. As displayed in Figure 2, we wanted to evaluate, on the one hand, whether any or both reflective strategies are more effective than the strategy that relies solely on clinical decision support systems (CDSS), namely, the non-reflective decision assistance (DA) strategy (observational comparison). On the other hand, we sought to evaluate whether a reflective strategy that additionally contains an A&F system—the self-reflective decision (SRD) strategy—is more effective than the CDSS-based strategy (the DA strategy) plus a corporate campaign—the decision information (DI) strategy—(experimental comparison).

**Figure 2** Timeline showing the deployment of the DE-imFAR de-implementation strategies (PDF format). FP: family physician; IHO: integrated healthcare organization; EEC: Ezkerraldea-Enkarterri-Cruces; BS: Barakaldo-Sestao; PIP: potentially inappropriate prescribing; N: number of family physicians; R:

randomization; DA: decision assistance; DI: decision information; SRD: self-reflective decision; CDSS: Clinical decision support systems; EHR: electronic health record; CVR: cardiovascular Risk; A&F: audit and feedback.

The DE-imFAR research protocol [12] was reviewed and approved by the Basque Country Clinical Research Ethics Committee (Reference: EOM2022018, March 30, 2022) and was registered in the U.S. National Library of Medicine ClinicalTrials.gov database (ClinicalTrials.gov Identifier NCT04022850, registered on July 17, 2019; last update on February 11, 2025). We used the CONSolidated Standards Of Reporting Trials (CONSORT) reporting guidelines for randomized controlled trials and the CONSORT 2025 checklist [see Additional File 1] [20-22]; and the Template for Intervention Description and Replication (TIDieR) checklist [see Additional File 2] [23] when writing this paper.

## 2.2 Participants

Eligibility criteria for the study were:

1. Physicians: FPs belonging to any of the 13 IHOs in Osakidetza with a non-zero annual incidence rate of PIP of statins at baseline (2021) with a minimum cluster size of  $n \geq 10$  patients.
2. Patients: All 40- to 74-year-old men and 45- to 74-year-old women with no history of statin use, low-density lipoprotein cholesterol levels between 70 and 189 mg/dL and/or total cholesterol between 200 and 289 mg/dL but without ischemic heart disease/CVD, and an estimated REGICOR score

<7.5% [24] who attended at least one appointment (despite of the reason for consultation) with any of the participating FPs during the study period (from May 2022 to May 2023).

### **2.3 Clinical Intervention**

The recommendations regarding when to initiate treatment in the primary prevention of CVD were described in detail in the DE-imFAR Phase II study protocol [12]. This recommended clinical practice follows both the Basque Health Service – Osakidetza and Spanish National Health System recommendations [13, 25] and several international guidelines [14-16]. There is an agreement among all guidelines that the decision to initiate statin therapy should be based on an estimation of each patient's CVR, among other factors. Thus, for the primary prevention of CVD, initiation of statins is not recommended in general for individuals aged 40 to 75 years with low CVR (REGICOR score <10%) and low-density lipoprotein cholesterol levels <190 mg/dL (i.e., as the DE-imFAR target population), noting that the presence of risk-enhancing factors should be taken into account when the CVR is close to 10%. Moreover, preventive activities should be focused on the promotion of healthy lifestyles through a healthful diet, regular physical activity, and smoking cessation.

### **2.4 De-implementation strategies**

FPs were exposed to one of the following additive de-implementation strategies (see [12] and Supplementary Table 1, Additional File 3] for a more detailed description of the strategies):

- a) Non-reflective decision assistance (DA) strategy: CDSS in the form of alerts and pop-up reminders integrated into OSABIDE, the Basque Health Service's electronic health record (EHR) system, with the aim of reminding, promoting and facilitating the recommended clinical practice for CVD primary prevention in accordance with evidence and guidelines and avoiding prescribing inertia. CDSS opened when FPs were i) estimating the CVR in the REGICOR calculator or ii) prescribing a statin in PRESBIDE (OSABIDE's computerized provider order entry [CPOE]). The PRESBIDE alert also included a link to an interactive media-based algorithm outlining the recommended clinical practice and a patient fact sheet. Behavior change techniques used included *prompts/cues, framing/reframing, and restructuring of the physical environment* [18].
- b) Decision information (DI) strategy: This strategy, which was added to the previous strategy, comprised a corporate campaign, run by the organization, entitled "Stopping low-value prescribing" (in Spanish: "*Abandono de prescripciones farmacológicas de escaso valor*") as well as the dissemination of evidence-based clinical practice guidelines for CVD primary prevention in low-risk patients. The aim of this strategy was to raise awareness of the problem of inappropriate statin prescribing and to provide FPs with standard clinical practice criteria based on independent scientific evidence for adequate CVD primary prevention. This evidence-based information was made available to FPs on the newly created "Adequacy and Implementation of Best Practices" webpage on the corporate intranets of the Barakaldo-Sestao (BS) and Ezkerraldea-Enkarterri-Cruces (EEC) IHOs and through several corporate campaign dissemination activities, such as news stories and notifications via mass e-mailing and/or internal newsletters. Several behavior change techniques were used to operationalize the strategy, including *instruction on how to perform a behavior, provision of information about social and health consequences, review of behavior goals, goal setting (behavior-organization level), communication from a credible source, and social support* [18].

