An evidence-based toolbox for the design and implementation of selective prevention of cardio-metabolic disease

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Introduction

Cardiometabolic disease in Europe

The steady rise in cardio-metabolic disease (CMD; cardiovascular disease, diabetes mellitus, chronic kidney disease) poses a major public health issue in most developed countries. Globally, 422 million people are currently diagnosed with diabetes mellitus [1]. This constitutes a nearly 400% increase since 1980. Further, cardiovascular disease (CVD) is currently the most common cause of mortality, accounting for 29.6% of all deaths (15.6 million deaths) worldwide [2]. These numbers are staggering – especially when considering the fact that CMDs are often preventable. That is, while more fixed factors, such as low socio-economic status or a family history of poor health, certainly contribute to the likelihood of developing a CMD, other equally significant precursors relate to maladaptive, yet changeable health behaviors. These include most importantly smoking, diet, and/or leading a sedentary lifestyle. Considering the persistent increase in each of these three key risk factors, rates of CMD will in all likelihood only continue to escalate [3-5].

In order to resolve this predicament, there is a clear and present need for early detection and intervention against the development of CMD.

CMD-prevention strategies

Preventive action targeting CMD can be classified in terms of the target population. In general, there are three avenues for preventive efforts:

1. **Universal prevention** focuses on the general population as a whole (national, local, community, school, etc.). With this approach, the entire population is considered to be at risk, with no regard to individual risk factors or predispositions. From this perspective, the whole population has potential to benefit from intervention.

2. **Indicated prevention** addresses already-diagnosed individuals, and/or individuals who display early signs of CMD, but who have not yet reached the point where a clinical diagnosis can be made.

3. **Selective prevention** targets sub-groups of the general population that are determined to be at increased risk of developing CMD. By use of various indicator and risk variables, these populations are identified and interventions are tailored to their needs and circumstances.

Past research suggests that universal prevention strategies (e.g. legislation targeting unhealthy behavior) alone are insufficient to effectively control increasing CMD rates [6]. Indeed, selective prevention is often considered crucial in preventive strategies, as early detection of the high-risk population presumably provides a significant window of time for lifestyle changes. This argument is supported by studies from England and Wales indicating that a 54% reduction in CMD-mortality rates, observed between 1981 and 2000, was largely due to behavioral changes and preventive statin prescription in particular high-risk, pre-symptom populations (e.g. a 35% decrease in smokers) [7]. Thus, complementing universal preventive efforts with selective prevention initiatives (SPIs) may be the most effective way to intervene against CMD.

In spite of the theoretical practicality of SPIs, implementing such programs is often complicated by the inherent difficulty of accurately and reliably identifying the high-risk population. In the Netherlands, however, an innovative identification process of the high-risk population has generated interesting results. This program – the so-called Prevention Consultation, Cardiometabolic Risk module – comprises a stepwise process: A) A voluntary health risk assessment of the segment of the general population deemed...
to be at risk by virtue of their age (45-70 year-old, non-CMD-diagnosed individuals are invited). B) A health assessment by a GP of those people who were identified as potentially being at increased risk of developing CMD in step A. In this step, the true high-risk population is identified. C) Within the cardiovascular risk management (CVRM) program provided in general practice, individually tailored preventive action is then taken to reduce the risk level in the identified population [8]. While pilot data indicates somewhat low patient responsiveness to the program, the implementation of this SPI in the primary care sector suggests budding potential for effective identification and treatment of the high-risk population [9, 10]. While auspicious in a Dutch setting, however, implementing this program in other EU countries may not be straightforward given considerable between-country differences in health care systems [11, 12].

The implementation of selective prevention initiatives – primary care
In addition to the accurate identification of the high-risk population, other key determinants of the success of CMD-prevention programs relate principally to compliance of the target group, support from professionals and health care authorities during implementation, adequate logistics and funding, and effective incorporation of the program into standard health services [13-15]. Identifying persons at high risk of CMDs is generally more efficient when these efforts are structurally embedded in health care [16]. To this end, primary care in particular may play an important role in facilitating patient uptake and compliance with any CMD-prevention efforts. This is principally due to the continuous relationship between GPs and their patients, and the central role of primary care in most community health services. Again, however, there exists relatively extensive variation within the EU in terms of national investment in primary care and its role in prevention. For instance, primary care health expenditure per capita is nearly three times higher in Luxembourg and Switzerland than it is in most of the Eastern European countries [17].

The importance of contextual factors for the success of prevention programs
Various factors may be central to whether an SPI will be successful. These primarily relate to:

- Practical organization of health care system (e.g. the remuneration of professionals for preventive activities, whether people are obliged to register with a GP, etc.).
- The extent to which GPs view prevention as a part of their responsibilities (i.e. do they perceive their job as including treatment of illness only, or does it also involve encouraging otherwise healthy patients to take preventive measures?).
- Social and cultural norms and values that may facilitate or interfere with preventive efforts (e.g. the acceptability of intervening in people's lifestyle).

Taking these issues into account, we will first work towards generating an innovative and generic approach to identify the high-risk population and implement preventive action. Dependent on the local setting in each country, this broad approach to prevention will then be tailored to accommodate any between-country variation in the aforementioned factors.

