

## Check-up examination: recommendations in adults

Vanessa Virgini, Claudine Meindl-Fridez, Edouard Battegay, Lukas Zimmerli

Division of Internal Medicine, University Hospital Zurich, Switzerland

### Summary

Check-up examinations, or periodic health examinations (PHEs), have gained in importance during the last decades and are nowadays among the most common reasons for consultations in primary care settings. The aim of PHEs is to identify risk factors and early signs of disease, but also to prevent future illness by early intervention. Therefore, each PHE should include counselling, immunisation and physical examination according to the patient's age and gender. However, deciding whether to screen a patient and choosing the most appropriate screening method can be challenging for general practitioners. The U.S. Preventive Service Task Force (USPSTF) provides updated recommendations on different existing preventive care measures based on relevant literature review. The aim of this review is to provide an updated statement of recommendations regarding preventive care measures based mostly on the guidelines derived from the USPSTF and the Swiss Medical Board. Among the major updates, there is no recommendation anymore to routinely screen for breast cancer and prostate cancer in asymptomatic adults. Since 2013, however, the USPSTF recommends annual screening for lung cancer with low-dose CT in patients aged 55 to 80 years with a smoking history of  $\geq 30$  pack years. During PHEs, the physician should be alert to the patients' hidden agendas, which are the reason for one third of all consultations in primary care.

**Key words:** *periodic health examination; check-up; screening; counselling; immunisation; hidden agenda*

### Introduction

Check-up examinations are among the most common reasons for adults to seek medical attention. Between 2002 and 2004, approximately 44 million adults per year underwent a periodic health examination (PHE) in the United States [1]. Data from Canada showed that "general medical examination" was the second most common reason for medical visits after hypertension, with a total of 10.5 million examinations per year [2]. A check-up examination is defined as health care motivated by the need to assess general health and prevent future illness rather than to attend to symptoms [3]. Other terms, such as PHE, annual physical or preventive health examination, are often used. However, all these

expressions exclude preventive care provided during other visits, e.g., due to chronic or acute illness [4].

### Historical perspective

In the 19th century the British physician Horace Dobell, considered to be the father of mass screening in the United Kingdom, outlined an argument for the periodic examination of healthy persons [5]. He suggested that PHEs could be a way to identify "these earliest evasive periods of defect in the physiological state, and to adopt measures for their remedy". However, developments beyond medical practice were proved to have more influence in promoting PHEs. In fact, life insurance companies were suddenly interested in using the applicants' medical history records and diagnoses to assess their financial risk [6]. Life insurance companies were interested in both one-time examinations for applicants and periodic examinations for existing policyholders with the aim of decreasing their risk for death [7]. Their profit motives influenced the conceptions of PHE by focusing the examination on physical defects of applicants and policyholders. It was recommended to take a thorough medical history together with an extensive physical examination from head to toe, multiple blood and urine tests, medical imaging and electrocardiograms [8]. In 1921 an uncontrolled study by the Metropolitan Life Insurance Company reported that policyholders undergoing a PHE had a 28% reduction in expected mortality within the subsequent 5 years [9]. In 1922 the American Medical Association officially promoted PHEs and published a detailed manual on the recommended examination objects and interpretation of results in the following year [10]. However, while public acceptance increased, medical professionals began to question the value of PHEs moving towards individualised check-up examinations. A more selective and evidence-based approach according to an individual's risk profile was conceptualised rather than performing complete annual examinations entailing a large number of laboratory tests. In 1968 the World Health Organization (WHO) commissioned a comprehensive review of screening worldwide, which contained ten principles to be applied before considering screening for a particular disease [11]. In 1975 Frame and Carson performed a literature review assessing the accuracy of screening measures and their impact on altering disease progression and mortality with respect to 36 major medical conditions [12–15].