c) Self-reflective decision (SRD) strategy: This strategy consisted of an A&F system component that was added to the CDSS (DA) and knowledge dissemination (DI) strategies described above. The rationale of the strategy was to provoke FPs reflection on their performance/practice through access to data on inappropriate prescribing of statins for the primary prevention of CVD and to facilitate clear and specific goal setting, at individual and organizational levels, to reduce inappropriate statin prescribing and increase healthy lifestyle promotion according to recommendations. A total of three personalized A&F reports were sent by e-mail to eligible FPs from the BS and EEC IHOs on month 1, 6 and 9 of the study. The A&F reports provided each FP with a summary of their individual performance over a specified period and compared it to organizational (each IHO and global) performance indicators through a dynamic dashboard. The displayed indicators were related to rates of inappropriate prescribing of statins and of healthy lifestyle promotion actions within the study population, and of CVR documentation in patients newly prescribed statins with no diagnosed CVD. The last two A&F reports also included a link to a short voluntary goal-setting exercise to improve the adequacy of statin prescribing in CVD primary prevention. The behavior change techniques used were, among others, *feedback on behavior*, *drawing attention to discrepancy between current behavior and goal*, *goal setting (behavior)*, *commitment*, and *review of outcome goals* [18].

## 2.5 Group allocation

As explained elsewhere [12], the DE-imFAR de-implementation strategies, aiming to improve the primary prevention of CVD, were additively deployed under real world conditions of PC in Basque Health Service – Osakidetza. Due to the technical requirements at the organizational level that oblige a system-wide implementation of any CDDS tool into OSABIDE, the non-reflective DA strategy, was applied to all FPs from the 13 IHOs of Osakidetza. In addition to this first strategy, eligible FPs belonging only to two (BS and EEC) of the 13 IHOs, in which the experimental trial was previously commissioned [18], were

randomly assigned to receive either the DI or the SRD plus the DI strategy. The allocation sequence within these two groups was generated using a specific restricted randomization scheme by one member of the research team. The sequence was concealed at the coordinating center. All FPs were allocated to the study groups after having agreed to participate through an opt-out strategy. Data analysts and the staff in charge of measurements were blind to group allocation.

## **2.6 Outcome measures**

To facilitate the evaluation of the impact of this de-implementation of low-value prescribing initiative in terms of public health, we have applied the Reach, Effectiveness, Adoption, Implementation, and Maintenance (RE-AIM) framework [26]. The outcomes reported in this paper include:

### **2.6.1 Reach**

We used healthy lifestyle counseling and statin prescribing data extracted from OSABIDE (the EHR) and PRESBIDE (the OSABIDE's CPOE) to compare the rates of patients from the target population who were treated according to the recommended clinical intervention for CVD primary prevention (i.e., no prescribing of statins and counseling on a healthy lifestyle [healthful diet, physical activity and smoking cessation]) in each de-implementation strategy group in both measurement periods. Characteristics of participants and representativeness data were extracted from information recorded by FPs in the EHR under routine clinical practice.

### **2.6.2 Effectiveness**

The primary effectiveness outcome was the differences among groups in pre-to-post change (from baseline to 12 months after target FPs' exposure to the de-implementation strategies) in the likelihood of receiving a PIP of statins and of provision of advice on lifestyle modifications, in patients from the target population eligible for CVD primary prevention. Secondary measures of effectiveness also included the change in the likelihood of CVR (REGICOR score) documentation in the EHR, from baseline to 12 months after FPs' exposure to these strategies, in patients with a new statin prescription but without ischemic heart disease/CVD. Prescribing data (PRESBIDE), provision of each type of healthy lifestyle advice, and CVR estimation data were captured by the EHR system.

### **2.6.3 Adoption**

We examined the adoption of the recommended CVD primary prevention clinical intervention by FPs in each de-implementation strategy group. To do so, we measured the percentage of eligible FPs with a reduction in the rates of PIP of statins and/or an improvement in the rates of provision of healthy lifestyle counseling from baseline to 12 months after their exposure to the compared de-implementation strategies. Data on prescribing and healthy lifestyle counseling were obtained from the EHR.

### **2.6.4 Implementation**

As detailed elsewhere [12], documented records and process indicators of the execution of and FPs' exposure to the de-implementation strategies' actions together with personalized contacts were used to assess implementation fidelity's dimensions of the adherence and dose [27-29]. In short, the degree of adherence to the planned execution of each de-implementation strategy and its active ingredients was assessed by comparing two sources of information: i)

the protocol for the de-implementation strategies [see reference 12 Supplemental File 1]; and ii) the documented records of the execution process for each strategy. Dose, defined as the extent to which the recipients actually received the components of the de-implementation strategies, was assessed through process indicators of the FPs' exposure to the de-implementation strategies' actions (accesses to the corporate intranets where the dissemination contents and A&F reports were hosted). Additionally, after the field implementation period, all FPs of the SRD group were contacted by the research team through phone calls and personalized emails to confirm the reception and interaction with the A&F reports.

