Systematic Review of Guidelines on Cardiovascular Risk Assessment

Which Recommendations Should Clinicians Follow for a Cardiovascular Health Check?

Bart S. Ferket, MD; Ersen B. Colkesen, MD; Jacob J. Visser, MD, PhD; Sandra Spronk, PhD; Roderik A. Kraaijenhagen, MD, PhD; Ewout W. Steyerberg, PhD; M. G. Myriam Hunink, MD, PhD

Objective: To appraise guidelines on cardiovascular risk assessment to guide selection of screening interventions for a health check.

Data Sources: Guidelines in the English language published between January 1, 2003, and May 2, 2009, were retrieved using MEDLINE and CINAHL. This was supplemented by searching the National Guideline Clearinghouse, National Library for Health, Canadian Medical Association Infobase, and G-I-N International Guideline Library.

Study Selection: We included guidelines developed on behalf of professional organizations from Western countries, containing recommendations on cardiovascular risk assessment for the apparently healthy population. Titles and abstracts were assessed by 2 independent reviewers. Of 1984 titles identified, 27 guidelines met our criteria.

Data Extraction: Rigor of guideline development was assessed by 2 independent reviewers. One reviewer extracted information on conflicts of interest and recommendations.

Results: Sixteen of 27 guidelines reported conflicts of interest and 17 showed considerable rigor. These included recommendations on assessment of total cardiovascular risk (7 guidelines), dyslipidemia (2), hypertension (2), and dysglycemia (7). Recommendations on total cardiovascular risk and dyslipidemia included prediction models integrating multiple risk factors, whereas remaining recommendations were focused on single risk factors. No consensus was found on recommended target populations, treatment thresholds, and screening tests.

Conclusions: Differences among the guidelines imply important variation in allocation of preventive interventions. To make informed decisions, physicians should use only the recommendations from rigorously developed guidelines.


CARDIOVASCULAR DISEASE (CVD) is the leading cause of mortality in Western society, accounting for approximately one-third of total mortality. Much of the burden of CVD can potentially be relieved by primary prevention, that is, reducing CVD incidence in the apparently healthy population. Detecting and treating those at highest CVD risk is regarded as an essential complement to a population-based approach. The primary care physician plays a pivotal role in providing prevention on the individual level and is thus essential for the success rate of this strategy. However, most physicians find implementing even rudimentary preventive services difficult, and the management of increased CVD risk remains suboptimal.

Although historically controversial, cardiovascular health checks have now been widely accepted as a means to efficiently detect high-risk individuals in primary care practice. As a result of the Diabetes, Heart Disease and Stroke pilot studies, UK citizens aged 40 to 74 years will be offered a cardiovascular health check every 5 years. This includes a questionnaire on risk factors and measurement of weight, hip to waist ratio, blood pressure, and total cholesterol level. People at high risk for developing diabetes undergo measurement of glucose levels. In the United States, cardiovascular health checks are already common practice as part of the periodic health examination. In the absence of a blueprint for the content of cardiovascular health checks, decisions on selection of appropriate individual screening interventions should be guided by the best available medical evidence. For translating research into clin-
recognition, transparency, and independence of guidelines.9,10 Guidelines are systematically and provide a validated instrument and assessed potential conflicts of interest. Finally, we examined recommendations from rigorously developed guidelines in detail to guide primary care physicians in deciding which screening interventions to use within a cardiovascular health check.

**METHODS**

To identify appropriate guidelines, a literature search was performed by using MEDLINE and CINAHL between January 1, 2003, and May 2, 2009. We supplemented this by searching the following 4 guideline-specific databases: the National Guideline Clearinghouse (United States), National Library for Health on Guidelines Finder (United Kingdom), Canadian Medical Association Infobase (Canada), and G-I-N International Guideline Library (http://www.g-i-n.net). We restricted our search to national guidelines from the United States, Canada, the United Kingdom, Australia, and New Zealand and to international guidelines written in English.

The MEDLINE search syntax served as a basis for all search strategies. The syntax consisted of the following 3 elements intersected by the Boolean term “AND”: (1) subject headings and free text terms for interventions regarding the health check content (ie, risk assessment, screening, early detection, early diagnosis, early intervention, periodic evaluation, periodic examination, periodic check-up, prevention, and risk management); (2) subject headings and free text terms for conditions that could define high risk for CVD and CVD outcomes that should be prevented (ie, arteriosclerosis, atherosclerosis, hypertension, hyperlipidemia, diabetes, cardiovascular disease, coronary heart disease, cerebrovascular disease, peripheral vascular disease, heart failure, and aortic aneurysm); and (3) publication types and title words that cover clinical practice guidelines (ie, practice guideline, guideline, guidance, standards, statement, position paper, position statement, recommendation, and consensus). A search on a number of Web sites of guideline development organizations was performed for additional relevant guidelines (the full search strategy is available on request from the authors).

Retrieved references were considered guidelines if they met the Institute of Medicine definition. We only considered guidelines recommending cardiovascular risk assessment specifically aimed to prevent a first CVD event. We excluded guidelines if they (1) did not contain recommendations involving the apparently healthy adult population, (2) were entirely focused on early detection of CVD, (3) were not produced on behalf of a professional organization, or (4) were not applicable to Western countries. In addition, only guidelines pro-

| Figure. Summary of guideline search and review process. Numbers of guidelines at each step of the process are indicated. Group totals may exceed the reported numbers for the excluded articles at abstract and full text level because several reasons for exclusion were allowed. CMA indicates Canadian Medical Association; CVD, cardiovascular disease; and NGC, National Guideline Clearinghouse. | 1984 Citations identified
| 277 NGC
| 140 National Library for Health
| 41 G-I-N
| 58 CMA Infobase
| 1259 MEDLINE
| 114 CINAHL
| 19 Web sites |
| 245 Duplicates |
| 1739 Titles reviewed |
| 1416 Excluded |
| 323 Abstracts reviewed |
| 209 Excluded |
| 17 No useful information
| 76 Not part of guideline
| 2 Not English language
| 16 Not most recent version
| 5 Target population <18 y
| 2 Not produced by specialty organization
| 7 Not applicable to selected countries
| 17 Not pannational or national
| 21 Not focused on screening
| 31 Not asymptomatic population
| 18 Background piece |
| 114 Full text reviewed |
| 87 Excluded |
| 1 Irretrievable
| 13 Not part of guideline
| 4 Developed before 2003
| 3 Not produced by specialty organization
| 10 Not pannational or national
| 6 Background piece
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| 4 Adapted from existing guideline
| 4 Other reasons |
| 27 Included guidelines |