In 1979 the Canadian Task Force analysed 78 conditions and examined the strength of available evidence for the effectiveness of screening measures in reducing disease-specific morbidity and mortality [16]. The group introduced rules of evidence to evaluate the quality of reported data and subsequently updated its recommendations. Finally, in 1984 the US Preventive Service Task Force (USPSTF), a panel formed by the US Department of Health and Human Studies, began to evaluate specific preventive interventions in 60 medical conditions by using explicit criteria and rules of evidence. The group published their first recommendations in 1989 and have issued several updates since then [17].

### Assessing and grading the evidence

The USPSTF provides annual reports to the US Congress by identifying critical evidence gaps in research related to clinical preventive services and recommends priority areas that deserve further examination [18]. The different preventive care measures are evaluated and ranged in a specific recommendation grade based on relevant literature review (grades A, B, C, D and I, see tables 1 and 2) [19]. In Switzerland, the Swiss Medical Board (SMB), an inter-

disciplinary group consisting of independent experts from medicine, law, ethics and economics, was founded in 2011. The aim of the panel is to assess the cost-effectiveness of various medical procedures [20].

Further expert committees are responsible for providing guidelines regarding specific medical fields, such as the American Diabetes Association (ADA), the American Thyroid Association (ATA), the European Society of Cardiology (ESC), the European Society of Hypertension (ESH) or the Swiss Atherosclerosis Association (AGLA). This review is mostly based on the USPSTF and SMB recommendations, but also on the opinions of other expert groups.

### Elements of a check-up examination

As previously described, the aim of PHEs is to identify risk factors and early signs of disease and also to prevent future illness through early intervention. Therefore, the PHE has to include counselling, immunisation and physical examination tailored to patient's age and sex. Another important component is the so-called "case finding", which involves screening based on the patient's known risk factors in the context of a concomitant disease (e.g., hypertension)

**Table 1:** Preventive care services recommended for men, as recommended by the USPSTF [111].

Primary prevention	Age (y)								Time intervals	Grade
	16	35	45	50	55	65	75	80		
<b>Counselling</b>										
Lifestyle									At each PHE <sup>a</sup>	C
Smoking									At each PHE	A
Alcohol									At each PHE	B
Sexual behaviour									At each PHE	B
<b>Immunisation</b>										
Standard									Review at each PHE	Swiss guidelines <sup>j</sup>
Influenza									Yearly <sup>b</sup>	Swiss guidelines <sup>j</sup>
Pneumococcus									Once <sup>c</sup>	Swiss guidelines <sup>j</sup>
<b>Cardiovascular disease</b>										
Hypertension									Every 1–2 y based on BP <sup>d</sup>	A
Lipid disorders									Every 5 years	A
Diabetes mellitus									Every 3y <sup>e</sup>	B
Obesity									At each PHE <sup>f</sup>	B
AAA									Once <sup>g</sup>	B
<b>Cancer</b>										
Colorectal cancer									Colonoscopy every 10y <sup>h</sup>	A
Lung cancer									1x/y with LDCT <sup>i</sup>	B*
Prostate cancer									Not recommended routinely <sup>k</sup>	D*
<b>Thyroid disorders</b>									Not recommended routinely	I
<b>Depression</b>									at each PHE	B

AAA = abdominal aortic aneurysm; BP = blood pressure; LDCT = low-dose computed tomography; PHE = periodic health examination; y = year

\* controversial recommendations

<sup>a</sup> only in targeted patients

<sup>b</sup> in specific risk populations (patients with chronic disease or immunosuppression) <65y

<sup>c</sup> only in specific risk populations (patients with chronic disease or immunosuppression)

<sup>d</sup> every 2 years if BP <120/80 mm Hg, yearly if BP 120–139/80–89 mm Hg

<sup>e</sup> in patients with other cardiovascular risk factors

<sup>f</sup> from 6 years old

<sup>g</sup> in smokers; repeat every 2–3 years if AAA 3–3.9 cm, every 6 months if 4–5.4 cm

<sup>h</sup> alternatives to colonoscopy: faecal occult blood testing once a year, or sigmoidoscopy every 5 years combined with FOBT every 3 years

<sup>i</sup> only recommended by the US Preventive Service Task Force, still controverted in Switzerland

<sup>j</sup> from the Swiss Federal Office of Public Health

<sup>k</sup> not recommended by the US Preventive Service Task Force, recommended by expert committees

or a positive family history (e.g., premature coronary heart disease in a first-degree relative). Furthermore, physicians need to be aware of “hidden agendas”, as patients often use PHE as a reason for consultation to raise the issue of a specific problem that troubles them.