#### **2.6.5 Other study covariates**

Potential confounders that may bias the estimated effect of the de-implementation strategies on changes in PIP of statins or healthy lifestyle promotion actions were also measured, both at a) physician level: n of patients attended and averaged values of their sociodemographic variables (i.e., average age, proportion of women, average CVD risk, etc.), baseline incidence rate of PIP of statins or healthy lifestyle promotion actions, etc., as applicable; and b) patient level: sociodemographic variables (age, sex, socioeconomic status) and clinical variables (baseline CVR and cholesterol level, presence of hypertension, prescribed antihypertensives, and smoking status).

#### **2.7 Analysis**

Frequencies and proportions were used to describe patient sociodemographic characteristics, and to calculate cumulative rates of PIP of statins and healthy lifestyle counseling at patient level as well as the rates of FPs who improved the provision of the recommended clinical practice in the CVD primary prevention at physician level. To perform the experimental and observational comparative effectiveness evaluation of decreases in PIP of statins and

increases in healthy lifestyle counseling among the three strategy groups, we first calculated the change in the rates from baseline to 12 months after FP exposure to the de-implementation strategies and the relative risk reduction with the corresponding 95% confidence intervals (CIs). Afterwards, multilevel analysis, i.e., generalized logistic mixed-effects models (PROC GLIMMIX), were used to estimate baseline and multivariate adjusted within- and between-group differences, adjusted odds ratios (aORs), and 95% CIs, taking into account the hierarchical and multicenter structure of data, with patients clustered within FPs, FPs nested within PC centers and PC centers nested within IHOs. Treatment group, time of measurement, time-group interaction and measured covariates, were considered as fixed effects. IHOs, PC centers and FPs were included as random effects on the intercept. This logistic models allow to estimate the average change in the odds of receiving a PIP of statins or advice on lifestyle modifications (i.e., change in the log-odds of the outcome), taking into account both the initial differences and the overall trends before and after the deployment of the compared strategies. Specifically, the group by time interaction term tests the differential change in the odds of the outcome for the different groups and time periods. Restricted maximum likelihood ratio tests and the Akaike information criteria were used to estimate the modeled parameters (fixed and random) and to determine the best covariance structure for our data, respectively. Likelihood ratio tests (significance criterion,  $p < 0.05$ ) were used to simplify the models following a backward strategy.

Finally, to compare the degree of adoption of the recommended CVD clinical intervention at physician level among groups, first, differences from pre-to-post average rates were calculated for each FP and then, logistic mixed effects models were used to estimate the likelihood (aORs and the corresponding CIs) of having reduced (yes/no) the rate of PIP of statins or improved (yes/no) the rate of each and all healthy lifestyle promotion actions, respectively.

For sample size calculation for the primary outcome in the worst-case scenario, namely, the change in annual incidence of PIP of statins within the experimental comparison, we hypothesized decreases of 20% in the DI strategy group and 50% in the SRD strategy group. Considering a baseline rate of statin PIP of 7.4% in FPs with an incidence rate of statin PIP > 0% with a minimum cluster size  $n \geq 10$  patients, an average cluster size of 39 patients, an intra-class correlation coefficient of 0.01 and a coefficient of variation of 0.63, we estimated that we needed 58 FPs for each experimental arm to achieve a statistical power of over 80% with an alpha of 0.05.

### 3 Results

According to the estimated annual incidence rate of PIP of statins at baseline (2021), out of a total of 1498 FPs across the 13 IHOs of Osakidetza, 621 FPs met the eligibility criteria for trial inclusion of having a non-zero incidence rate and a minimum cluster size of  $n \geq 10$  patients. Therefore, 503 FPs from 11 IHOs constituted the DA non-randomized arm (active comparator group) (Figure 1). Eligible FPs from two of the IHOs (BS and EEC) ( $n= 118$ ) were randomly assigned to additionally receive one of two increasingly intensive reflective strategies: i) a DI strategy based on knowledge dissemination ( $n=59$ ) and ii) the DI strategy plus A&F, that is, the SRD strategy ( $n=59$ ). Overall, 23,456 eligible patients attended at least one medical appointment with one of the 621 FPs included during the baseline period (2021), while 30,672 eligible patients attended over the field study implementation period (May 2022-May 2023). Sociodemographic and clinical characteristics of the baseline and implementation period samples in each group are summarized in Table 1.