The SPIMEU project
The SPIMEU project – on which this document is based – focuses specifically on the need for early detection and intervention against the development of CMD. Taking into account the considerable variation in EU member states’ health care systems (specifically in terms of quality, extensiveness, and organization), we focus on how best to mobilize and implement effective selective prevention initiatives in the EU at large. The main objectives of the SPIMEU project therefore relate to establishing the feasibility of implementing CMD selective prevention initiatives (SPIs) in five different national health care systems in the EU (see Table 1). Specifically, we investigated the potential of evidence-based SPIs in the Netherlands, Greece, the Czech Republic, Sweden, and Denmark. In order to do this, we designed five work packages
(WPs) focusing on various feasibility aspects of selective prevention in terms of intervention design, implementation, and effectiveness. Thus, we examined the practical and structural organization of past and current SPIs in Europe (WP4). We then investigated the barriers and facilitators of patient and GP attitudes to selective prevention of CMD (WP5 & 6). In WP 7 and 8, we developed and tested the feasibility of a generic CMD SPI in the five partner countries. Based on our empirical results from these WPs as well as on the broader literature, we aim to create a “toolbox” of sorts, containing evidence-based tools and “do’s and don’ts” for future SPIs. Specifically, we will generate a generic framework for CMD SPIs that can be tailored and implemented across various national settings in the EU.

Given the principal importance of systemic and operational context when it comes to designing and implementing health care initiatives, we include a brief description of the characteristics of the five different health care systems included in SPIMEU.

**Table 1 Health care system characteristics in the SPIMEU partner countries**

<table>
<thead>
<tr>
<th>Country</th>
<th>Universal health care</th>
<th>Type of health care system*</th>
<th>Level of primary care orientation**</th>
<th>GP gatekeeping</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sweden</td>
<td>Yes</td>
<td>NHS</td>
<td>Medium</td>
<td>Partial</td>
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<tr>
<td>Denmark</td>
<td>Yes</td>
<td>NHS</td>
<td>High</td>
<td>No</td>
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<tr>
<td>The Netherlands</td>
<td>Yes</td>
<td>SHI</td>
<td>High</td>
<td>Full</td>
</tr>
<tr>
<td>Czech Republic</td>
<td>Yes</td>
<td>Transitional</td>
<td>Medium</td>
<td>No</td>
</tr>
<tr>
<td>Greece</td>
<td>Yes</td>
<td>NHS</td>
<td>Low</td>
<td>No</td>
</tr>
</tbody>
</table>

*Transitional: Former Semashko (Soviet) system  
NHS: National Health Service based system  
SHI: Social Health Insurance based system  

**Method**

The SPIMEU project comprised five empirical WPs, designed to investigate different aspects of selective prevention methodology and implementation. In Table 2, we have outlined each of these WPs in terms of their aim and method.

**Table 2 Aim, method, and principal output of work packages 4-8**

<table>
<thead>
<tr>
<th>WP</th>
<th>Aim</th>
<th>Method (N)</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>Identification and evaluation of SPIs implemented in the EU.</td>
<td>Survey (28 key persons, 66 experts).</td>
<td>Characteristics and assessment of 27 CMD SPIs implemented in the EU.</td>
</tr>
<tr>
<td>5</td>
<td>Evaluation of common barriers/facilitators of uptake and compliance with SPIs in European primary care systems.</td>
<td>Systematic Review (39 articles)</td>
<td>A synthesis of the evidence on barriers/facilitators into four categories: Structural, organizational, professional, and social.</td>
</tr>
<tr>
<td>6</td>
<td>Assessment of GP and patient attitudes towards selective prevention in the five partner countries.</td>
<td>Surveys (575 GPs, 1354 patients)</td>
<td>Overview of attitude and opinions of a multi-national population of GPs and patients.</td>
</tr>
<tr>
<td>7</td>
<td>Development of practical, step-wise implementation method for SPIs.</td>
<td>RAND/UCLA appropriateness method** (14 experts)</td>
<td>A set of 31 recommendations for implementation.</td>
</tr>
<tr>
<td>8</td>
<td>Development and implementation of a patient identification and recruitment method based on results from preceding WPs.</td>
<td>Feasibility study (22 GPs, 474 patients)</td>
<td>Feasibility assessment of selective prevention implementation methods in five EU countries.</td>
</tr>
</tbody>
</table>

* WPs 1-3 were not empirical WPs, relating instead to project coordination, steering committee tasks, and dissemination of the results. As such, they are not included in the table.
**A validated method to synthesize the evidence and expert opinion on a given topic.**

**Results: Tools for the design and implementation of CMD SPIs**

By synthesizing the overall results from the SPIMEU project, we identified a series of themes and variations in terms of barriers and facilitators of CMD SPIs. These relate to a broad range of issues, including practical (e.g. SPI funding structure), methodological (e.g. SPI implementation method), and psychological (motivating patient/health professional participation) matters. On this basis, we make a series of recommendations that may serve to inform current and future preventive initiatives. Where possible, we have supplemented these recommendations with evidence-based suggestions – or tools – that may be employed to heed the recommendations. We have arranged these issues and tools in four central categories (see Table 3):

1. Funding and stakeholders,
2. Risk assessment and identification of the target patient population,
3. Motivating participation and engagement of health professionals,
4. Motivating participation and engagement of patients.