## Primary prevention

Counselling and immunisations are the cornerstones of primary prevention. In fact, when compared with secondary or tertiary prevention, these preventive measures are harmless, and they have been shown to be clearly more cost-effective [21]. For these reasons, evidence-based primary prevention should be part of the PHE for all patients.

## Counselling

### Lifestyle

Although a healthy lifestyle has been associated with a decreased incidence of cardiovascular disease, there is only a limited health benefit when behavioural counselling is

applied to all patients in primary care settings (Grade C) [22]. Therefore, the USPSTF recommends intensive lifestyle counselling for patients with risk factors for cardiovascular and diet-related chronic disease (Grade B) [23].

### Smoking

Physicians have been shown to be in a strategic position to support their patients in smoking cessation [24]. Although tobacco use has been reduced worldwide, it still remains an important cause of morbidity and death, with 9,000 deaths associated with tobacco consumption each year in Switzerland [25, 26]. Therefore, clinicians should provide smoking cessation interventions for all patients who smoke tobacco (Grade A) [27]. Several meta-analyses have demonstrated a strong correlation between the number and the duration of counselling sessions and the abstinence rate [28]. Interventions to help patients quit smoking can be based on the 5 A's, a validated five-step algorithm, in which patients are asked about their smoking habits, advised to quit smoking, assessed if they are ready to quit smoking, assisted in their attempt to quit smoking, and finally arranged for follow-up counselling sessions after smoking cessation [28]. This

**Table 2:** Preventive care services for women, as recommended by the USPSTF [111].

Primary prevention	Age (y)									Time intervals	Grade
	16	21	26	45	50	55	65	75	80		
<b>Counselling</b>											
Lifestyle										At each PHE <sup>a</sup>	C
Smoking										At each PHE	A
Alcohol										At each PHE	B
Sexual behaviour										At each PHE	B
<b>Immunisation</b>											
Standard										Review at each PHE	Swiss guidelines <sup>l</sup>
Influenza										Yearly <sup>b</sup>	Swiss guidelines <sup>l</sup>
Pneumococcus										Once <sup>c</sup>	Swiss guidelines <sup>l</sup>
HPV										Once (+ revaccination) <sup>d</sup>	Swiss guidelines <sup>l</sup>
<b>Cardiovascular disease</b>											
Hypertension										Every 1–2 y based on BP <sup>e</sup>	A
Lipid disorders										Every 5 years <sup>f</sup>	A
Diabetes mellitus										Every 3 y <sup>f</sup>	B
Obesity										At each PHE <sup>g</sup>	B
<b>Cancer</b>											
Colorectal cancer										Colonoscopy every 10 y <sup>h</sup>	A
Lung cancer										1x/y with LDCT <sup>i</sup>	B*
Cervical cancer										Every 3–5 y	A
Breast cancer										Not recommended routinely <sup>j</sup>	D*
<b>Thyroid disorders</b>										Not recommended routinely	I
<b>Depression</b>										At each PHE	B
<b>Osteoporosis</b>										Maximum every 2 years <sup>k</sup>	B

BP = blood pressure; HPV = human papilloma virus; LDCT = low-dose computed tomography; PHE = periodic health examination; y = year

\* controversial recommendations

<sup>a</sup> only in targeted patients

<sup>b</sup> in specific risk populations (patients with chronic disease or immunosuppression) <65 y

<sup>c</sup> only in specific risk populations (patients with chronic disease or immunosuppression)