**Table 1** Participating patients' characteristics

	Baseline period				Implementation period			
	DA (n=18960)	DI (n=2091)	SRD (n=2405)	TOTAL (n=23456)	DA (n=25219)	DI (n=2680)	SRD (n=2773)	TOTAL (n=30672)
<b>Female, n (%)</b>	11193 (59.03%)	1333 (63.75%)	1461 (60.75%)	13987 (59.63%)	14761 (58.53%)	1630 (60.82%)	1685 (60.76%)	18076 (58.93%)
<b>Male, n (%)</b>	7767 (40.97%)	758 (36.25%)	944 (39.25%)	9469 (40.37%)	10458 (41.47%)	1050 (39.18%)	1088 (39.24%)	12596 (41.07%)
<b>Age (years), mean (SD)</b>	60.81 (8.80)	60.88 (8.82)	60.46 (8.85)	60.72 (8.81)	59.24 (8.74)	58.79 (8.77)	59.24 (8.75)	59.09 (8.74)
<b>Total cholesterol (mg/dl), mean (SD)</b>	222.21 (30.56)	227.10 (26.97)	226.09 (27.39)	225.13 (30.00)	221.44 (30.33)	226.38 (25.90)	226.74 (27.15)	224.85 (29.76)
<b>REGICOR score (%), mean (SD)</b>	3.32 (1.54)	3.36 (1.51)	3.39 (1.51)	3.36 (1.53)	3.30 (1.54)	3.41 (1.57)	3.43 (1.52)	3.38 (1.54)
<b>Current smoker, n (%)</b>	3567 (18.81%)	416 (19.89%)	506 (21.04%)	4489 (19.14%)	4211 (16.70%)	483 (18.02%)	525 (18.93%)	5219 (17.02%)
<b>Former smoker, n (%)</b>	3631 (19.15%)	376 (17.98%)	417 (17.34%)	4424 (18.86%)	5518 (21.88%)	557 (20.78%)	586 (21.13%)	6661 (21.72%)
<b>Non-smoker, n (%)</b>	11762 (62.04%)	1299 (62.12%)	1482 (61.62%)	14543 (62.00%)	15490 (61.42%)	1640 (61.19%)	1662 (59.94%)	18792 (61.27%)
<b>Antihypertensive medication use, n (%)</b>	5702 (30.07%)	681 (32.57%)	827 (34.39%)	7210 (30.74%)	7364 (29.20%)	826 (30.82%)	963 (34.73%)	9153 (29.84%)

Note: DA: decision assistance; DI: decision information; SRD: self-reflective decision; n: number of patients; SD: standard deviation; REGICOR: cardiovascular risk (CVR) score.

### 3.1 Implementation

All strategies were performed from May 5, 2022, to May 5, 2023 (Figure 2). All three de-implementation strategies were deployed as planned in the protocol without adaptations. Specifically, the reminders and alerts with their associated messages and resources (the DA strategy) were integrated into the EHR on May 5, 2022. All participating FPs belonging to any of the 13 IHOs were exposed to this strategy as these alert messages opened each time an FP estimated the CVR and/or started the process of prescribing a statin.

The first action of the DI strategy, an email to all FPs from the EEC and BS IHOs notifying the 'go-live' date of the "Stopping low-value prescribing" campaign, was sent on May 5, 2022. In addition, on the same day, a news story on the launch of the corporate campaign with links to the newly created webpages was published on both corporate intranets. Subsequently, to revitalize the campaign, regular news stories were published on the EEC and BS IHO intranets to inform FPs of updates of the content and educational materials on the specific webpages on their intranets. All eligible FPs from these two IHOs received and were exposed to this second strategy as planned.

A total of three A&F reports were sent by e-mail to the FPs from the SRD group, together with instructions on how to interpret the reports. The first A&F report, sent on June 9, 2022, showed data on global performance indicators across the Basque Health Service – Osakidetza concerning the CVD primary prevention clinical practice in low-risk patients. The FPs received the second and third A&F reports on November 3, 2022 and February 10, 2023, respectively. Information gathered from email and phone call contacts with SRD group FPs confirmed that only 40% (n = 20) of them interacted with these mailings and were actually exposed to at least one A&F report reflecting an implementation failure.

### 3.2 Effectiveness

As displayed in Table 2, baseline rates of PIP of statins were 5.6%, 7.8%, and 7% in the DA, DI, and SRD groups, respectively. After FPs' exposure to the corresponding de-implementation strategies, rates of PIP of statins decreased significantly to 3.6%, 3.8%, and 4.4% ( $p < 0.001$ ) in the DA, DI and SRD groups, respectively. The highest pre-to-post reduction in the rate of PIP of statins was observed in the DI group that was exposed to a dissemination campaign in addition to the CDSS (absolute risk difference = 4%; Risk Ratio (RR): 0.49; 95% CI: 0.38-0.62). Regarding healthy lifestyle promotion, an overall decrease was observed from pre- to post-rates, only the decrease observed in the pre-to-post healthful diet promotion rates in all three groups being statistically significant ( $p < 0.001$ ). A significant increase, from 10.3% to 12.4%, was observed in the rate of CVR documentation in patients with a new statin prescription and no diagnosed ischemic heart disease or CVD in the DA group (RR: 1.20; 95% CI: 1.06-1.36) .

**Table 2** Baseline and 12-month implementation periods rates and pre-to-post Risk Ratios of new PIP of statins; provision of healthy lifestyle counseling and of the recommended CVD prevention practice; and CVR documentation.