### Table 3 Toolbox sections

<table>
<thead>
<tr>
<th>Category</th>
<th>Issue</th>
</tr>
</thead>
<tbody>
<tr>
<td>Funding &amp; stakeholders</td>
<td>1.1 To the furthest extent possible, all central stakeholders (e.g. policy makers, health care professionals) should be involved in the design and implementation process of SPIs.</td>
</tr>
<tr>
<td></td>
<td>1.2 To maximize success and effect of SPIs, funding of the initiatives should be sustainable over time.</td>
</tr>
<tr>
<td>Risk assessment &amp; target population identification</td>
<td>2.1 In order to facilitate accurate and efficient identification of the high-risk population, the definition of this population should be clear and concise, and take into account age and pre-existing conditions.</td>
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<tr>
<td></td>
<td>2.2 For optimum accuracy and validity, locally validated risk-assessment tools will likely yield the best results in terms identifying the target population.</td>
</tr>
<tr>
<td>Health professionals – recruitment and engagement</td>
<td>3.1 The initiative should accommodate health professionals’ existing workload and time constraints.</td>
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<td>3.2 A clear, evidence-based protocol for the implementation of the initiative should be made available to all participating health professionals.</td>
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<td>3.3 If needed, education in selective prevention and training in the specific initiative protocol should be made available to health professionals and their staff.</td>
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<td>Patients – recruitment and engagement</td>
<td>4.1 Patient apprehensions related to potential health-check outcomes, should be anticipated and assuaged pre-implementation.</td>
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<td>4.2 Patients’ feelings of powerlessness to affect their own health should be anticipated and counteracted before and during implementation.</td>
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<td></td>
<td>4.3 Lack of patient knowledge in terms of the causes of and susceptibility to CMD, as well as its potential severity, should also be anticipated and counteracted pre-implementation.</td>
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<tr>
<td></td>
<td>4.4 Patients’ potential time constraints (work/family, etc.) and/or other practical obstacles (geography, financial, etc.) may impact on their likelihood of showing up for a health check and should be accommodated to the furthest extent possible throughout implementation.</td>
</tr>
<tr>
<td></td>
<td>4.5 Method of invitation to participate in the SPI should be evidence-based and optimally consist of an invitation from the patient’s GP, supplemented with information on the purpose and nature of a health check.</td>
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1. **Funding and stakeholders**

   1.1 *To the furthest extent possible, all central stakeholders (e.g. policy makers, health care professionals) should be involved in the design and implementation process of SPIs.*
In our systematic review of existing CMD SPIs in the EU, we identified a total of 27 initiatives currently implemented in 16 EU countries. While the design, target population, and implementation methods varied considerably among these initiatives, a relatively clear common denominator of the identified SPIs related to the continuous participation of policy makers and primary health care workers. Specifically, while the design and implementation of SPIs typically represented a shared responsibility among all stakeholders, policy makers (and to some extent public health organizations) were mostly involved in the developmental phases of the SPI, whereas health care workers typically spearheaded the execution of the project. While our review did not include an assessment of the effectiveness of the identified SPIs, the sheer prevalence of implemented SPIs within the EU speaks to the fruitful nature of collaboration between central stakeholders as well as to the general feasibility of these types of interventions. Organizing and encouraging such collaborations may thus be key in the advancement of CMD SPIs.

In addition to the mobilization and organization of various stakeholders, the procurement of adequate subsidies for all stages of the design and implementation process is paramount to the success of an SPI. This becomes abundantly clear when reading through this toolbox, where most – if not all – of the tools require continuous funding to realize effectively.

1.1.1 Identify and organize key stakeholders in CMD prevention: For maximum inclusiveness and effect, CMD SPIs should involve as many key stakeholders as practical in the design and implementation of the initiative. For instance, the “Healthy lifestyle interventions to combat noncommunicable disease – a novel nonhierarchical connectivity model for key stakeholders” policy statement from the main cardiology and cardiovascular medical professional associations in the US and Europe, expounds this point exactly [18]. This document maps out all organizations with a stake in the prevention of cardiovascular disease, thus providing a clear idea of who could (and perhaps should) be approached for collaboration when designing and implementing preventive initiatives. These include everything from professional medical organizations and educational systems to health insurance companies and government, to media outlets and the food industry. The policy statement also outlines potential lines of communication between these different stakeholders, illustrating how to connect and collaborate effectively for anyone interested. Using organized efforts such as these to facilitate productive, interdisciplinary collaborations targeting CMD prevention may prove useful in the design and implementation of comprehensive CMD SPIs.

1.2 To maximize success and effect of SPIs, funding of the initiatives should be sustainable over time. Existing SPIs within the EU vary somewhat in terms of the funding schemes employed to sustain them over time. Of the 19 EU SPIs identified in our WP4 review, 50% were subsidized by health care insurance, 44% by policy makers, 32% by public health organizations, and 13% by patients. In 8 countries funding was reported as unclear. The capital to continuous single-funded SPIs typically came from health insurance, municipal health organizations, or the government. Multi-funded SPIs were financed by municipal authorities, government, patient organizations, and/or health care insurance. There is currently no evidence to support either funding scheme (single- vs. multi-source) as being better than the other. However, stable funding throughout the life of the initiative is obviously imperative to its success, and should to the farthest extent possible be secured in full pre-implementation. Tool #1.1.1 above may be useful to this end as well.

2. Risk assessment & identification of the target population

2.1 In order to facilitate accurate and efficient identification of the high-risk population, the definition of this population should be clear and concise, and take into account age and pre-existing conditions.

In the WP7 consensus meeting we discussed the importance of defining the target population at the outset of any CMD SPI. Selective prevention is, by its very definition, focused on treating a
subsection of the general population that is deemed to be at risk. In order to access this population systematically and accurately, it must first be defined. Through our consensus meeting expert discussions, we arrived at two recommendations for the definition of the high-risk population relevant to CMD SPIs.