**Citations identified**

- 1984
- NGC: 277
- National Library for Health: 140
- G-I-N: 41
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**Included guidelines**

- 27

**Duplicates**

- 245

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  - Adapted from existing guideline
  - Early detection of CVD
  - Not pannational or national
  - Not produced by specialty organization
  - Developed before 2003
Reproduced or updated from 2003 onward were eligible for inclusion to be more certain about the currency of guidelines.12

Review of titles and abstracts was assessed independently by two of us (B.S.F. and E.B.C.). For an article to be excluded, both reviewers had to agree that the article was ineligible. For abstracts, discrepancies between the reviewers were discussed and resolved by consensus. The final selection for full data extraction was made by the first reviewer (B.S.F.) because of the broad array of potentially eligible guidelines.

**GUIDE LINE QUALIT Y ASSESSMENT**

We used the 7-item Rigor of Development domain of the Appraisal of Guidelines Research and Evaluation (AGREE) instrument13 to determine the quality of development for each included guideline. This domain considers the reporting of (1) methods to search for evidence; (2) criteria for selecting the evidence; (3) methods for formulating the recommendations; (4) health benefits, adverse effects, and risks; (5) supporting evidence; (6) procedures for external expert review; and (7) the update process. Each item is rated on a 4-point Likert scale. In conformity with the instructions,14 two of us (B.S.F. and J.J.V.) independently rated the 7 items. A group member is reported recused when a relevant area is under discussion.

**RECOMMENDATION EXTRACTION**

We used the search and Evaluation (AGREE) instrument15 to determine the quality of development for each included guideline. This domain considers the reporting of (1) methods to search for evidence; (2) criteria for selecting the evidence; (3) methods for formulating the recommendations; (4) health benefits, adverse effects, and risks; (5) supporting evidence; (6) procedures for external expert review; and (7) the update process. Each item is rated on a 4-point Likert scale. In conformity with the instructions, two of us (B.S.F. and J.J.V.) independently rated the 7 items.

Table 1. Characteristics of 27 Guidelines and 32 Recommendations

<table>
<thead>
<tr>
<th>Guidelines by Medical Condition, y</th>
<th>Organization Responsible for Guideline Development</th>
<th>Country Applied</th>
<th>AGREE Rigor Score, %</th>
<th>Conflicts of Interest</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total cardiovascular risk</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NICE,19 2008</td>
<td>National Institute for Health and Clinical Excellence</td>
<td>United Kingdom</td>
<td>98</td>
<td>EI, SCI</td>
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<tr>
<td>SIGN,14 2007</td>
<td>Scottish Intercollegiate Guidelines Network</td>
<td>United Kingdom</td>
<td>83</td>
<td></td>
</tr>
<tr>
<td>AHA1,17 2007</td>
<td>American Heart Association</td>
<td>United States</td>
<td>76</td>
<td>SCI, SCI1, SCI2</td>
</tr>
<tr>
<td>AHA2,16 2006</td>
<td>American Heart Association and American Stroke Association</td>
<td>United States</td>
<td>71</td>
<td>SCI1</td>
</tr>
<tr>
<td>NZGG,18 2003</td>
<td>New Zealand Guidelines Group</td>
<td>New Zealand</td>
<td>67</td>
<td>EI, FPO, SCI1, SCI2</td>
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<tr>
<td>WHG,21 2007</td>
<td>World Health Organization</td>
<td>International</td>
<td>60</td>
<td></td>
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<tr>
<td>ESC1,20 2007</td>
<td>European Society of Cardiology</td>
<td>Europe</td>
<td>55</td>
<td></td>
</tr>
<tr>
<td>CDS,26 2006</td>
<td>Canadian Cardiovascular Society</td>
<td>Canada</td>
<td>50</td>
<td>EI, SCI1, SCI2</td>
</tr>
<tr>
<td>NHF1,31 2005</td>
<td>National Heart Foundation of Australia and Cardiac Society of Australia and New Zealand</td>
<td>Australia</td>
<td>43</td>
<td>SCI1</td>
</tr>
<tr>
<td>JBS,32 2005</td>
<td>Joint British Societies</td>
<td>United Kingdom</td>
<td>19</td>
<td></td>
</tr>
<tr>
<td>ACS,48 2004</td>
<td>American Cancer Society, American Diabetes Association, and American Heart Association</td>
<td>United States</td>
<td>14</td>
<td></td>
</tr>
<tr>
<td>ESC2,39 2007</td>
<td>European Society of Cardiology</td>
<td>Europe</td>
<td>14</td>
<td>SCI1, SCI2</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>USPSTF1,35 2008</td>
<td>US Preventive Services Task Force</td>
<td>United States</td>
<td>95</td>
<td>EI</td>
</tr>
<tr>
<td>NHLBI,36 2002 (updated 2004)</td>
<td>National Heart, Lung, and Blood Institute; National Institutes of Health; and US Department of Health and Human Services</td>
<td>United States</td>
<td>50</td>
<td></td>
</tr>
<tr>
<td>NHF2,37 2001 (still valid 2009)</td>
<td>National Heart Foundation of Australia and Cardiac Society of Australia and New Zealand</td>
<td>Australia</td>
<td>45</td>
<td></td>
</tr>
<tr>
<td>ACS,38 2004</td>
<td>American Cancer Society, American Diabetes Association, and American Heart Association</td>
<td>United States</td>
<td>14</td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>USPSTF2,39 2007</td>
<td>US Preventive Services Task Force</td>
<td>United States</td>
<td>81</td>
<td>EI, SCI</td>
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<tr>
<td>AHA2,38 2006</td>
<td>American Heart Association and American Stroke Association</td>
<td>United States</td>
<td>71</td>
<td>SCI1</td>
</tr>
<tr>
<td>BHS,1,37 2004</td>
<td>British Hypertension Society</td>
<td>United Kingdom</td>
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<td></td>
</tr>
<tr>
<td>ACS,48 2004</td>
<td>American Cancer Society, American Diabetes Association, and American Heart Association</td>
<td>United States</td>
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<td></td>
</tr>
<tr>
<td>Dysglycemia</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>USPSTF3,40 2008</td>
<td>US Preventive Services Task Force</td>
<td>United States</td>
<td>95</td>
<td>EI, SCI</td>
</tr>
<tr>
<td>NHMRC,41 2001 (updated 2005)</td>
<td>National Health and Medical Research Council</td>
<td>Australia</td>
<td>79</td>
<td>FPO</td>
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<tr>
<td>ESC3,42 2007</td>
<td>European Society of Cardiology and European Association for the Study of Diabetes</td>
<td>Europe</td>
<td>74</td>
<td></td>
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<td>CDA,43 2008</td>
<td>Canadian Diabetes Association</td>
<td>Canada</td>
<td>74</td>
<td>EI, FIP, SCI1, SCI2</td>
</tr>
<tr>
<td>CTF,44 2005</td>
<td>Canadian Task Force on Preventive Health Care</td>
<td>Canada</td>
<td>69</td>
<td>SCI1</td>
</tr>
<tr>
<td>AACE,45 2007</td>
<td>American Association of Clinical Endocrinologists</td>
<td>United States</td>
<td>50</td>
<td>SCI1</td>
</tr>
<tr>
<td>CCS,46 2006</td>
<td>Canadian Cardiovascular Society</td>
<td>Canada</td>
<td>50</td>
<td>EI, SCI1, SCI2</td>
</tr>
<tr>
<td>IDF1,47 2005</td>
<td>International Diabetes Federation</td>
<td>International</td>
<td>48</td>
<td>FIP, SCI1, SCI2</td>
</tr>
<tr>
<td>IDF2,48 2007</td>
<td>International Diabetes Federation</td>
<td>International</td>
<td>24</td>
<td>EI, FIP, SCI1, SCI2</td>
</tr>
<tr>
<td>ADA,49 2009</td>
<td>American Diabetes Association</td>
<td>United States</td>
<td>17</td>
<td>SCI1</td>
</tr>
<tr>
<td>ACS,50 2004</td>
<td>American Cancer Society, American Diabetes Association, and American Heart Association</td>
<td>United States</td>
<td>14</td>
<td></td>
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<tr>
<td>DUK,51 2006</td>
<td>Diabetes UK</td>
<td>United Kingdom</td>
<td>10</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: AGREE, Appraisal of Guidelines Research and Evaluation; EI, editorial independence declared; FIP, funding by industrial partner reported; FPO, funding by external public organization reported; SCI, statement about conflicts of interest of group members present.

