

# Health checks in general practice: evidence first, not last

Alberto López-García-Franco<sup>1</sup>, Héctor Pardo-Hernández<sup>2</sup>,  
David Fraile-Navarro<sup>1</sup>, Pablo Alonso-Coello<sup>2,3,4</sup>

<sup>1</sup> Centro de Salud Dr. Mendiguchía Carriche (Leganés), Madrid, Spain

<sup>2</sup> Iberoamerican Cochrane Centre, Biomedical Research Institute Sant Pau (IIB Sant Pau), Barcelona, Spain

<sup>3</sup> CIBER Epidemiología y Salud Pública (CIBERESP), Barcelona, Spain

<sup>4</sup> Department of Clinical Epidemiology and Biostatistics, McMaster University, Hamilton, Ontario, Canada

## KEY WORDS

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## ABSTRACT

Despite being ubiquitous in primary care, there is no accepted consensus on the definition and main components of health checks. They range from periodic health evaluations with a general physician, through the screening and diagnostic tests derived from these visits, to broader screening programs. Health checks may promote a fluid patient–provider relationship, improve the delivery of some preventive measures, and reduce the patient’s anxiety. However, they can also expose patients to overdiagnosis and unnecessary interventions.

Research on the benefits, harms, and cost-effectiveness of health checks is limited. As a consequence, health checks and screening programs are implemented in several countries and supported by national scientific societies based chiefly on their potential benefits on surrogate outcomes. There is also substantial variability regarding the target population (eg, initial age), tests, or intervals.

We call for a rigorous assessment of the net effect of all health checks, taking into consideration common biases (eg, sticky-diagnosis and slippery-linkage biases), patient-important outcomes, potential adverse events, cost-effectiveness, as well as equity and feasibility of the proposed programs.

**Introduction** Health checks typically involve visits to a health care provider with the aim of identifying risk factors and early signs of preventable diseases through a varied array of screening tests.<sup>1–3</sup> Generally speaking, the common denominator of health checks is opportunistic early disease detection. As such, they range from periodic health evaluations with a general physician, through the screening and diagnostic tests derived from these visits, to broader screening programs. Nevertheless, and despite being ubiquitous in primary care, the definition and main components of health checks vary widely.<sup>3</sup>

The rationale behind health checks relies on the possibility of preventing or delaying the onset of disease through the management of symptoms and the modification of behaviors and lifestyle risk factors.<sup>3</sup> Health checks may promote a fluid patient–provider relationship, improve the delivery of some preventive measures, and reduce the patient’s anxiety.<sup>4</sup> However, health checks can

also expose patients to overdiagnosis and unnecessary interventions.

Research on the benefits, harms, and cost-effectiveness of health checks is limited. Two systematic reviews, one by Krogsbøll et al<sup>5</sup> published in the *British Medical Journal* in 2012, and another by Si et al<sup>6</sup> published in the *British Journal of General Practice* in 2014,<sup>6</sup> have recently reviewed the available evidence on the effects of health checks. Krogsbøll et al<sup>5</sup> conducted a Cochrane systematic review and included 16 studies that randomized 182 880 adults to either health check screening for more than 1 disease risk factor (76 403 participants) or to no health checks (106 477 participants). They excluded trials focused exclusively on geriatric populations as well as observational studies. The authors found no evidence to support health checks, with an increase in new clinical diagnosis and no reduction in morbidity or overall cardiovascular or cancer mortality.

## Correspondence to:

Héctor Pardo-Hernández,  
Carrer Sant Antoni Maria Claret, 167,  
Pavelló 18, 08025 Barcelona, Spain,  
phone: +34 935 537 832,  
e-mail: hpardo@santpau.cat  
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In contrast to Krogsbøll's review,<sup>5</sup> Si et al<sup>6</sup> focused on general practice-based health checks, regardless of whether they screened for more than 1 disease or risk factor, and took into consideration surrogate outcomes. This review included 6 randomized controlled trials (RCTs) (4 of which were included by Krogsbøll et al)<sup>5</sup> and found statistically significant although clinically small improvements in surrogate outcomes, specifically reductions in total cholesterol levels, blood pressure, or body mass index. However, there was no decrease in total mortality and an unexpected increase in cardiovascular mortality.

Both of these reviews suffered from some limitations. Most importantly, there were potential biases inherent to the design of the included studies, especially with regards to performance and detection bias due to the lack of blinding of participants. Krogsbøll et al<sup>5</sup> also reported difficulties finding information on some of the prespecified outcomes, for example, harms. Si et al<sup>6</sup> reported risk of bias due to the proportion of patients lost to follow-up in the included studies. Furthermore, these reviews did not assess the economic implications of health checks, and the information they provided on potential adverse events was limited to overdiagnosis or anxiety and worry levels. There was no information on complications related to the follow-up investigations, the proportion of false positives, or overtreatment.