2.1.1 **Age range**: The target population for CMD SPIs should include (but not necessarily be limited to) individuals (of both sexes) between 40 and 70 years old. This recommendation is based on the current evidence base that shows that it is people within this age range who are most likely to be at risk of CMDs, and for whom preventive efforts are most likely to pay off (WP7 statement #22).

2.1.2 **Pre-existing conditions**: By definition, the high-risk population for SPIs does not include people who have been, or are currently, in treatment for hypertension, diabetes mellitus, cardiovascular disease, chronic renal damage, and/or hypercholesterolemia (WP7 statement #19).

2.2 *For optimum accuracy and validity, locally validated risk-assessment tools will likely yield the best results in terms identifying the target population.*

Another point made in the WP7 consensus meeting related to the selection of risk-assessment tools for CMD SPIs. There was unanimous agreement that to the furthest extent possible, CMD risk assessment should be conducted by use of validated measures (WP7 statement #20). This recommendation was based on the presumably greater efficacy of local over generic assessment tools in terms of accuracy, reliability, and cultural appropriateness. Indeed, when implementing the WP8 feasibility study, we used only locally validated risk assessment instruments to identify the high-risk populations in the respective partner countries. We do note, however, that while each SPIMEU country employed local solutions for the identification of the high-risk population, the risk-assessment tools were quite similar in content and format. As such, in the event that no locally validated assessment tool is available, adapting one from a similar country may be feasible.

3. **Health professionals – motivating participation and engagement**

3.1 *The initiative should accommodate health professionals’ existing workload and time constraints.*

In our systematic review of the evidence in WP5, we found that one of the most frequently reported barriers to GP participation and/or attrition in SPIs related to increased workload (in terms of participant invitation, health check, and administration) and time constraints. In other words, GPs were often overwhelmed and demotivated by the added responsibilities involved in implementing an SPI. Our evidence indicates that these practical and motivational barriers may be overcome by creating an environment (i.e. implementation method) that is more conducive to GP participation – namely by reducing responsibilities and reimbursing time and extra work load. This may be achieved in different ways depending on the local health-care setting.

3.1.1 **Sharing the burden**: In Denmark the primary care system includes general practice and municipal health centers. The latter component serves the entire population with primary prevention measures, including for example smoking cessation and dietary advice. On the other hand, GPs are tasked with managing and coordinating secondary prevention, such as treatment for hypertension, hypercholesterolemia, or diabetes. A current Danish prevention project refers patients at risk of CMD to either their GP or a health center depending on their level of risk [19]. Specifically, those deemed at high risk are invited to a...
health check and dialogue at their GP. Those at medium risk (i.e. people who have no physical ailments, but do engage in risky health behaviors such as smoking, drinking, etc.), however, are referred to a health center for lifestyle intervention. In this way the high-risk population is divided into different categories based on need, thus spreading the burden across multiple treatment facilities.

3.1.2 Providing support staff: Given sufficient funding, the selective prevention initiative may incorporate administrative personnel to undertake all things related to the identification and recruitment of high-risk patients, thus minimizing the workload for health professionals. For example, in conducting the SPIMEU feasibility study (WP8), the Dutch and Danish research teams were responsible for recruiting patients to participate in the initiative, administering and scoring patient risk assessments, and inviting patients to a health check at their GP. Following this protocol, the GPs’ main responsibilities included providing access to their patient lists and performing health checks for those patients who made an appointment. An expanded version of this protocol could be to even let support staff (e.g. a specially trained nurse) conduct most, if not all of the health check (blood work, lung function tests, dialogue, etc.).

3.1.3 Incentivizing GP participation: Some of the most commonly reported barriers for GP participation in selective prevention initiatives relate to the often inadequate financial reimbursement for the time and effort that GPs and their staff put in. On the other hand, one of the most significant facilitators of participation in selective prevention initiatives pertains to sufficient financial incentives and reimbursement for practitioners. For instance, a national SPI in the Czech Republic centers on biannual invitation to all citizens over 18 years old for a CMD-risk assessment at their GP. The government reimburses patients for the cost of the health check, which also represents an important source of income for GPs. Since the inception of this initiative in 1995, Czech GPs are among the most likely in all of Europe to practice active selective prevention of CMD (WP6). Indeed, in our survey study of GPs in the SPIMEU partner countries, we found that 69% of participating Czech GPs practiced selective prevention. This was considerably higher than in the four other SPIMEU countries (average = 40%). In other words, the evidence suggests that a CMD SPI that incorporates financial incentives may contribute to motivating GP participation in spite of existing workloads and time constraints.

3.2 A clear, evidence-based protocol for the implementation of the initiative should be made available to all participating health professionals.

Results from past studies strongly suggest that for SPIs to be implemented successfully and sustained in practice over time, practitioners and their staff need access to and/or training in a clear and actionable selective prevention protocol that is tailored to the given setting and health care system. For example, past research has found that lack of GPs’ awareness of existing selective prevention guidelines represented a central barrier to this kind of practice [20-22]. Similarly, other studies report that inconsistent, unclear, or too many guidelines not only confused practitioners, but ultimately discouraged them from participating wholeheartedly or at all in SPIs [22, 23]. Other research has cited the lack of tailored evidence-based protocols for the implementation of SPIs as
a fundamental barrier to GP participation (WP5). Devising clear and feasible protocols may be achieved by referring to past and current SPIs.