<sup>d</sup> 1st vaccination possible between 11 and 26 years

<sup>e</sup> every 2 years if BP <120/80 mm Hg, yearly if BP 120–139/80–89 mm Hg

<sup>f</sup> only in patients with cardiovascular risk factors

<sup>g</sup> from 6 years old

<sup>h</sup> alternatives to colonoscopy: faecal occult blood testing once a year, or sigmoidoscopy every 5 years combined with FOBT every 3 years

<sup>i</sup> only recommended by the US Preventive Service Task Force, still controverted in Switzerland

<sup>j</sup> recommended by the US Preventive Service Task Force, not recommended routinely by the Swiss Medical Board

<sup>k</sup> for patients with risk factors for osteoporosis <45 y

<sup>l</sup> from the Swiss Federal Office of Public Health

algorithm can be used for further lifestyle issues, such as physical inactivity, alcohol misuse and consumption of illicit drugs.

#### *Alcohol use*

Alcohol misuse is also one of the most common preventable causes of morbidity and death [29]. It has been shown that one in five individuals is engaged in unhealthy or risky alcohol consumption in Switzerland [25]. Various systematic reviews showed the efficacy of counselling interventions among patients with alcohol misuse [30, 31]. These interventions have also been confirmed to be cost-effective [32]. For these reasons, the USPSTF recommends that physicians screen all their patients for alcohol misuse, and provide brief behavioural counselling sessions to reduce alcohol intake for those who have a risky alcohol consumption (Grade B) [33]. There are various available tools, the most validated being the ten-item AUDIT (alcohol use disorders identification test) questionnaire, with the best sensitivity and specificity for screening unhealthy alcohol use [34]. The four CAGE (cut-down, annoyed, guilty, eye-opener) questions are less sensitive for screening the whole spectrum of alcohol misuse (for example to distinguish alcohol misuse from alcohol abuse or dependence), but can be used to quickly find out if the patient has a problem regarding alcohol consumption [35].

#### *Sexual behaviour*

As sexually transmitted infections (STIs) are associated with morbidity and potential complications, the USPSTF recommends high intensity behavioural counselling interventions for sexually active patients (Grade B) [36]. In fact, several meta-analyses have shown that high-intensity behavioural counselling can reduce the incidence of STIs up to thirty percent [37, 38].

### **Immunisation**

#### *Standard immunisation*

Clinicians should assess standard immunisation at periodic health examinations and, if indicated, proceed to revaccination. Based on the guidelines of the Swiss Federal Office of Public Health, patients between twenty-five and twenty-nine years or patients considering travelling to endemic parts of the world should receive a revaccination against diphtheria, tetanus and pertussis [25]. A revaccination against diphtheria and tetanus should then be repeated once at forty-five years and every ten years for patients over sixty-five years. Vaccination against poliomyelitis, hepatitis B virus and measles-mumps-rubella should be assessed and completed if necessary.

#### *Immunisation against influenza*

Each year, infections with seasonal influenza are responsible for 100,000 to 250,000 medical consultations, 1,000 to 5,000 hospitalisations, and 400 to 1,500 deaths in Switzerland, in particular among patients older than 65 years [25]. An annual immunisation of all patients over sixty-five years of age could significantly reduce the disease burden and the associated costs. It has been shown that influenza-associated pneumonia and hospitalisations could be reduced by 50% and mortality by 70% in that population with

influenza immunisation [39]. Specific populations should also be immunised against influenza before 65 years, such as health care workers, and patients with chronic diseases (cardiac or pulmonary disease, renal insufficiency, diabetes mellitus) or immunosuppression (including HIV-infected individuals).