1 Relationship with industry is reported by any group member.

2 A group member is reported recused when a relevant area is under discussion.

3 Minimum possible score (see the eTable15-41 [http://www.archinternmed.com] for item scores per guideline). Reproducibility of the 2 reviewers’ average rigor scores was good, with an intraclass correlation coefficient of 0.78. We ranked included guidelines according to their average scores. Moreover, editorial independence from the funding body and external funding and disclosure of relationships with industry by individual guideline group members were assessed by one reviewer (B.S.F.).

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vice was not considered. Subsequently, a recommendation matrix grouped by screen-detectable conditions was constructed. Each matrix was divided into (1) a methods section, (2) target group and delivery of screening, (3) recommended screening tests, and (4) thresholds for follow-up. Strength of recommendation was classified as “for,” “consider,” “not for not against,” “insufficient evidence,” and “against.” If possible, cardiovascular risk factors were classified into major, underlying, and emerging risk factors according to the World Heart and Stroke Forum 2004 scientific statement. In this report, we present only the recommendations of guidelines with an average rigor score of 30% or higher (indicating considerable rigor).

## RESULTS

The search retrieved 1984 titles, of which 323 were identified as potentially eligible. Many were excluded on the basis of the abstract (n = 209) and on review of the full report (n=87). Finally, 27 guidelines relevant to cardiovascular risk assessment were included (Figure). Table 1 summarizes the selected guidelines, together with the rigor score and conflict of interest results, categorized by the following screen-detectable conditions: total cardiovascular risk, dyslipidemia, hypertension, and dysglycemia (diabetes mellitus, impaired glucose tolerance, and/or impaired fasting glucose). Eleven guidelines did not report that they were developed independently from funding organizations or have a statement about conflicts of interest of group members. The development of 2 guidelines (from the New Zealand Guidelines Group [NZGG] and the National Health and Medical Research Council [NHMRC]) was funded by external governmental sources. Guidelines from the Canadian Diabetes Association (CDA) and the International Diabetes Federation (IDF1 and IDF2) were financially supported by industry partners. Although sponsors did not take part in the development of these guidelines, commercial organizations were allowed to comment on draft versions of the IDF1. Only 2 guidelines (from the American Heart Association [AHA1] and the CDA) reported that recusal of group members with conflicts of interest was accomplished when relevant areas were under discussion.