3.2.1 **Relevant steps in SPI protocols**: In our review of CMD SPIs within the EU, several common characteristics of implemented SPIs emerged. Notably, these included six basic steps:

1. Identification of the target population (74% of identified SPIs; see point 2 above).
2. Survey risk assessment of the target population (70%; see point 3 above).
3. Physical examination (85%).
4. Laboratory tests (81%).
5. Specific interventions for high-risk patients (74%).
6. A patient follow-up system (67%)

3.2.2 **SPIMEU selective prevention feasibility protocol**: As an example of a tailored protocol for an SPI, we refer to the one developed for the SPIMEU feasibility study (WP8). Here, we developed a two-step protocol, including a *core method* and a *tailored method*. The core method was uniform across countries, and specified the definition of the target population (in terms of age and medical history), the use of a validated risk assessment tool to identify the target population, and comparable risk evaluation methods. The tailored method, on the other hand, allowed each individual partner country to adapt the initiative to local settings. This related most prominently to the number of participating GPs, the method of patient invitation and communication, and the selection of a validated risk assessment tools. Using this protocol, all partner countries in the SPIMEU project were able to source an eligible, target population.

3.3 **If needed, education in the efficacy of selective prevention and training in the specific initiative protocol should be made available to health professionals and their staff.**

Past studies have found that significant barriers to GP uptake of SPIs relate to their lack of education/training in communicating risk and lifestyle information to patients [20, 22, 24-27]. For those SPIs that include an IT component, insufficient GP training in its functionality also represents a significant barrier. Noted facilitators of GP uptake include sufficient training in the given SPI protocol and motivational counseling more generally. Sufficient GP knowledge of the benefits of selective prevention also stands out as a key facilitator of GP motivation to participate in an SPI. In light of this, it would seem pertinent in any SPI to ensure that participating GPs have the background knowledge and skill to execute the SPI protocol accurately and confidently. This may be achieved by providing introductory training programs for participating GPs, centering on both the benefits of selective prevention and concrete know-how relevant to the given protocol (including for instance comprehensive knowledge of referral options). In this context, it is also crucial that the protocol be absolutely clear and unambiguous with logical step-by-step instructions tailored to the given clinical setting (see 4.2 above).

4. **Patients – motivating participation and engagement**

4.1 **Patient apprehensions related to potential health-check outcomes, should be anticipated and assuaged pre-implementation.**
In both WP5 and WP6, results indicated that patient worries associated with the outcome of a potential CMD health check was a deciding factor in their willingness to get a health check. Specifically, our review article in WP5 identified ten studies that indicated that patient fear of a health-check outcome, or not wanting to know their risk of CMD, represented a significant barrier. On the other hand, another ten studies showed that wanting to be reassured of one's health, wanting to know one's risk of CMD, and/or having no trepidation of a health-check outcome, facilitated patient participation in health checks. Thus, it would seem that concern about one's health can be both adaptive and maladaptive. That is, worrying about one's health may inhibit preventive action (such as getting a health check), it can also have the opposite effect and facilitate this behavior – especially if the primary motivation is to ameliorate anxiety through reassurance and/or insight into individual risk. Alleviating patients' potential uneasiness in regards to health-check outcomes is therefore an important factor in terms of facilitating patient uptake of a CMD SPI [13, 28]. While research on how to mitigate health anxieties in order to facilitate preventive action is scarce, there are nonetheless several approaches that are theoretically sound. For instance, unequivocal information about the nature and purpose of a CMD-prevention health check might allay patient fears [28]. Similarly, the GPs' role in effectively communicating to their patients the importance of preventive health checks may also be a central factor in assuaging patient worries and motivating uptake.

4.1 Reducing patient worries about health-check outcome by providing information: In terms of overcoming any patient trepidations related to health-check outcomes, past research indicates the value of educating people about three particular aspects of health and disease screening [28]:

i. The nature and effects of the disease in focus (what are the symptoms? What is the (typical) prognosis? What are the causes/risk factors?)

ii. The relative risk of developing the disease (who is the high-risk population?)

iii. The benefits and specific procedure of a health-check (how does one get a health check? What happens during the health check? What happens after the health check in the event of increased CMD risk or diagnosis? What are the risks of not getting a health check?).

Such information could be dispensed via media campaigns and public service announcements to the general public. However, studies indicate that the efficacy of these types of campaigns might be significantly boosted if they are tailored to subgroups of the general populations (e.g. gender, age, race, culture) and dispensed through TV, newspaper advertisements, and pamphlets [28-30].

4.2 Patients' feelings of powerlessness to affect their own health should be anticipated and counteracted before and during implementation.

In our systematic review on patient willingness to get health checks (WP5), we found that perceived locus of control over one's health was a major factor. Specifically, high perceived internal locus of control (i.e. the belief that one can influence one's own health) increased receptiveness to health checks. By contrast, high perceived external locus of control (the belief that outside factors determine health) had the opposite effect. The extent to which patients feel able to influence their own health thus seems to underpin their openness to preventive action. Other research also indicates the importance of this factor in terms of sustained participation in behavioral medical interventions [31]. As such, in terms of the design and implementation of CMD SPIs, it would likely be advantageous to empower the high-risk population by emphasizing the
feasibility and potential of health-behavior change for reducing CMD risk. Below we list the central factors that should be taken into account.