Three earlier systematic reviews<sup>1,7,8</sup> reported similar results to that by Krogsbøll et al.<sup>5</sup> One review included RCTs and observational studies, as well as studies that focused on geriatric populations, showing a decrease in patients' health worries but no decrease in mortality, disability, or new diagnoses.<sup>1</sup> The other 2 reviews assessed the effect of calculating and communicating coronary risk and found no decrease in morbidity or mortality rates.<sup>7,8</sup>

Given the above, the currently available evidence does not allow us to draw firm conclusions on the effectiveness of health checks. Health check and screening programs are implemented in several countries and supported by national scientific societies, with substantial variability regarding target population (eg, initial age), tests, or intervals. Often, these programs are justified based chiefly on the potential benefits of health checks on surrogate outcomes.<sup>9</sup> Hence, there is a clear need for rigorously assessing the net effect of health checks, taking into consideration truly patient-important outcomes and other crucial aspects.

**Patient-important outcomes** First and foremost, any assessment of the appropriateness of health checks should steer clear of surrogate outcomes. Surrogate outcomes substitute "hard" clinical endpoints (mortality, major cardiovascular events, serious adverse events, etc) on the basis that they may predict clinical benefit or harm.<sup>10</sup> As such, cholesterol levels may substitute cardiovascular mortality, and glucose levels may substitute

blindness and amputation among diabetes patients. Si et al<sup>11</sup> argue that surrogate outcomes in health check studies are valid risk factors for chronic disease. However, surrogate outcomes may conceal harmful effects, especially due to the shorter follow-up they require.<sup>12</sup>

While surrogate outcomes can expedite research and facilitate the development of new drugs and interventions, they can lead to misinterpretation of research findings, since they replace outcomes that are more relevant and understandable for patients but that may require longer follow-up periods and larger study populations.<sup>12</sup> As such, surrogate outcomes have served to justify the use of lipid-lowering drugs that do not reduce coronary events<sup>13</sup> as well as antihypertensive interventions with no real effect on the incidence of strokes.<sup>14</sup>

**Undesirable effects** The significance of identifying all true positives for a given condition should compensate the effects of the interventions provided to diagnose and treat these patients. Whether early detection will have an effect on the overall prognosis should also be weighed up. For instance, there has been an increase in the diagnosis of breast cancer in early stages without a corresponding decrease in the diagnosis of advanced stages. While it can be argued that early breast cancer screening potentially saves lives due to early detection, overdiagnosed women with harmless cancers are exposed to the deleterious undesirable effects associated with treating these cancers.<sup>15</sup> Likewise, men diagnosed with prostate cancer may be offered treatment interventions associated with urinary incontinence and erectile dysfunction.<sup>16</sup> However, it has been estimated that close to 45% of newly detected prostate cancers will have a neutral effect on the health status of the patient.<sup>16</sup>

Another matter to consider is the proportion of false positives associated with screening interventions. False positives are exposed to unnecessary diagnostic tests and interventions that may carry side effects, oftentimes severe. Recommendations as simple as calcium and vitamin D supplements may put patients at higher risk of lithiasis and cardiovascular disease.<sup>17,18</sup> In addition, false positives often present anxiety and other subjective symptoms, including pain and lower libido, which may persist over time.<sup>19,20</sup>

Lung cancer screening is another illustrative example. The National Lung Screening Trial evaluated the effect on cancer mortality of screening with low-dose helical computer tomography (CT) compared with chest radiography for early lung cancer detection.<sup>21</sup> It included 54 454 patients between 55 and 74 years of age with a history of smoking of at least 30 pack-years. The authors reported a 20% reduction in lung cancer mortality and a 6.7% reduction in all-cause mortality. However, the CT group presented 96.4% of false positives compared with 94.5% in the radiography group. One in five patients (24.2%) in the CT

group and 6.9% of the patients in the radiography group had positive screening results, of which 1.4% and 1.6%, respectively, presented with clinically relevant adverse events associated with diagnostic evaluation procedures.

Last but not least, the proportion of false negatives must also be contemplated. False negatives in health checks can be a result of screening errors but also of sampling errors and other shortcomings associated with diagnostic tests. A health technology assessment on this matter<sup>22</sup> identified 13 studies that do not provide strong evidence on the actual medical consequences of false negatives in practice, although they underline the risk of delayed diagnosis and treatment. Eight more studies included in this assessment also found evidence of a false reassurance among affected patients that led to altered subsequent decision making on health and risk behaviors. False negatives were also more likely to take legal action and seek economic compensation and, overall, were associated with decreased public trust in screening programs.<sup>22</sup>

The issue of false positives and negatives is closely associated with the thresholds set to determine risk of disease and/or recommendation for treatment. Increasing or lowering thresholds result in substantial variations in the individuals eligible for a given intervention. A clear example of this phenomenon is provided by the Rotterdam study.<sup>23</sup> This study evaluated the implications of implementing, in a homogenous population of Dutch individuals aged 55 years or older, 3 different clinical practice guidelines regarding administration of statins to reduce atherosclerotic cardiovascular disease. Depending on the guideline, the use of statins would be recommended for 52.0% to 96.4% of men and 35.5% to 65.8% of women.