#### *Immunisation against Streptococcus pneumoniae*

In 1993, Gardner et al. showed that pneumococcus immunisation could prevent more than 20,000 deaths in the United States, and that pneumococcal vaccine was used in only 14% of the cases in which an immunisation was primarily indicated [40]. Since then, efforts to promote pneumococcal vaccination have been made, but the burden of disease still remains very important [41]. Therefore, the Swiss Federal Office of Public Health recommends immunising risk populations with the 13-conjugated-valent vaccine [25]. The specific risk populations are characterised by chronic diseases (cardiac, pulmonary, hepatic, renal or haematological disorders), neoplasia, transplantation and immunosuppression (autoimmune disorders, HIV infection, medicine associated immunosuppression, immunodeficiency and functional or anatomical asplenia) [25]. Systematic immunisation of patients older than sixty-five years is not indicated any more.

#### *Immunisation against human papilloma virus*

The Swiss Federal Office of Public Health recommends immunisation against human papilloma virus (HPV) for all females between eleven and fourteen years, with a revaccination between fifteen and nineteen years [25]. Based on clinical evaluation, immunisation could be administered until the age of twenty-six years. Both vaccines available in Switzerland provide protection against HPV-types 16 and 18, responsible for cervical cancer. Only one vaccine provides immunisation against HPV-types 6 and 11, which have been associated with genital warts. Recommendations regarding immunisation against HPV among males to prevent penile or anal cancer and potentially transmission of the virus are emerging. In fact, the Australian National HPV Vaccination Program Register has recently recommended immunising young males against HPV [42]. However, systematic vaccination of males is not yet recommended in Switzerland.

#### *Other immunisations*

People with a negative history for varicella zoster virus (VZV) infection under 40 years of age should be actively immunised against VZV. The immunisation is especially recommended in women wishing to become pregnant or in healthcare workers. The Swiss Federal Office of Public Health recommends immunisation against hepatitis A virus for patients who have chronic liver disease, who live in endemic parts of the world, who use intravenous drugs, who are in contact with people living in endemic parts or using intravenous drugs, who work in specific laboratories or as drainers, and in men who have sex with men [25]. Immunisation against tick-borne encephalitis virus is indicated in people living in endemic parts of the world [25].

## Screening

Screening tests are designed to identify a disease among asymptomatic individuals. Based on the WHO guidelines, screening tests should adhere to various principles [11]. First, the condition should be a relevant health issue and include a latent phase where validated tests can be performed. The screening tests have to be not only economically acceptable but also in terms of balance of benefits and harms for the population. Finally, there should be an available and validated treatment for the diagnosed condition.

### Cardiovascular disease

#### *Hypertension*

Hypertension is defined as a systolic blood pressure >140 mm Hg and/or diastolic blood pressure >90 mm Hg [43]. As controlled hypertension is associated with a risk reduction of 50% for heart failure, 40% for cerebrovascular accidents and 25% for myocardial infarction, it is recommended to routinely screen for hypertension in patients 18 years or older (Grade A) [44, 45]. Recommendations concerning the intervals between blood pressure measurements are unclear. According to expert opinion, blood pressure should be measured every two years when systolic blood pressure is <120 mm Hg and diastolic blood pressure is <80 mm Hg and annually if the systolic and diastolic blood pressure values are 120–139 mm Hg and 80–89 mm Hg, respectively [45].

#### *Abdominal aortic aneurysm*

Men aged sixty-five to seventy-five years who have ever smoked should be screened once for abdominal aortic aneurysm (AAA) by ultrasonography (Grade B) [46]. Recommendations for men who have never smoked are unclear (Grade C). Routine screening for AAA in women is not recommended by the USPSTF (Grade E). A surgical intervention is required if an AAA  $\geq 5.5$  cm is diagnosed. Ultrasonography should be repeated in a two to three year interval for AAA of 3 to 3.9 cm, and every 6 months for those with a diameter from 4 to 5.4 cm [46, 47].