	Baseline period				Implementation period				Within group pre-to-post Risk Ratio (95% CI)
	Total n=23456	DA n=18960	DI n=2091	SRD n=2405	Total n=30672	DA n=25219	DI n=2680	SRD n=2773	
PIP, n (%)	1390 (5.9%)	1057 (5.6%)	164 (7.8%)	169 (7%)	1136 (3.7%)	912 (3.6%)	103 (3.8%)	121 (4.4%)	DA: 0.65 (0.59-0.71) DI: 0.49 (0.38-0.62) SRD: 0.62 (0.49-0.78)
PA advice, n (%)	11654 (49.7%)	9209 (48.6%)	1100 (52.6%)	1345 (55.9%)	15143 (49.4%)	12295 (48.7%)	1335 (49.8%)	1513 (54.6%)	DA: 1.00 (0.98-1.02) DI: 0.95 (0.89-1.00) SRD: 0.97 (0.93-1.02)
Dietary advice, n (%)	8412 (35.9%)	6533 (34.7%)	832 (39.8%)	1047 (43.5%)	9594 (31.3%)	7649 (30.3%)	889 (33.2%)	1056 (38.1%)	DA: 0.88 (0.86-0.90) DI: 0.83 (0.77-0.90)

									SRD: 0.87 (0.82-0.93)
<b>SM cessation advice, n (%)</b>	12554 (53.5%)	9904 (52.2%)	1159 (55.4%)	1491 (62%)	16445 (53.6%)	13337 (52.9%)	1422 (53.1%)	1686 (60.8%)	DA: 1.01 (0.99-1.03) DI: 0.96 (0.91-1.01) SRD: 0.98 (0.94-1.02)
<b>*Recommended CVD practice, n (%)</b>	7705 (32.8%)	5992 (31.6%)	751 (35.9%)	962 (40%)	9050 (29.5%)	7212 (28.6%)	838 (31.3%)	1000 (36.1%)	DA: 0.90 (0.88-0.93) DI: 0.87 (0.80-0.94) SRD: 0.90 (0.84-0.97)
	<b>n=5402</b>	<b>n=4145</b>	<b>n=591</b>	<b>n=666</b>	<b>n=4779</b>	<b>n=3865</b>	<b>n=460</b>	<b>n=454</b>	
<b>**CVR documentation, n (%)</b>	580 (10.7%)	429 (10.3%)	83 (14%)	68 (10.2%)	605 (12.7%)	480 (12.4%)	66 (14.3%)	59 (13%)	DA: 1.20 (1.06-1.36) DI: 1.02 (0.76-1.38) SRD: 1.27 (0.92-1.77)

Note: CVD: cardiovascular disease; CVR: cardiovascular risk; EHR: electronic health record; DA: decision assistance; DI: decision information; SRD: self-reflective decision; n: number of patients; PIP: potentially inappropriate prescribing; PA: physical activity; SM: smoking; aOR: adjusted odds ratio; CI: confidence interval. All pre-to-post differences were statistically significant at  $p < 0.001$  except for PA and SM cessation advice ( $p > 0.05$ ). \*No PIP and all three healthy lifestyle (diet, physical activity and smoking cessation) promotion actions. \*\* CVR estimation and documentation in the EHR in patients newly prescribed statins with no diagnosed ischemic heart disease or CVD.

Concerning the study's main hypothesis on the observational comparative effectiveness among the de-implementation strategies for reducing the odds of receiving a PIP of statins (Table 3, first and second columns), though the reduction obtained by the DI and SRD strategies were 33% (aOR: 0.77; 95% CI: 0.58-1.01) and 6% (aOR: 0.94; 95% CI: 0.73-1.23), respectively, higher compared to the change from the DA strategy, estimated differences did not reach statistical significance ( $p = 0.07$ ). Nonetheless, when comparing the two reflective strategies together (DI + SRD) with the non-reflective (DA), a significant difference ( $p = 0.038$ ) was observed, being the odds of receiving a PIP of statins 19% less likely (aOR: 0.81; 95% CI: 0.66-0.99). In the experimental

comparison between the reflective strategies (SRD vs. DI) (Table 3, third column), no differential effect was associated with the A&F -provided in the SRD strategy but not in the DI strategy ( $p = 0.33$ ).

**Table 3** Effectiveness of de-implementation strategies in reducing PIP of statins and increasing healthy lifestyle promotion actions for CVD primary prevention in low-risk patients, and in increasing CVR documentation in the EHR in patients newly prescribed statins.

		All strategies Observational comparison		Reflective vs non-reflective strategies Observational comparison			Reflective strategies Experimental comparison		
		Difference in pre-to-post risk reduction among groups aOR (95% CI)	p-value of group*time interaction	DA	Difference in pre- to-post risk reduction among groups aOR (95% CI)	p-value of group*time interaction	DI	Difference in pre-to-post risk reduction among groups aOR (95% CI)	p-value of group*time interaction
<b>New PIP</b>	DA	1.00	0.07	DA	1.00	0.04	DI	1.00	0.33
	DI	0.77 (0.58-1.01)		DI+SRD	0.81 (0.66-0.99)		SRD	1.20 (0.83-1.73)	
	SRD	0.94 (0.73-1.23)							
<b>PA advice</b>	DA	1.00	0.06	DA	1.00	0.02	DI	1.00	0.58
	DI	0.86 (0.74-0.99)		DI+SRD	0.88 (0.79-0.98)		SRD	1.06 (0.87-1.28)	
	SRD	0.91 (0.79-1.04)							
<b>Dietary advice</b>	DA	1.00	0.13	DA	1.00	0.05	DI	1.00	0.54
	DI	0.92 (0.77-1.09)		DI+SRD	0.89 (0.78-1.00)		SRD	0.93 (0.74-1.17)	
	SRD	0.86 (0.73-1.01)							
<b>SM cessation advice</b>	DA	1.00	0.06	DA	1.00	0.02	DI	1.00	0.55
	DI	0.85 (0.74-0.99)		DI+SRD	0.88 (0.79-0.98)		SRD	1.06 (0.87-1.29)	
	SRD	0.91 (0.79-1.05)							
<b>CVR documentation</b>	DA	1.00	0.10	DA	1.00	0.40	DI	1.00	0.18
	DI	1.35 (0.91-1.99)		DI+SRD	1.14 (0.84-1.54)		SRD	0.69 (0.40-1.19)	
	SRD	0.96 (0.63-1.45)							