**Resource use and cost considerations** Since all initiatives financed by health systems are implemented at the expense of forsaking other ones, the costs associated with health checks allude to the concept of opportunity cost. In this sense, it is important that the decision to finance health check programs, as well as the population that will be potentially eligible, is informed not only by the best available evidence on effects but also on cost-effectiveness. As highlighted by a health economic analysis of new-born hearing screening, the cost-effectiveness of screenings present ample variations regarding incremental costs per additional identified case, depending on whether the screening is applied universally, to high-risk populations, or not implemented at all.<sup>24</sup>

**Considerations on implementation** The strategies used to inform patients potentially eligible for health checks should be explicit and allow the patient to gauge the balance between the desired and undesired effects. Furthermore, these strategies must avoid alarming the general population unnecessarily. Public health campaigns to

promote cancer screenings sometimes rely on fear, guilt, and other persuasive tools instead of providing information that will help patients to determine whether they should undergo a health check.<sup>25</sup> Another key aspect that needs to be balanced is the potential for unanticipated indirect effects. For example, a study by Zeliadt et al<sup>26</sup> revealed that smokers would be less likely to quit the habit if an effective lung cancer screening program was offered.

The practicality and viability of the health checks must also be contemplated. Besides the logistic implications, the pertinence and periodicity of the corresponding interventions and follow-up must be carefully established. Bearing in mind that health screenings have a direct benefit only for those who test positive, the repercussions on the remaining participants should be minimal. All potentially eligible patients must also have equal access to the information and interventions associated with the proposed measures. Special emphasis must be placed on reaching out to underserved communities, who are less likely than affluent patients to visit a physician for any reason. Thus, health checks provide a good opportunity to detect early (and late) symptoms of disease as well as health education interventions among these populations.<sup>27</sup>

**Implications for research** The effectiveness of health checks must be assessed through rigorously designed RCTs with adequate statistical power and follow-up. Special emphasis must be placed on avoiding common biases associated with studies on screening programs. These include sticky-diagnosis bias (attributing the same cause of death to people with serious diseases) and slippery-linkage bias (failing to attribute the cause of death to a screening or its adverse events), among others.<sup>28</sup>

**Conclusions** The currently available evidence on the effectiveness of health checks is limited. Health systems, scientific societies, and other stakeholders responsible for the implementation of health checks programs should inform their policies taking into account patient-important outcomes, potential adverse events, and implementation strategies. The target population and thresholds for screening and treatment must also be carefully weighed up to control for the proportion of false positives and the cost-effectiveness of the proposed programs.

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# Badania okresowe w podstawowej opiece zdrowotnej: najpierw dowody, potem działanie

Alberto López-García-Franco<sup>1</sup>, Héctor Pardo-Hernández<sup>2</sup>,  
David Fraile-Navarro<sup>1</sup>, Pablo Alonso-Coello<sup>2,3,4</sup>

1 Centro de Salud Dr. Mendiguchía Carriche (Leganés), Madryt, Hiszpania

2 Iberoamerican Cochrane Centre, Biomedical Research Institute Sant Pau, Barcelona, Hiszpania

3 CIBER Epidemiología y Salud Pública (CIBERESP), Barcelona, Hiszpania

4 Department of Clinical Epidemiology and Biostatistics, McMaster University, Hamilton, Ontario, Kanada

## SŁOWA KLUCZOWE

metody masowych badań przesiewowych, metody prewencji pierwotnej, podstawowa opieka zdrowotna, wczesne rozpoznanie, wskaźniki stanu zdrowia

## STRESZCZENIE

Nie istnieje powszechnie przyjęta definicja i zakres rutynowych badań kontrolnych w podstawowej opiece zdrowotnej, mimo ich częstego wykonywania. Mogą one obejmować tylko okresowe badanie ogólnolekarskie, poprzez testy przesiewowe i diagnostyczne wynikające z tego badania, aż po systematyczne programy badań przesiewowych. Rutynowe badania mogą sprzyjać kontaktom pacjenta ze świadczeniodawcą, usprawniać prowadzenie działań profilaktycznych i zmniejszać lęk pacjenta. Mogą one też jednak narażać pacjenta na przediagnozowanie i niepotrzebne interwencje.

Istnieje niewiele badań na temat korzyści, skutków ubocznych i opłacalności badań okresowych. Dlatego badania okresowe i programy przesiewowe są wprowadzane w niektórych krajach i przyjmowane przez narodowe towarzystwa naukowe głównie w oparciu o ich korzystny wpływ na zastępcze punkty końcowe. Istnieją także znaczące różnice dotyczące zalecanej populacji (np. wieku rozpoczęcia badań) oraz rodzaju i odstępów czasowych wykonywanych testów.

Wzywamy do rygorystycznej analizy efektów netto badań okresowych, biorącej pod uwagę częste rodzaje błędów systematycznego (np. błąd etykiety, błąd umykającego związku), punkty końcowe ważne dla pacjentów, potencjalne działania niepożądane oraz równość dostępu i wykonalność proponowanych programów.

### Adres do korespondencji:

Héctor Pardo-Hernández,  
Carrer Sant Antoni Maria Claret,  
167, Pavelló 18, 08025 Barcelona,  
Hiszpania, tel.: +34 935 537 832,  
e-mail: hpardo@santpau.cat

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