#### *Obesity*

Prevalence of obesity has increased by 10% to 40% in Europe during the last decade among both adults and children [25]. Obesity, defined as a body-mass-index (BMI) >30.0 kg/m<sup>2</sup> (in children defined as age and genderspecific BMI at  $\geq 95$ th percentile) has been associated with an increased risk to develop cardiovascular and cerebrovascular disease, as well as cancer and diabetes mellitus [48, 49]. A systematic screening for obesity with BMI calculation is recommended in all patients, beginning at the age of six years (Grade B) [49, 50]. Patients with a BMI >30 kg/m<sup>2</sup> should be offered multimodal behavioural interventions (Grade B), as intensive behavioural counselling has been shown to reduce weight and cardiovascular risk factors and to improve glucose tolerance [50]. Time intervals between BMI measurements are still uncertain.

#### *Lipid disorders*

Screening for cholesterol disorders is recommended every five years for men aged thirty-five years or older (Grade

A) and for women with cardiovascular risk factors aged forty-five years or older (Grade A) [51]. Recommendations regarding women who are not at increased cardiovascular risk are not clear (Grade C) [51]. However, screening guidelines concerning lipid disorders differ between expert groups. AGLA recommends screening for lipid disorders among all individuals aged forty years or more, regardless of gender [52]. Based on the AGLA recommendations, screening for lipid disorders should be repeated every five years for low-risk patients (ten-year cardiovascular risk <10%) and every two to five years for intermediate-risk patients (ten-year cardiovascular risk 10%–20%) [52]. Lipid-measurement should then be repeated more frequently based on the clinical situation for patients with a high or very high risk (ten-year cardiovascular risk >20%, confirmed coronary heart disease, atherosclerosis, diabetes mellitus with end-organ damage such as stroke, coronary heart disease and nephropathy, or glomerular filtration rate <60 ml/min/1.73 m<sup>2</sup>). ESC recommends screening for lipid disorders in men aged forty years or more, in women aged fifty years or more or in post-menopausal women, even if asymptomatic [53].

Several studies have demonstrated a risk reduction of 30% for developing cardiovascular disease among individuals with high total or low HDL cholesterol who take statins [54]. AGLA provides indications to initiate a lipid-lowering therapy based on the different ten-year risk groups. Although there is no upper age limit for screening lipid disorders, the initiation of a statin-therapy among patients older than seventy-five years of age should be evaluated individually [55]. Furthermore, physicians must be aware that in a high-risk primary prevention setting, a meta-analysis did not find evidence for the benefit of statin therapy on all-cause mortality [56].

### Osteoporosis

Screening for osteoporosis with bone-densitometry (DXA) is recommended for all women aged sixty-five years or older (Grade B) and for younger females with an increased risk to develop osteoporosis [57]. Routine screening for osteoporosis among asymptomatic men without risk factors is not recommended (Grade I) [57]. The ten-year risk can be assessed by using the FRAX-instrument (Fracture Risk Assessment), based on clinical data, such as age, BMI, family history, tobacco use and alcohol consumption [58]. Lifestyle counselling concerning healthy diet and exercise promotion is recommended for all post-menopausal women to prevent bone-loss, whereas pharmacological intervention is indicated among women aged 50 years or older with a history of vertebral or hip fracture, a femoral or spine T-score of -2.5 or lower at DXA or a T-score of -1 to -2.5 together with an elevated FRAX-score [59]. According to the USPSTF, there is currently insufficient evidence to recommend vitamin D and calcium supplementation in primary prevention (Grade I) [60].

### Depression

All patients should be screened for depression in primary care settings (Grade B) [61]. There are various available screening tools, but it has been shown that asking only two short questions ("Over the past two weeks, have you felt

down, depressed, or hopeless?” and “Over the past two weeks, have you felt little interest or pleasure in doing things?”) may be as effective to screen for depression compared to more elaborated questionnaires [62]. Once depression is detected, clinicians should apply standard diagnostic criteria to assess the type and severity of depression.