Seventeen of the 27 guidelines had an average rigor score equal to or greater than 50%. Recommendations for total cardiovascular risk assessment extracted from these guidelines are demonstrated in Table 2, excluding the recommendation of the AHA2 guidelines that did not explicitly describe treatment thresholds. Advice concerning screening primarily for single risk factors (dyslipidemia, hypertension, and dysglycemia) are tabulated in Tables 3, 4, and 5. The full recommenda-

<table>
<thead>
<tr>
<th>Method to formulate recommendations</th>
<th>Method to evaluate evidence</th>
<th>Target group</th>
<th>Strategy</th>
<th>Strength of recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Consensus development conference; informal consensus or formal voting if evidence sparse</td>
<td>Systematic review; review of published systematic reviews</td>
<td>Aged ≤40 y; prioritize those at ≥20% risk using Framingham and preexisting record of risk factors; self-presenting</td>
<td>Record-based screening; opportunistic screening/ case finding</td>
<td>For</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Considerations of costs</th>
<th>CEA; cost-impact analysis; systematic review of CEA studies</th>
<th>Systematic review of CEA studies</th>
<th>CEA; cost-impact analysis</th>
<th>Systematic review of CEA studies</th>
<th>Systematic review of CEA studies</th>
<th>Systematic review of CEA studies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost-effectiveness; cost-impact analysis</td>
<td>Systematic review of CEA studies</td>
<td>Women aged ≥20 y; first-degree relative with premature CVD or familial dyslipidemia</td>
<td>Opportunistic screening/ case finding</td>
<td>Not specified, population screening is not warranted</td>
<td>Opportunistic screening/ case finding</td>
<td>Opportunistic screening/ case finding</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Strength of recommendation</th>
<th>For</th>
<th>For</th>
<th>For</th>
<th>For</th>
<th>For</th>
<th>For</th>
<th>Consider</th>
</tr>
</thead>
</table>

(continued)
tion matrices of all 27 guidelines are available on request from the authors.

**AREAS OF AGREEMENT**

Recommendations of 16 of 17 guidelines supported risk assessment. In general, there was consensus on how screening tests should be administered to the target population. A selective screening approach based on prior knowledge of patient characteristics (record-based screening) or during nonpreventive patient visits (case finding or opportunistic screening) was advocated in 10 of 17 guidelines. A mass screening approach was suggested as an alternative by only 1 guideline (from the National Heart, Lung, and Blood Institute [NHLBI]).

Many guidelines recommended integrating age, sex, smoking, blood pressure, and lipid levels into total cardiovascular risk assessment by using prediction models (Tables 2 and 3). In only 2 hypertension guidelines (from the US Preventive Services Task Force [USPSTF] and the AHA2 guidelines) were treatment decisions merely guided by elevated blood pressure levels (Table 4). The recommended prediction models were all based on the concept that CVD is best predicted by multiple risk factors and that these risk factors interact. If a risk score was not recommended as a primary screening test, it was frequently used to guide treatment in a second stage for individuals with elevated single risk factors (USPST1 and NHLBI guidelines).

Thresholds for initiation of treatment were based on short-term (5- or 10-year) risk for CVD, with exceptions often made for those with extreme levels of single risk factors. In general, the same thresholds across guidelines were used for the initiation of treatment with aspirin, statins, and antihypertensives. The guideline from the European Society of Cardiology for total cardiovascular risk assessment (ESC1) used a higher threshold for the use of aspirin because of the risk for major gastrointestinal tract bleeding. The ESC1 guideline may represent a common, cautious European viewpoint. However, we did not observe a more conservative attitude with respect to preventive treatments among the European guidelines compared with the others.

Guidelines that specifically covered dysglycemia screening were mainly focused on selecting individuals for interventions to lower glucose levels and did not report or were short on initiation of statin

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**Table 2. Recommendations for Screening for Total CVD Risk in 7 Guidelines (continued)**

<table>
<thead>
<tr>
<th>Major risk factors</th>
<th>Screening Tests</th>
<th>NICE</th>
<th>SIGN</th>
<th>AHA1</th>
<th>NZGG</th>
<th>WHO</th>
<th>ESC1</th>
<th>CCS Step 1</th>
<th>CCS Step 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Framingham, CHD/stroke events at 10 y</td>
<td>Framingham, CHD/stroke events at 10 y</td>
<td>Framingham, general CVD events at 10 y</td>
<td>Framingham, general CVD events at 5 y</td>
<td>WHO/ISH CVD risk prediction charts, CHD/stroke events at 10 y</td>
<td>SCORE, general CVD mortality at 10 y</td>
<td>Framingham, CHD events at 10 y</td>
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<tr>
<td>Age</td>
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<td>Sex</td>
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<td>Blood pressure</td>
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<td>TC level</td>
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<td>LDL-C level</td>
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<td>HDL-C level</td>
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<td>TG levels</td>
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<td>Underlying risk factors</td>
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<td>Overweight/obesity</td>
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<td>Physical inactivity</td>
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<td>Family history of premature CVD</td>
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<td>Genetic/racial factors</td>
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<td>Emerging risk factors</td>
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<td>Apolipoprotein/ lipoprotein levels</td>
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<td>Glucose therapy for insulin resistance</td>
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<td>Prothrombotic markers</td>
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<td>C-reactive protein level</td>
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<tr>
<td>Subclinical atherosclerosis (LVH in history)</td>
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</tbody>
</table>

(continued)
and aspirin therapy (Table 5). Guidance for these treatments was based on single risk factors, and none of the recommendations contained models predicting CVD. Fasting glucose level was usually the test of first choice, except for 1 guideline (ESC3) in which an antecedent risk score for developing type 2 diabetes mellitus was recommended.

Although guidelines did not make firm statements about screening intervals, frequently reported periods of screening for individuals at low risk were 5 years for total cardiovascular risk and dyslipidemia screening, 2 years for hypertension screening, and 3 years for dysglycemia screening. Only 2 guidelines based these intervals on modeling studies (NZGG and USPSTF3).

**AREAS OF DISAGREEMENT**

We found no consensus on target populations for screening among the

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**Table 2. Recommendations for Screening for Total CVD Risk in 7 Guidelines (continued)**