Note: CVD: cardiovascular disease; CVR: cardiovascular risk; EHR: electronic health record; PIP: potentially inappropriate prescribing; DA: decision assistance; DI: decision information; SRD: self-reflective decision; PA: physical activity; SM: smoking; aOR: adjusted odds ratio; CI: confidence interval.

Within the overall decrease in the provision of healthy lifestyle advice, the likelihood of providing counseling on a healthy lifestyle decreased more in the DI and SRD strategies than in the DA strategy (Table 3). Specifically, in FPs exposed to the DI strategy, the likelihood of providing physical activity and smoking cessation advice was 15% lower (aOR for physical activity: 0.86; 95% CI: 0.74-0.99; aOR for smoking cessation: 0.85; 95% CI: 0.74-0.99) as compared to the pre-to-post change observed in the DA strategy. However, again, the group by time interaction term for testing a differential change in the probability was not statistically significant (group by time interaction p-value = 0.06). When comparing the two reflective strategies with the non-reflective strategy, after the deployment of the strategies, the odds of receiving advice on physical activity or smoking cessation was reduced by 12% in the group of FPs exposed to the reflective strategies (DI + SRD), compared to the change in odds in the non-reflective (DA) group over the same period. With regard to the experimental comparison between the reflective strategies, the differences in the change of the odds of receiving any of the healthy lifestyle promotion actions after strategies deployment were not significant ( $p > 0.5$ ).

Finally, regarding the secondary effectiveness outcome measure, change in the likelihood of CVR documentation in the EHR in patients newly prescribed statins with no diagnosed ischemic heart disease or CVD, no significant differences were found in any of the comparisons among strategies (Table 3).

### **3.3 Reach and adoption**

The rate of low-risk patients receiving the recommended CVD primary prevention clinical intervention (Reach) (i.e., no prescribing of statins and counseling on all three healthy lifestyle behaviors), was 32.8% in the baseline period and 29.5% after FPs' exposure to the de-implementation strategies (Table 2). Therefore, the RR of receiving the recommended care in the implementation period compared to the baseline period was around 10% less likely in all groups ( $p < 0.001$ ).

Regarding physician adoption of the recommended CVD primary prevention clinical intervention [see Supplementary Table 2, Additional File 3], more than 20% of the FPs improved the recommended CVD primary prevention intervention (i.e., both practices, avoiding PIP of statins and providing advice on all three healthy lifestyle behaviors), with higher rates observed in the reflective groups (27.1% in the DI and 25.4% in the SRD group, respectively). A 74%, 72.9%, and 71.2% of FPs from the DA, DI, and SRD groups, respectively, reduced PIP of statins from baseline levels to those observed after the 12-month implementation period. And lastly, a third of FPs from the SRD (33.9%) and DI (32.2%) groups improved all healthy lifestyle promotion actions. However, differences between the compared groups in the mentioned recommended care provision rate were all not significant ( $p > 0.27$ ).

#### **4 Discussion**

The results of the present study showed that the DE-imFAR de-implementation strategies that target clinical decision-making and were developed through a systematic, comprehensive, and theory- and evidence-based framework were moderately effective in reducing PIP of statins for CVD primary prevention in low-risk patients. Differences among the three strategies when evaluating comparative effectiveness did not reach statistical significance. Nonetheless, it

seem that reflective strategies were associated with greater reductions in PIP compared to non-reflective strategies relying solely on reminders. However, the strategies studied were not successful in triggering increases in the provision of healthy lifestyle counseling.

Reducing low-value care in healthcare settings is a global priority, and further research is needed to identify effective and efficient strategies to de-implement low-value practices [30, 31]. Notably, de-implementation of these practices is challenging because of the many multilevel factors that consciously or unconsciously influence healthcare professionals to deliver low-value care [30, 32]. Behavioral science has been extensively applied for identifying factors that explain and influence behavior and designing techniques and interventions to enact behavior change of healthcare professionals [33-35]. Within the field of behavioral research, there is an emerging debate [11, 36] related to human decision-making through rational and unconscious paths and the potential of classical methods to enact behavior change based on influencing rational constructs (e.g., improving knowledge, raising awareness) versus the impact of simple and low-cost strategies based on insights from behavioral economics such as nudges or choice architecture techniques that target bounded rationality [37-40].

The DE-imFAR phase II project aimed to determine whether de-implementation reflective strategies that target physicians' conscious cognitive decision-making processes are better than strategies that rely on non-reflective or unconscious processes [12]. To do so, three strategies were implemented as planned in the protocol, without any adaptations, from May 5, 2022 to May 5, 2023: 1) a strategy that relies solely on CDSS in the form of reminders and alerts (the [non-reflective] DA strategy); 2) this first strategy and, in addition, a corporate campaign to promote the abandonment of low-value prescribing (the DI strategy); and 3) both the aforementioned strategies plus an A&F system (the SRD strategy).