## Cancer

### *Colorectal cancer*

All men and women aged fifty to seventy-five years should undergo screening for colorectal cancer (Grade A) [63]. Screening of people older than eighty-five years is clearly not indicated (Grade D), whereas screening among those between seventy-six and eighty-five years should be assessed individually (Grade C) [63]. The USPSTF recommends three possible screening procedures: colonoscopies every ten years, annual faecal occult blood testing (FOBT), or sigmoidoscopies every 5 years combined with faecal occult blood testing every three years. Although colonoscopy has been shown to have the best sensitivity and specificity, annual testing for faecal occult blood alone can also significantly reduce mortality [64]. Serious complications associated with colonoscopy occur in 25 cases per 10,000 procedures [65]. The screening method should therefore be chosen in a decision-sharing context. Moreover, there is insufficient evidence to recommend computed tomographic colonography and faecal DNA testing at the moment (Grade I) [63]. We recommend colonoscopy with the possibility of an immediate polypectomy as first-choice screening method, as polyps can evolve into cancer over the course of years. A population-based observation study from Switzerland showed that colorectal cancer screening by colonoscopy markedly reduced not only the incidence of colorectal cancer but also cancer-related death [66]. Furthermore, Swiss insurance companies cover the costs for screening colonoscopies since 2013.

### *Cervical cancer*

Cervical cancer is the third most common cause of cancer in females worldwide [67]. Several observational studies showed that cervical cytology testing can reduce mortality due to cervical cancer up to 60% and is associated with better cure rates [68, 69]. Therefore, screening for cervical cancer is recommended in all women aged twenty-one to sixty-five years with Papanicolaou testing (Grade A) [70]. Regarding screening intervals, women between thirty and sixty-five years of age should be screened every three years, or every five years if they wish a longer interval (Grade A). However, screening for cervical cancer is not indicated in women younger than twenty-one years or older than sixty-five years with adequate previous testing and no increased risk for cervical cancer (Grade D) [70].

## Case finding and controversies

Although clinical studies were able to provide strong evidence about screening methods to clarify international guidelines, robust data on benefits and harms regarding several screening tests are still lacking, and international recommendations are conflicting.

## Cardiovascular

### *Diabetes*

Screening for type 2 diabetes mellitus is recommended in adults with a sustained blood pressure  $\geq 135/80$  mm Hg (Grade B) [71]. The USPSTF concluded that there was insufficient evidence to recommend systematic screening for type 2 diabetes mellitus among adults with blood pressure values  $\leq 135/80$  mm Hg (Grade I), because long-term outcomes are still uncertain. However, ADA recommends screening for diabetes in asymptomatic adults of any age with a BMI  $\geq 25$  kg/m<sup>2</sup> who have at least one additional risk factor for diabetes (physical inactivity, severe obesity, high-risk ethnicity, hypertension, low HDL cholesterol or elevated triglyceride level, haemoglobin-A<sub>1c</sub>  $\geq 5.7\%$ , impaired fasting glucose, women with gestational diabetes or polycystic ovarian syndrome, positive history for cardiovascular disease, first-degree relative with diagnosed diabetes) or among all individuals  $\geq 45$  years of age, in three-year intervals (Grade B) [72]. The validated tests to screen for diabetes mellitus are haemoglobin A<sub>1c</sub> (normal if  $< 5.7\%$ ) or fasting blood glucose measurements (normal if  $< 5.6$  mmol/l), and oral glucose tolerance test (normal if 2h-plasma glucose  $< 7.8$  mmol/l).

### *Coronary heart disease*

Screening for coronary heart disease (CHD) among asymptomatic adults at low risk for cardiovascular events with resting or exercise electrocardiography and cardiac computed tomography (CT) is not recommended (Grade D) [73]. There is insufficient evidence to recommend screening for patients at intermediate or high risk for CHD events (Grade I). In order to assess a patient's risk level, clinicians may use the Framingham calculator, which provides the patient's ten-year risk assessment (high risk if greater than 20%, intermediate risk if 10 to 20%, low risk if less than 10%) or the AGLA risk calculator, respectively [52].