<table>
<thead>
<tr>
<th>Further screening</th>
<th>NICE</th>
<th>SIGN</th>
<th>AHA1</th>
<th>NZGG</th>
<th>WHO</th>
<th>ESC1</th>
<th>CCS Step 1</th>
<th>CCS Step 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspirin</td>
<td>NR</td>
<td>NR</td>
<td>10-y CVD risk ≥20% and controlled BP &lt;150/90 mm Hg; DM</td>
<td>10-y CHD/stroke risk ≥20%; DM</td>
<td>5-y CVD risk ≥15%</td>
<td>10-y CVD mortality ≥10% and controlled BP &lt;140/90 mm Hg</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Statins</td>
<td>10-y CHD/stroke risk ≥20%; aged ≥74 y and smoking or HTN</td>
<td>10-y CHD/stroke risk ≥20%; DM; LDL-C level ≥160 mg/dL; 10-y CHD/stroke risk ≥10% and ≥2 RFs; LDL-C level ≥130 mg/dL; 10-y CHD/stroke risk ≥10% and ≥2 RFs; LDL-C level ≥190 mg/dL</td>
<td>10-y CHD/stroke risk ≥20%; DM; LDL-C level ≥310 mg/dL; 10-y CHD/stroke risk ≥20% and ≥2 RFs; LDL-C level ≥130 mg/dL; 10-y CHD/stroke risk ≥10% and ≥2 RFs; LDL-C level ≥190 mg/dL</td>
<td>10-y CHD/stroke risk ≥15%; TC level ≥310 mg/dL; TC:HDL-C ratio ≥5.0; 10-y CHD/stroke risk ≥20%; 10-y CHD risk ≥5% (in elderly, ≥10%); 10-y CHD risk ≥5% (in elderly, ≥10%); 10-y CHD risk ≥15 mg/dL or LDL-C level ≥115 mg/dL; (DM2 or DM1) with microalbuminuria and TC level ≥115 mg/dL or LDL-C level ≥115 mg/dL; severe hyperlipidemia</td>
<td>5-y CVD risk ≥30%; 10-y CHD/stroke risk ≥20%; LDL-C level ≥130 mg/dL or LDL-C level ≥115 mg/dL; severe hyperlipidemia</td>
<td>10-y CHD risk ≥20%; 10-y CHD risk ≥15 mg/dL or LDL-C level ≥115 mg/dL; severe hyperlipidemia</td>
<td>Lipoprotein(a) level ≥0.3 g/L if TC:HDL-C ratio ≥5.0 or other major RFs indicate need for earlier and more intensive LDL-C level lowering; hsCRP level ≥3.0 mg/L indicates high risk; subclinical atherosclerosis</td>
<td></td>
</tr>
<tr>
<td>Antihypertensives</td>
<td>NR</td>
<td>10-y CVD risk ≥20% and BP ≥140/90 mm Hg; 10-y CVD risk ≥10%-19% and BP ≥160/100 mm Hg; (DM2 or DM1) and BP ≥140/90 mm Hg or ≥130/80 mm Hg if complications</td>
<td>10-y CHD/stroke risk ≥20% and BP ≥140/90 mm Hg; (DM2 or DM1) and BP ≥140/90 mm Hg or ≥130/80 mm Hg if complications</td>
<td>10-y CHD/stroke risk ≥20% and BP ≥140/90 mm Hg; (DM2 or DM1) and BP ≥140/90 mm Hg or ≥130/80 mm Hg if complications</td>
<td>10-y CHD/stroke risk ≥20%; BP ≥170/100 mm Hg</td>
<td>10-y CHD/stroke risk ≥30%; 10-y CHD risk ≥5% (in elderly, ≥10%); 10-y CHD risk ≥5% (in elderly, ≥10%); 10-y CHD risk ≥15 mg/dL or LDL-C level ≥115 mg/dL; (DM2 or DM1) with microalbuminuria and TC level ≥115 mg/dL or LDL-C level ≥115 mg/dL; severe hyperlipidemia</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Intensive lifestyle counseling</td>
<td>10-y CHD/stroke risk ≥20%; 10-y CVD risk ≥20%; 10-y CVD risk ≥20% and BP ≥160/100 mm Hg or TC level ≥310 mg/dL</td>
<td>10-y CVD risk ≥20%; DM; LDL-C level ≥160 mg/dL and 10-y CHD/stroke risk &lt;10%; and ≥2 RFs; LDL-C level ≥130 mg/dL and 10-y CHD/stroke risk ≥10% and ≥2 RFs; LDL-C level ≥190 mg/dL</td>
<td>10-y CVD risk ≥20%; DM; LDL-C level ≥160 mg/dL and 10-y CHD/stroke risk ≥10% and ≥2 RFs; LDL-C level ≥190 mg/dL</td>
<td>10-y CVD risk ≥20%; DM; LDL-C level ≥160 mg/dL and 10-y CHD/stroke risk ≥10% and ≥2 RFs; LDL-C level ≥190 mg/dL</td>
<td>10-y CVD risk ≥15%</td>
<td>10-y CHD/stroke risk ≥20%</td>
<td>NR</td>
<td>NR</td>
</tr>
</tbody>
</table>

(continued)
Table 2. Recommendations for Screening for Total CVD Risk in 7 Guidelines (continued)

<table>
<thead>
<tr>
<th>Screening intervals</th>
<th>Further risk assessment on an ongoing basis</th>
<th>Further risk assessment every 1-5 y, depending on clinical circumstances if 10-y CVD risk 10%-19%; further risk assessment in 5 y if 5-y CVD risk &lt;10%</th>
<th>Further risk assessment in 5 y if 5-y CVD risk 10%-15%; further risk assessment in 5-10 y if 5-y CVD risk &lt;10%</th>
<th>Further risk assessment every 2-5 y depending on clinical circumstances and resource availability if 10-y CHD/stroke risk &lt;10% and BP ≥140/90 mm Hg</th>
<th>Further risk assessment at regular (5-y) intervals if 10-y CVD mortality &lt;5%</th>
<th>More frequent testing if abnormal values or if treatment initiated</th>
<th>More frequent testing if abnormal values or if treatment initiated</th>
</tr>
</thead>
<tbody>
<tr>
<td>High-risk monitoring</td>
<td>Unnecessary, clinical judgment and patient preference should guide review of drug therapy and whether to review lipid profile</td>
<td>Monitor risk profile every 6-12 mo if 10-y CVD risk ≥20%</td>
<td>Further risk assessment at least annually; monitor risk profile every 3-6 mo if 5-y CVD risk ≥15%</td>
<td>Monitor risk profile every 3-6 mo if 10-y CHD/stroke risk ≥20%; monitor risk profile every 6-12 mo if 10-y CHD/stroke risk ≥10%-20%</td>
<td>Monitor risk profile if 10-y CVD mortality ≥5%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: ABI, ankle-brachial index; BP, blood pressure; CEA, cost-effectiveness analysis; CHD, coronary heart disease; CVD, cardiovascular disease; DM, diabetes mellitus; DM1, DM type 1; DM2, DM type 2; ECG, electrocardiography; HDL-C, high-density lipoprotein cholesterol; hsCRP, high-sensitivity C-reactive protein; HTN, hypertension; ISH, International Society of Hypertension; LBD-L, low-density lipoprotein cholesterol; UH, left ventricular hypertrophy; NR, not reported; PE, physical examination; RF, risk factor; SCORE, Systematic Coronary Risk Evaluation; TC, total cholesterol; TG, triglyceride; US, ultrasonography; *H12012, formal screening test (included in the prediction model); †H1350, additional screening test. For other abbreviations, see Table 1.