The results from our study suggest that the three strategies seemed to reduce PIP of statins after their deployment compared to baseline period rates. These results need to be interpreted with caution, given that they have been obtained from comparisons in a before-and-after observational study, and hence, may have been influenced by uncontrolled confounders. Nonetheless, in general, it can be concluded that using a systematic process involving the main players to design tailored strategies to improve healthcare based on an assessment of the specific determinants of the targeted practice in a given context does enhance the chance of success [35, 41]. In this sense, the Theoretical Domains Framework and the Behavior Change Wheel have been used to both identify determinants of low-value care and guide the design and implementation of successful strategies [17, 42, 43]. For example, one of the evaluated de-implementation strategies, reminders and alerts (the DA strategy), was developed and implemented to intervene in memory and attention processes that may unconsciously induce an inappropriate approach in CVD primary prevention in low-risk patients [18]. Reminders aim to reinforce and facilitate the desired behavior by drawing individuals' attention, increasing their presence in individuals' thinking, and requiring immediate action through fast and automatic mental processes [44]. Clinical decision support in the form of alerts and prompts integrated into an EHR that appear when a physician takes a specific action have shown significant potential to reduce redundant testing, inappropriate test orders, and rates of inappropriate prescribing by improving guideline compliance or providing clinicians with information on evidence-based care [45]. In line with this previous evidence, in our study, reminders and clinical decision support systems produced a significant pre-to-post reduction in the rate of PIP of statins.

However, our study's main questions were whether any or both de-implementation strategies that primarily target reflective thinking were more effective than those seeking to influence automatic decision-making processes. Our results showed that, on the one hand, although not statistically different from the

reduction in the rates of PIP obtained in the DA non-reflective strategy, the two increasingly intensive reflective strategies showed further reductions, specially the strategy based on the knowledge dissemination campaign. But on the other hand, when comparing both reflective strategies together to the non-reflective DA strategy, the reduction in the rates of PIP after physician exposure was significantly higher. This result although not conclusive, is in line with some de-implementation theories stating that an organizational culture that promotes, prioritizes, and increases awareness to reduce low-value care is associated with better results [46]. While the decision information strategies may activate reflective thinking through raising awareness, confronting the installed heuristics and knowledge, and prompting professionals to reflect on the consequences of their actions, the self-reflective strategy may work by social influences and social comparison mechanisms by raising visibility and accountability of one's own behavior [44, 47].

Further, we expected that the most reflective strategy, in which a combination of information (corporate campaign) and reflection (A&F) takes place, would be the one that would achieve the best results. Recent work suggests that a nudge could become more effective when it incorporates elements that prompt reflection, self-awareness, and internal deliberation, which could generate long-term, persistent, and sustainable behavior change [47, 48]. On the one hand, the provision of A&F, a summary report of healthcare professional's clinical performance over a specified period of time, has been shown to have a modest effect on low-value practice de-implementation [49]. On the other, recent evidence from analysis of studies comparing de-implementation strategies suggests that adding education or A&F increases the effect of a given strategy [50]. Even further, a recently published systematic review of randomized trials evaluating the effectiveness of de-implementation strategies in reducing low-value care use in PC, concluded that provider education interventions combined with A&F could be prioritized, as this strategy had a moderate certainty of evidence [51]. This is in line with the finding that a personalized prescribing portrait on statins coupled with evidence-based educational messages decreased (by 6%) the relative probability of new statin

prescribing for primary prevention in the first year after the portrait [52]. Moreover, a study assessing the effect of a multifaceted computer-guided intervention that consisted of a point-of-care decision support system, A&F, and training was associated with an improvement in cardiovascular disease risk measurement in primary healthcare [53, 54].

To explore this, the experimental comparison of the DE-imFAR phase II study aimed to isolate the effect of A&F beyond that of other strategies, such as reminders and informative-formative interventions that have shown to be effective. Nonetheless, we have not been able to thoroughly assess the potential of A&F as a strategy for deepening the decision-making process based on rational thinking and reflection by clinicians concerning their own practice. As recent A&F theory states for an A&F intervention to be successful a set of sequential processes must take place: goal setting, data collection and analysis, feedback, recipient interaction, perception, and acceptance of the feedback, followed by intention, behavior, and clinical performance improvement (the feedback cycle; CP-FIT) [55]. Feedback becomes less effective if any individual process fails, and therefore causes the feedback cycle to stop. Within the present study, we have failed to fully achieve the communication to and reception of the measured clinical performance by FPs. If actors are not engaged in reflection through mindful thinking, automatic thinking may predominate; and thus, unconsciously maintain the *status quo* and impede adoption of the desired behavior [10]. In addition, this strategy may also have failed due to reactance by creating friction or unexpected interpretation [44].