4.2.1 **Educating the high-risk population about the nature of CMD:** In order to empower patients to manage their risk of CMD, educating them about the nature of CMDs, how these diseases develop, and how individual risk of CMDs can be reduced through behavioral changes, is imperative [32-34]. Past research has shown positive results of patient education in terms of disease management and engagement in health interventions [35]. It would seem that such education would naturally fall under the responsibility of the GP. However, GPs often lack the necessary training to educate effectively in a clinical context [34]. Thus, patient uptake of, and sustained participation in CMD SPIs may be bolstered by providing GP training in patient education about the nature and management of CMD risk. This strategy should take into account tool 3.1 above concerning GPs’ workload and scheduling issues. Providing patients at risk of CMD with additional practical CMD educational materials – such as information pamphlets, booklets, and/or media – may also help empower this population to take up and stick with CMD SPIs.

4.2.2 **Providing support, advice, and guidance for behavior change:** In addition to educating the high-risk population, providing continuous practical support to patients participating in an SPI may similarly empower them and retain their participation over time. Past research has indicated that increased patient access to their GP clinic (e.g. via email and/or an IT-support system) for advice and guidance may encourage health behavior considerably [31].

4.2.3 **Community health-behavior intervention:** Another approach that may complement the aforementioned tools, relates to mass-media awareness campaigns that target the high-risk population at large. These are relatively common in many countries, and are usually delivered to a wide audience through social media, tv, radio, newspapers, etc. [36]. These types of interventions are typically designed to effect change in individuals’ decision processes regarding a certain issue (e.g. attending a health check) – for example by supplying them with relevant information (e.g. health or disease facts). In terms of facilitating positive health behavior (e.g. attending preventive health checks), however, past research indicates the key importance of accounting for individuals’ self-efficacy and the broader social context in which they exist [19, 30, 37, 38]. Specifically, in contrast to people with high self-efficacy, those with low self-efficacy will most likely not be successful in changing their behavior in response to information about CMD alone [29, 30]. However, if this information were accompanied by practical, stepwise instruction on how to change their behavior for the better (i.e. instilling participants with a sense of self-efficacy), the likelihood of successful behavior change would presumably be much greater. For example, in an evaluation of a community CVD-awareness campaign, Maibach et al. [38] were able to increase participants’ belief in their self-efficacy from pre- to post-intervention. This was achieved by empowering participants with specific, usable advice on how to minimize risk of CVD throughout the campaign. In turn, the augmentation of self-efficacy mediated the increased adoption of relevant health behaviors in the target population. Numerous other studies support these findings [29, 31, 37], further endorsing...
the efficacy of combining awareness with practical, how-to advice in changing health behavior.

In addition to self-efficacy, the broader norms that govern the social context in which the individual operates are at least of equal importance in terms of facilitating health-behavior change through awareness campaigns. Indeed, the perceived social norms within one’s social network and broader social categories are highly influential in terms of individual behavior. A plethora of research has shown strong, positive associations between the extent to which the individual perceives a certain behavior as norm-based, and his or her likelihood of engaging in that behavior (e.g. [39, 40]). In light of this, it follows naturally that suggesting to the individual that similar others regularly engage in a given behavior (e.g. attending regular health checks) may implore him or her to follow suit. Examples of these types of approaches to health-behavior change are numerous and generally highly effective [30, 39-42].

In sum, to empower and motivate the target population to engage in health behaviors such as attending health checks, an awareness-campaign approach that focuses on self-efficacy and social norms may produce positive results in this respect.

4.3 Lack of patient knowledge in terms of the causes of and susceptibility to CMD, as well as its potential severity, should also be anticipated and counteracted pre-implementation.

In our review of the evidence on patient facilitators and barriers to uptake of SPIs (WP5), we found that patients’ feelings of susceptibility to CMDs and/or their beliefs about CMD severity represented significant factors in terms of uptake (reported in 13 studies). Particularly, feeling healthy and less susceptible to CMD, and/or perceiving CMDs as less debilitating conditions was associated with lower participation rates. While the former attitude may be well-founded (that is, someone who leads a healthy lifestyle may in fact be less susceptible to CMD), the latter is surely based in misconception considering the fact that cardiovascular disease is the leading cause of death for both men and women [17]. Further, given the potential subtlety of CMD manifestation early in its development (e.g. high blood pressure is relatively asymptomatic), it is not uncommon for people at elevated risk to feel healthy. In other words, people’s lack of knowledge and misapprehensions about CMD may give rise to a false sense of health, and thus impact negatively on their motivation to take up a CMD SPI. In light of this, creating awareness around the subtleness of CMD symptoms, as well as the severity and general risk of CMD, may in all likelihood boost participation rates in CMD SPIs. It may therefore be advantageous for implementation efforts to prime the high-risk population by disseminating information about the causes and nature of CMDs, and encouraging preventive health care. This may be accomplished by employing health promotion strategies akin to those outlined in Recommendation 4.2 above.

4.4 Patients’ potential time constraints (work/family, etc.) and/or other practical obstacles (geography, financial, etc.) may impact on their likelihood of showing up for a health check and should be accommodated to the furthest extent possible throughout implementation.

The results of our systematic review of barriers and facilitators of patient health check participation (WP5) revealed several common themes across studies in terms of specifically practical barriers/facilitators. These related mainly to time issues and primary care access. Specifically, our review indicated that lack of time (due to family and/or work) was a significant barrier, whereas working flexible hours or being retired (and thus presumably having more free time) facilitated health checks. These findings dovetailed nicely with other results from our review
that indicated that walk-in health checks and easy geographical access to a GP facilitated participation in health checks. Further, we also found evidence that suggested that low SES might facilitate health check attendance in one setting, but inhibit it in another (high SES was consistently a facilitator). Overall, our findings highlights the fact that time and access issues, as well as SES, can impact significantly on the likelihood of patients attending health checks. While past research indicates the inherent difficulty in circumventing these issues, there are some options that may be advantageous to incorporate in an SPI.