| Thresholds (continued) | | |
|-------------------------|------------------|------------------|------------------|------------------|------------------|------------------|
| NICE | SIGN | AHA1 | NZGG | WHO | ESC1 | CCS Step 1 | CCS Step 2 |
| initiated | frequent | frequent | frequent | frequent | frequent | frequent | frequent |
| | testing | testing | testing | testing | testing | testing | testing |
| | if | abnormal | values | or if | treatment | initiated | initiated |
| | | | | treatment | initiated | | |

Recommendations (Tables 2, 3, 4, and 5). Target groups varied from middle-aged and younger adults with and without risk factors to unspecified patients asking for screening themselves. From these recommendations, health checks that included assessment of lipid levels, blood pressure, and dysglycemia could be designed that would start at 20 years of age (using the NLHBI, USPSTF2, and ESC3 guidelines) or that would start at middle age (eg, using the guidelines from the Scottish Intercollegiate Guidelines Network [SIGN] and the NHMRC guidelines).

Guidelines on total cardiovascular risk, dyslipidemia, and hypertension screening (Tables 2, 3, and 4) disagreed on tests to be performed in addition to those primarily recommended. The most frequently recommended risk modifiers not included in formal risk assessment were a family history of premature CVD, obesity, and socioeconomic deprivation. In the total cardiovascular risk recommendations, only 1 prediction model (the ASSIGN score) was used that incorporated some of these risk factors, namely, family history and socioeconomic status in addition to the major risk factors. Other total cardiovascular risk guidelines provided instructions for simple multiplication of the predicted risk by the relative risk of the additional risk factor (guidelines from the National Institute for Health and Clinical Excellence [NICE] and Canadian Cardiovascular Society [CCS]) or only made general statements about the relative contribution to the total cardiovascular risk estimation (SIGN, AHA1, NZGG, and ESC1 and guidelines from the World Health Organization [WHO]).

Recommendations for dysglycemia screening (Table 5) varied in strength. For example, for a 60-year-old patient without risk factors, screening could both be not supported and recommended at the same time, depending on which guideline the physician follows. Discrepancies in decision making could also occur with regard to the initiation of treatment guided by total cardiovascular risk (Table 2). Apart from differences in thresholds indicating high risk, recommended risk models varied over the use of data sets, predictors, and end points, including fatal and nonfatal CVD outcomes. For example, the NICE, SIGN, CCS, and NHLBI guidelines all used a threshold of 20% to define high risk. The NICE guidelines recommended the 1991 Framingham model using coronary artery disease and stroke events as a composite end point, whereas the CCS and NHLBI guidelines used Framingham models for predicting coronary artery disease alone (ie, without stroke). The SIGN guideline endorsed the ASSIGN score, which includes coronary artery disease, heart failure, aortic aneurysm, peripheral arterial disease, and stroke. Because of this lack of consistency, making comparisons of recommended indications for aspirin, statin, and antihypertensive therapy and intensive lifestyle changes is not straightforward.
We identified 27 guidelines involving cardiovascular risk assessment that could be performed within a cardiovascular health check. A great variation in rigor of development and transparency about conflicts of interest was found among the guidelines. Guidelines on screening for total cardiovascular risk and dyslipidemia embraced, to a different extent, decision making based on multiple risk factors. This approach contrasted with the recommendations for hypertension and dysglycemia screening, which focused on single risk factors. Most of the guide-
lines supported a selective screening strategy. We found differences between guidelines with respect to the selection of target groups, screening tests in addition to those for major CVD risk factors, and treatment thresholds. Different statements about strength were given to recommendations that considered comparable patient populations with respect to dysglycemia screening. No firm recommendations could be

<p>| Table 4. Recommendations for Screening for Hypertension in 2 Guidelines |</p>
<table>
<thead>
<tr>
<th>USPSTF2</th>
<th>AHA2</th>
</tr>
</thead>
<tbody>
<tr>
<td>AGREE rigor score, %</td>
<td>81</td>
</tr>
<tr>
<td>Method to evaluate evidence</td>
<td>Systematic review; review of published systematic reviews</td>
</tr>
<tr>
<td>Method to formulate recommendations</td>
<td>Formal consensus and voting</td>
</tr>
<tr>
<td>Consideration of costs</td>
<td>NR</td>
</tr>
<tr>
<td>Target group</td>
<td>Aged $\geq$ 18 y</td>
</tr>
<tr>
<td>Strategy</td>
<td>Opportunistic screening/case finding</td>
</tr>
<tr>
<td>Strength of recommendation</td>
<td>For</td>
</tr>
</tbody>
</table>

### Screening Tests

**Major risk factors**
- Age
- Sex
- BP
- Smoking

**Underlying risk factors**
- Overweight/obesity
- Physical inactivity

### Thresholds

- **Antihypertensives**
  - BP $\geq$ 140/90 mm Hg

- **Intensive lifestyle counseling**
  - BP $\geq$ 140/90 mm Hg

- **High-risk monitoring**
  - Rescreen every year if SBP 120-139 mm Hg and/or DBP 80-99 mm Hg; rescreen every 2 y if BP $< 120/80$ mm Hg, but optimal interval for screening not known

- **Screening intervals**
  - Rescreen regularly if BP $\geq$ 140/90 mm Hg, at least every 2 y in most adults and more frequently in minority populations and elderly persons