With regard to lifestyle promotion actions, overall and similar slight decreases were observed from pre-to-post rates of patients having received advice across the three strategies and lifestyles, without significant differences being found between the strategies. It is known that a lack of time and/or skills, low self-confidence, expected outcomes, and low motivation among FPs are the main barriers that impede healthy lifestyle promotion actions in primary

prevention consultations for CVD [18]. However, within the present study, the lack of clear improvements in healthy lifestyle advice may be due to all three deployed strategies having focused mainly on reducing PIP of statins without offering specific implementation strategies to enable healthy lifestyle promotion by FPs. Special attention should be placed on ensuring equal effort is dedicated to the design and enactment of both de-implementation and implementation strategies that need to operate in parallel, especially when the reduction of one practice should be accompanied by an increase in an alternative evidence-based practice. Finally, when analyzing the degree of adoption at physician level, though the reflective strategies groups had promising additional improvement rates in providing the recommended care and of advice on all healthy lifestyle behaviors over the non-reflective strategy, differences did not reach statistical significance.

Several limitations of this study should be recognized. The first limitation lies in the planned comparisons with respect to the active comparator group as before-and-after quasi-experimental comparisons limit internal validity, making it difficult to disentangle the effects of time, secular trends, or other external influences [36]. Second, the study is also subject to a high risk of contamination derived from the randomization at FP level, since some of them share the same IHO and PC center. Third, another potential source of confounding that may contribute to the observed effects could derive from differences among IHOs in organizational culture, implementation maturity, patient mix, and baseline prescribing norms, as the DA group includes all FPs belonging to any of the 11 IHOs, while the DI and SRD groups include FPs from only 2 IHOs, which may differ systematically. Four, there may be limitations in the generalizability of the results to other health care systems even in Europe. However, the main limitation of the study is related to its fidelity. One of the main objectives of the DE-imFAR phase II study was to isolate the effect of A&F with respect to other de-implementation strategies that have shown some effectiveness in reducing low-value prescribing. Though the three additive strategies compared were implemented as planned in the protocol during the

study period without any adaptations, exposure of physicians to A&F was limited (only 40%), and hence, we are unable to assess its full potential. If one of the dimensions of fidelity of a potentially effective intervention is not achieved as planned (e.g., limited actual exposure), then it is likely that its effects are diminished [56]. Further research is needed in order to determine the impact of each of the strategies and especially the contribution of A&F within multifaceted strategies. Lastly, we would like to remark that the results could be interpreted differently considering the potential effect associated with the effort of carrying out the intervention. That is, we do not have robust, conclusive arguments to assert that the effect of the additional strategies -that seek to maximize professional reflection, but also require more effort and resource use- in terms of reduction in PIP is superior to simpler, cheaper strategies seeking to encourage changes in decision-making that do not imply deep reflection, such as the use of reminders and alerts.

## **5 Conclusions**

The DE-imFAR de-implementation strategies that targeted clinicians' decision processes seemed to reduce inappropriate prescribing of statins for the primary prevention of CVD. Results suggest that among the strategies evaluated those aimed to activate reflective decision processes are associated with greater PIP reduction. Though conclusive evidence has not been obtained due to the methodological characteristics of the study and some fidelity issues, our study may contribute to scientific knowledge about the effectiveness of strategies to de-implement low-value prescribing and the procedures used to design and develop such strategies based on well-known implementation research frameworks.

**Abbreviations**

CVD	cardiovascular disease
CVR	cardiovascular risk
PC	primary care
FP	family physician
IHO	integrated healthcare organization
PIP	potentially inappropriate prescribing
A&F	audit and feedback
CDSS	clinical decision support systems
DA	decision assistance
SRD	self-reflective decision
DI	decision information
TIDieR	Template for Intervention Description and Replication
CONSORT	CONsolidated Standards Of Reporting Trials

EHR	electronic health record
CPOE	computerized provider order entry
BCT	behavior change techniques
EEC	Ezkerraldea-Enkarterri-Cruces
BS	Barakaldo-Sestao
aOR	adjusted odds ratio
CI	confidence interval
RR	risk ratio
PA	physical activity advice
SM	smoking cessation advice
CP-FIT	Clinical Performance Feedback Intervention Theory

### **Ethics approval and consent to participate**

The DE-imFAR research protocol was reviewed and approved by the Basque Country Clinical Research Ethics Committee (Reference: EOM2022018, approved on 30 March 2022) and was registered in the U.S. NLM ClinicalTrials.gov database (ClinicalTrials.gov Identifier NCT04022850. <https://clinicaltrials.gov/study/NCT04022850>. Registered 17 July 2019; Last update 11 February 2025). The participants provided their written informed

consent to participate in this study. The Primary Care Research Unit of Bizkaia is explicitly authorized by the Healthcare Directorate of Osakidetza—Basque Health Service to extract and use data from EHRs for research purposes.

**Consent for publication**

Not applicable.

**Data availability**

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

**Competing interests**

The authors declare no competing interests.

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### **Author contributions**

AS and JIP conceived the idea and were the study guarantors. They were primarily responsible for the study design and planning, obtained funding, were responsible for project coordination and supervision, analysis and interpretation of results, and developed and drafted the manuscript. RSdR, IL, RSV, JAQ, RR, AE, CM, MM-C, MM, CG-R, LV, VM, NM-I, ML, MGSdT and AG-A were coinvestigators and collaborated in the study design, study execution and/or interpretation of results. AS, JIP and AG-A designed and performed the statistical analysis. ML and NM-I were involved in editing and reviewing the manuscript. All authors read and approved the final version of the manuscript.

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