4.4.1 Support staff: The amount of time and resources that GPs have at their disposal is directly related to their availability for appointments. This would presumably account for at least some of the difficulty in booking appointments reported by patients who work rigid daytime schedules, and/or have their free time eaten up by family responsibilities. Similar to tool #3.1 above, this issue might be dealt with by employing GP support staff. Past research has suggested different types of assistance for this purpose, typically including patient navigators, physician assistants [28], or nurse-led initiatives. Here, non-GP staff take on various duties (including basic health checks) to off-load the GP and create greater access for patients [43]. These initiatives necessarily rely on relatively extensive training and detailed protocols so that the given support staff may tackle whatever responsibilities they are tasked with effectively (e.g. a health check).

4.4.2 After-hours access: Currently there are various after-hours primary care models implemented in Europe. Many of these involve after-hours primary care centers or primary care cooperatives. The former model involves primary care centers – staffed by doctors, nurses, and administrative support staff – where patients can present with or without an appointment. In the latter model, GPs within a region or municipality form multiple, rotating groups which, with the support of auxiliary staff, provide primary care in large, non-profit organizations [44]. The latter model is currently implemented in Denmark and the Netherlands[44, 45] and has been somewhat instrumental in off-loading GPs’ workloads and alleviating busy emergency departments [46]. However, systems like these may serve a third purpose by allowing patients, who cannot schedule preventive health checks during normal working hours, to make appointments at an after-hours primary care center or cooperative. Dependent on local resources, however, SPIs may need to employ extra staff for this specific purpose (particularly for walk-in centers where appointments are not possible).

4.4.3 Mobile health service/Reimbursement of transportation costs: Our findings suggested that lack of geographical access to a GP and/or health center significantly impeded patients who might otherwise be motivated and willing to get a health check. Similar discoveries have been made in past research as well [47, 48]. This issue may be of particular relevance in rural or suburban settings, or in cities with poor public transport systems. Potential solutions to this barrier may be for GPs to offer home visits and/or organize regular (e.g. annual) mobile health clinics that cater to health check demand. These approaches have shown some success in past research focusing on hard-to-reach populations [49, 50].
4.5 Method of invitation to participate in the SPI should be evidence-based and optimally consist of an invitation from the patient’s GP, supplemented with information on the purpose and nature of a health check.

Our systematic review of patient facilitators and barriers to the uptake of an SPI suggested that the method and content of the invitation to the initiative was a central factor in patients’ choice to participate or not. Specifically, not actively inviting patients and limited patient knowledge of the purpose and content of a health check, were identified as barriers. By contrast, facilitators included effective invitation strategies and having access to clear and unambiguous information about the health check. Effective invitation methods generally included receiving a personal invite from the GP or health center which, if not responded to, was followed up with a reminder or second invitation. The use of outreach workers in the invitation process was also identified as a facilitator. Indeed, in our feasibility study (WP8) four countries sent out paper invitations, addressed to the patient from the research team (i.e. to the patient an unknown entity). This resulted in a relatively low response rate, ranging from 30% to 50%. The Czech team, however, instructed GPs to invite their patients personally by letter or during consultation. This resulted in a 100% response rate. On this basis, it seems the invitation process of a given SPI may maximize patient uptake by including three basic steps:

1. Patients should be invited by their GP.
2. Non-responders should be followed up with a second invitation or reminder to respond.
3. The invitation should be supplemented with clear and specific information about the purpose, benefits, and specific content of a health-check (What happens during the health check? What happens after the health check in the event of increased CMD risk or diagnosis? What are the risks of not getting a health check?)

Discussion

The overarching aim of the SPIMEU project centered on how best to design and implement CMD SPIs in European countries. To this end, we executed five empirical work packages (WPs) that explored different aspects of CMD selective prevention in primary care. Specifically, we reviewed past and present SPIs, examined the facilitators and barriers to SPI uptake among both health professionals and patients, and tested the feasibility of a generic SPI model in five different countries. The results indicated a variety of barriers and facilitators that were common across national contexts in terms of efficient implementation of SPIs. Based on these findings, we developed a set of generic recommendations and tools – listed above – which we hope will help develop and focus current and future SPIs. However, while we found definite commonalities in terms of the obstacles and facilitators of CMD SPIs, given the systemic, attitudinal, and cultural differences between countries, the proposed toolbox may not always apply equally across the board. For example, tool #3.1.3 (incentivizing GP participation) may not be particularly useful in a country such as Denmark where there currently is a relatively large patient-to-GP ratio. That is, many Danish GPs are encumbered by heavy workloads and tight schedules, and may thus be reluctant to take on more work regardless of monetary incentives. Indeed, in this scenario, introducing support staff (tool #3.1.2) or sharing the extra workload with other primary care agents (tool #3.1.1) may be more appropriate and effective. By contrast, other tools have broader relevance and value regardless of systemic or national context. For instance, tool #4.2.3 (community health-behavior intervention) targets rather fundamental human psychological dynamics (i.e. self-efficacy, motivation, social norms) that are pertinent to behavior change in a broad range of cultural and national settings [36, 39, 40, 51].