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| Table 5. Recommendations for Screening for Dysglycemia in 7 Guidelines |
| --- | --- | --- | --- | --- | --- | --- | --- |
| USPSTF3 | NHMRC | NHMRC | ESC3 | CDA | CTF | AACE | CCS |
| AGREE rigor score, % | 95 | 79 | 79 | 74 | 74 | 69 | 50 |
| Method to evaluate evidence | Meta-analysis for drug and lifestyle effects; systematic review; review of published systematic reviews | Systematic review; review of published systematic reviews | Systematic review; review of published systematic reviews | Systematic review; review of published systematic reviews | Systematic review; review of published systematic reviews | Systematic review | Systematic review; review of published systematic reviews |
| Method to formulate recommendations | Formal consensus and voting; balance sheets | Formal consensus | Formal consensus | Formal consensus | Formal consensus | Formal consensus | Formal consensus |
| Consideration of costs | Review of CEA studies | NR | Review of CEA studies | NR | NR | NR | NR |
| Target group | Aged $\geq$ 18 y | Aged $\geq$ 45 y and BMI $\geq$ 30; aged $\geq$ 55 y and high-risk ethnicity | Aged $\geq$ 55 y; aged $\geq$ 45 y and first-degree relative with DM; women and previous gestational DM; and high-risk ethnicity | Aged $\geq$ 18 y | Aged $\geq$ 40 y and $\geq$ 1 RI $^a$; patients who diagnosed as having DM | Aged $\geq$ 30 y and $\geq$ 1 RI $^c$ | Aged $\geq$ 40 y and $\geq$ 1 RI $^d$ |
| Strategy | Opportunistic screening/case finding | Opportunistic screening/case finding | Opportunistic screening/case finding | For | NRI | For | For |
| Strength of recommendation | Insufficient evidence to make one | For | Insufficient evidence to make one | For | For | For | For |

**Abbreviations:** DBP, diastolic blood pressure; SBP, systolic blood pressure. For other abbreviations, see Tables 1, 2, and 3.
made for screening intervals in people at low risk for developing a first cardiovascular event.

Previously published reviews of CVD prevention guidelines were not systematically performed or did not use a validated instrument to assess the quality of identified guidelines. We used a sensitive search strategy to identify guidelines and the AGREE instrument to select guidelines of considerable quality. This article can therefore be of additional value to already available guideline compendiums and libraries such as the US National Guideline Clearinghouse and the UK National Library for Health because these libraries depend on submissions by guideline organizations. Although a guideline synthesis tool can be found on the National Guideline Clearinghouse Web site, this tool is only available for a sample of US guidelines. Despite a number of strengths, there are several limitations that could have biased our findings. First,
Table 5. Recommendations for Screening for Dysglycemia in 7 Guidelines (continued)

<table>
<thead>
<tr>
<th>USPSTF3</th>
<th>NHMRC</th>
<th>NHMRC</th>
<th>ESC3</th>
<th>CDA</th>
<th>CTF</th>
<th>AACE</th>
<th>CCS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Intensive lifestyle counseling</strong></td>
<td>Attention to lifestyle if DM</td>
<td>DM; IFG</td>
<td>DM; IFG</td>
<td>DM; IGT; high score values on the noninvasive risk score</td>
<td>DM; IFG; IGT</td>
<td>DM; IFG; IGT</td>
<td>Confirmatory FPG level ≥ 100 mg/dL or 2hPG level ≥ 140 mg/dL</td>
</tr>
</tbody>
</table>
| **High-risk monitoring** | | | Retest in 1 y if IFG | Retest in 1 y if IFG | Retest more frequently than every 3 y if primary FPG ≥ 100 mg/dL or RF
d | NR | NR | NR |
| **Screening intervals** | ADA recommends every 3 y | Optimal interval for screening not known | Rescreen every 3 y | Rescreen every 3 y | Rescreen annually | Rescreen annually | Rescreen annually |

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); FINDRISC, Finnish type 2 diabetes risk score; FPG, fasting plasma glucose; HbA1c, hemoglobin type A1c; IFG, impaired fasting glucose; IGT, impaired glucose tolerance; OGTT, oral glucose tolerance test; RPG, random plasma glucose; 2hPG, 2-hour postload plasma glucose. For other abbreviations, see Tables 1 and 2.

°SI conversion factors: To convert glucose to millimoles per liter, multiply by 0.0555; HDL-C, LDL-C, and TC to millimoles per liter, multiply by 0.0259; TG to millimoles per liter, multiply by 0.0113.

a Includes family history of DM, overweight/obesity, and high-risk ethnicity.
b Includes smoking and increased age.
c Includes family history of DM, overweight/obesity, high-risk ethnicity, and sedentary lifestyle.
d Includes family history of DM and overweight/obesity.
e Includes men 45 years or older, women 50 years or older, multiple cardiovascular risk factors, extreme level of a single cardiovascular risk factor, and duration of DM longer than 15 years with age older than 30 years.

The AGREE instrument considers the whole guideline and is not intended for individual recommendations. However, a global appraisal will probably reflect the quality of the individual recommendations to some extent. Second, AGREE evaluates a guideline’s construction process and not the quality of its content. It is beyond the scope of this review to appraise the quality of the evidence underpinning the recommendations. However, an analysis of underlying evidence should be considered when evaluating guidelines. One would expect that the quality of the development methods correlates with the quality of the content, but it may be possible to create a solid guideline with a poor process. Third, only 2 reviewers rated the AGREE rigor items, and a more precise estimate would be obtained if we could have used more resources. Finally, our search strategy’s sensitivity could be improved. We did not use a search engine for an Internet search, and therefore we might have missed some eligible guidelines.

The finding that many guidelines recommended multivariable risk assessment conforms with historical developments. The rationale of its use is explained by studies showing that arbitrary elevations of single risk factors are of little clinical relevance when they are interpreted separately from other risk factors.94 The performance of multivariable risk assessment mainly depends on the selection of appropriate risk predictors. Prediction models using the traditional major risk factors may be updated through inclusion of emerging risk factors.47 However, the additional prognostic value is often questionable.48,49 Few of the reviewed guidelines used a prediction model incorporating 1 or more of the emerging risk factors. The value of general statements about their contribution to risk seems ambiguous if consistency of health care is intended.