In this way, the presented recommendations may highlight more or less omnipresent issues, but the extent to which these can be dealt with using the suggested tools (or at all) may differ depending on local settings. In other words, an entirely generic, one-size-fits-all solution to the design and implementation of CMD SPIs, may be impractical if not impossible in a European context. In all likelihood, certain
components of a given SPI will nearly always need to be tailored to the specific national context and system in which they will be implemented. As such, while we have presented a set of general recommendations and tools, the onus is ultimately on the stakeholders of a given SPI to decide which tools are relevant to their particular project, and how these tools are best tweaked and implemented in the relevant setting. In Figure 1 below, we have provided an overview process flowchart of how the toolbox might be implemented.
**Strengths and Limitations**

One of the main strengths of this toolbox is the comprehensiveness of the WPs that inform each of the recommendations and tools outlined above. WP 4 (which reviewed existing SPIs in Europe) drew on evidence from all 28 EU member states, and WP 5 (health professionals’ attitudes towards SPIs) reviewed studies from all over the world. WP 6, 7, and 8 collected data mainly from the five SPIM-EU countries. However, it should be noted that these countries (the Netherlands, the Czech Republic, Greece, Sweden, and Denmark) are good representations of the different types of health care systems that currently exist in
Europe (see Table 1). As such, the recommendations and tools that we have developed based on SPIMEU data, presumably apply and/or can be adapted to many different settings within the EU.

Another strength relates to the methodological rigor of each of the empirical WPs that underpin the toolbox. The evidence generated from these WPs comprises three reviews (one based on key informants and experts (WP 4), as well as two systematic literature reviews (WP 5)), two multi-national survey studies (WP 6), an international expert consensus meeting (WP 7), and a multi-national feasibility study (WP 8) (see Table 2). The reviews were executed according to validated review guidelines. Similarly, the consensus meeting was conducted using the validated Rand/UCLA appropriateness method (the RAM) [52] and included 14 internationally renowned experts in cardiology, epidemiology, and/or general practice. Finally, the WP 8 feasibility study directly tested the practicality of implementing a generic SPI in each SPIM-EU country. The collection of high-quality evidence generated in each of these WPs, places us in a unique position to create the evidence-based, state-of-the-art SPI toolbox detailed above.

In terms of limitations, the SPIM-EU project timeline often did not allow for adequate follow-up studies. This left a few questions that emerged from our initial findings unanswered. For example, the association between SES and the likelihood of engaging in preventive health behavior was quite ambiguous, with some studies indicating a positive relationship and others a negative one. Given the social inequality in lifestyle-related disease that currently exists in most of the world, not least in the EU [53-57], it would certainly seem germane to examine this relationship further to clarify exactly how these two variables relate.

Another limitation relates to the validation of the toolbox. That is, while the recommendations and tools listed above have been derived from the evidence generated in the SPIMEU project combined with results from the literature, some have as yet not been tested. For example, while past research may suggest that mobile health-check services (tool #4.4.3) might get at hard-to-reach populations, this has – to our knowledge – not been attempted in the context of SPI implementation. We therefore strongly encourage potential users of this toolbox to record their implementation methods and results for evaluation and amendment purposes. A concerted and sustained effort to revise and update this toolbox will secure its relevance and applicability over time.

Future Directions

While this toolbox is comprehensive in scope, there are nonetheless certain matters that we have been unable to draw firm conclusions about. One issue that is particularly worth noting relates to GP (de)motivation to participate in SPIs. In the above sections we have identified various barriers, including insufficient funding, increased workload, lack of knowledge of available protocols, etc. However, another factor that may dissuade GPs from engaging with SPIs might relate to more fundamental matters. Particularly, we believe that the somewhat ambiguous nature of the evidence for the effectiveness of such programs (e.g. in terms of cost-effectiveness, feasibility, high-risk population identification, health check invitation and attendance) likely plays a significant role in the extent to which GPs choose to participate or not. For instance, the cost-effectiveness of SPIs has yet to be conclusively demonstrated, and while some studies indicate a positive impact of SPIs on health and health behavior, others report small, mixed, or no effects [10, 58]. Thus, we argue that this opacity in the evidence base may contribute to GPs’ reluctance to participate in selective preventive efforts. To remedy this situation more research is needed to clearly identify the value and feasibility of SPIs in combating CMD. To this end, we propose three main avenues for future research: 1) High-quality studies (e.g. RCTs, stepped-wedge trials) that account for the various limitations of past research. 2) Assessing the effectiveness of current and past SPI programs (e.g. a metaanalysis of those programs identified in WP4 that also report effect sizes) in terms of feasibility, cost-effectiveness, effectiveness of patient invitations, health-check attendance, and overall health outcomes over time. 3) Encouraging current and future SPIs to incorporate comprehensive and rigorous impact evaluation components as core features in their programs.
Conclusion

We set out to create a generic toolbox for the implementation of CMD SPIs in Europe. In line with this goal, we executed five empirical work packages, each designed to uncover different aspects of SPI design and methodology. We then synthesized the results into a set of more or less universally significant (at least within the EU) overall recommendations for the design and implementation of CMD SPIs. Each of these recommendations was supplemented with practical suggestions on how to heed the given piece of advice. We acknowledge that these tools may not always apply equally across different systemic, political, and cultural landscapes. However, we hope that they at least can inspire solutions, if not be adapted directly to a given setting, and thus hopefully contribute to the reduction of CMD.
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