Implementation of cardiovascular risk assessment into practice has been shown to be difficult.50 It is questionable whether the generally recommended opportunistic screening strategy could overcome this problem. Arguments in favor of opportunistic screening originate from disappointing results of population-based periodic health examinations and nurse-led cardiovascular health checks.31,52 Although health information technology may in part solve difficulties,53 the sheer volume of preventive care tasks per patient visit would put an overwhelming pressure on the workload of primary care physicians.54 Periodically inviting individuals for a preventive visit using already recorded determinants could be a valuable alternative. The workload and cost-effectiveness of this strategy will depend on risk factor distributions in the selected target populations and applied thresholds that indicate elevated risk. Given the controversy about target populations, treatment thresholds, and screening intervals, we advocate a decision-analytic approach to resolve these issues.55

Although guidelines on total cardiovascular risk, dyslipidemia, and hypertension all agreed on added value with screening, those on screening for dysglycemia sometimes disagreed. The case for dysglycemia screening has been uncertain in the absence of randomized trials but becomes stronger with the rising prevalence of overweight.56 Because CVD is by far the leading cause of mortality in persons with diabetes mellitus, preventing CVD seems more cru-
cial than reducing microvascular complications. Although intensive lowering of glucose levels in longstanding diabetes has not been shown to reduce CVD, in patients with newly diagnosed diabetes it may be beneficial. The efficacy of statins has been shown in a meta-analysis of 14 randomized controlled trials. The use of aspirin therapy in diabetes, however, is still controversial. Included guidelines were predominantly focused on selection of individuals for therapy to lower glucose levels but were not unanimous with regard to statins. Some guidelines advised that all patients with diabetes should receive a statin, whereas most allocated statins only to those with raised cholesterol levels in addition to diabetes. However, sustained benefits of statins are seen even in diabetic patients with low cholesterol levels, and thus it is argued that the decision for statin therapy in diabetics should also be based on total cardiovascular risk irrespective of initial cholesterol levels. Recommended risk models do not incorporate dysglycemia as a covariate or perform poorly in estimating CVD risk in diabetes. Prediction models specifically developed for people with dysglycemia exist but have to be validated. Integration of dysglycemia screening within a cardiovascular health check thus remains complex.

Some guidelines provided recommendations to select high-risk individuals for aspirin use. Recommended treatment thresholds for aspirin were predominantly the same as those for statins and fixed according to sex and age. These recommendations contrast with the recent conclusions of the USPSTF, which established its guidance on an assessment of the net benefit of aspirin, determined by the potential preventable number of CVD events and the potential harm due to gastrointestinal tract hemorrhages. The USPSTF’s thresholds for aspirin use depend on age and sex because the risk for serious bleeding increases with age and among men. The approach for aspirin use as demonstrated in the USPSTF guideline could lead to more individualized decision making. However, this approach can be made more sophisticated through expression of the benefit and harm in utility measures and might then also be applicable to the provision of other preventive treatments.

CONCLUSIONS

We identified guidelines providing recommendations for various screening interventions that can be performed within cardiovascular health checks. By using different recommendations, there are several ways to integrate multiple screening interventions into a single program. Although methods for guideline adaptation are available, our purpose was not to create one international set of recommendations. Nevertheless, physicians can easily adopt the presented recommendations applicable to their own health context. However, they should be wary of the differences, which can have important consequences for selection of individuals for preventive interventions. In addition, physicians should be able to balance the utility and disutility of potential lifelong preventive treatment. Complete and unbiased information on benefits and harms is thus desirable. Transparency about how judgments have been made within guidelines allows physicians to make informed decisions on adopting recommendations. Disclosure of conflicts of interest allows the industry influence on guideline development and the professional integrity of guideline group members to be assessed. The AGREE rigor scores of many guidelines demonstrated poor quality, and several guidelines lacked statements about conflicts of interest. We therefore encourage physicians to use the tabulated guidelines with higher AGREE rigor scores and unambiguous declarations about conflict of interest from this review for organizing their cardiovascular health checks.

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Online-Only Material: The eTable is available at http://www.archinternmed.com.

REFERENCES

21. Graham I, Atar D, Borch-Johnsen K, et al; European Society of Cardiology (ESC); European Association for Cardiovascular Prevention and Rehabilitation (EACPR); Council on Cardiovascular Nursing; European Association for Study of Diabetes (EASD); International Diabetes Federation Europe (IDF-Europe); European Stroke Initiative (EUSI); Society of Behavioural Medicine (ISBM); European Society of Hypertension (ESH); WONCA Europe (European Society of General Practice/ Family Medicine Council); National Heart Foundation of England; European Atherosclerosis Society (EAS). European guidelines on cardiovascular disease prevention in clinical practice: full text: Fourth Joint Task Force of the European Society of Cardiology and other societies on cardiovascular disease prevention in clinical practice (constituted by representatives of nine societies and by invited experts). Eur J Cardiovasc Prev Rehabil. 2007;14(suppl 2):S11-33.
Screening for High-Risk Cardiovascular Disease

A Challenge for the Guidelines

Cardiovascular disease is the leading cause of mortality worldwide, resulting in more than 17 million deaths in 2008. Early detection and treatment of high-risk patients has been endorsed as an important strategy to prevent cardiovascular events. The Institute of Medicine has emphasized the importance of evidence-based medicine expressed through guideline recommendations as a means to improve patient outcomes. Health care providers involved in preventive medicine are called on to initiate therapies to prevent cardiovascular disease through the use of guidelines issued by multiple groups. Yet concerns remain about the process by which guidelines might be developed, and a lack of congruence among their recommendations is one reason for low implementation by health care providers.

In this issue of the Archives, Ferket and colleagues report the results of their systematic review of guidelines containing recommendations for the assessment of cardiovascular risk in apparently healthy adults. Their study focuses on 27 guidelines from professional organizations in Western countries. The process of guideline development is evaluated using the Appraisal of Guidelines Research and Evaluation (AGREE) instrument, and guideline recommendations are summarized qualitatively in matrix groups that include the patient target group, screening tests recom...