The SMB recently considered that screening for CHD among patients at intermediate or high risk could be performed with cardiac CT instead of invasive coronary angiogram if medical imaging is required [20]. However, physicians and patients need to be aware that cardiac CT can lead to incidental findings, as it enables visualisation of both cardiac and extracardiac structures. Suspicious pulmonary nodules represent in particular the vast majority of clinically significant extracardiac incidental findings [74], and may lead to further potentially invasive procedures, such as bronchoscopies or needle biopsies. A future challenge will be to quantify the benefit arising from searching for extracardiac findings in randomised controlled long-term studies for both the patient and the health care system [74]. In the light of the current available data, we therefore suggest cardiac CT in patients at intermediate risk when the result is reasonably expected to lead to change in management upon reclassification to a lower or higher risk group.

### **Thyroid disorders**

Screening for thyroid dysfunction is subject to controversies worldwide. ATA recommends screening for thyroid dysfunction by measuring thyroid stimulating hormone (TSH) every five years among patients thirty-five years of

age or older, even if they are asymptomatic [75]. Although prevalence of thyroid dysfunction is high, particularly for subclinical and overt hypothyroidism (4 and 2%, respectively), the USPSTF concluded that there is insufficient evidence to recommend or advise against screening with TSH measurement among asymptomatic adults (Grade I) [76–78]. However, it has recently been shown that thyroid dysfunction may be associated with adverse clinical outcomes even if subclinical. For instance, studies have reported that subclinical hypothyroidism may be associated with an increased risk of developing CHD and heart failure, in particular if TSH  $\geq 10$  mU/l [79, 80]. In subclinical hypothyroidism with TSH 5–10 mU/l a reduction of all-cause mortality was observed whereas for subclinical hyperthyroidism all-cause mortality and cardiovascular morbidity were increased, respectively [81]. Nevertheless, further studies are needed to clarify the benefits of systematic screening in asymptomatic persons.

## Cancer

### *Lung cancer*

As lung cancer is the leading cause of cancer death in the United States, and as it is associated with a poor outcome if diagnosed at an advanced stage, the USPSTF recently updated the recommendations regarding screening [82, 83]. In fact, it is recommended since 2013 to proceed to annual screening for lung cancer with low-dose CT (LDCT) in patients aged fifty-five to eighty years with a smoking history of thirty pack-years, who are currently smoking or have quit smoking within the past fifteen years (Grade B) [82]. Several studies, including a large randomised, controlled trial, have reported evidence that annual screening for lung cancer with LDCT among high-risk individuals can significantly reduce the number of lung cancer-associated deaths (relative reduction in mortality of 20% [95% confidence interval 6.8–26.7, p-value = 0.004]) [84]. For patients who have quit smoking more than fifteen years ago, or for those with limited life expectancy or contraindications to undergoing curative lung surgery, screening is not indicated or should be ceased [82]. However, the SMB recently stated that screening for lung cancer with positron-emission tomography/CT is not recommended [20].

In this controversial situation, and in the light of the available data, we only recommend screening for lung cancer with LDCT if patient and physician are committed to pursue follow-up investigations as detection of abnormalities often require further evaluation involving needle biopsy and/ or surgery. We would like to underline, that prevention, rather than screening, is the most effective strategy for reducing the long-term burden of lung cancer, and doctors should therefore provide smoking cessation interventions for all patients who smoke tobacco (see above).

### *Breast cancer*

In past years, screening for breast cancer was recommended in Switzerland for all women aged fifty to seventy-four years. In fact, the USPSTF stated in 2009 that screening mammography is recommended every two years in women between fifty and seventy-four years of age (Grade B) [85]. Nevertheless, based on the analyses of several random-

ised controlled trials and observational studies conducted between 1963 and 1991, the SMB changed its guidelines in December 2013. They concluded that screening for breast cancer with mammography presented an unfavourable cost-effective rate [20, 86]. In fact, most studies have shown that screening for breast cancer was associated with a limited reduction in mortality. Among 1,000 regularly screened women, only one to two deaths due to breast cancer could be avoided compared with 1,000 women who were not regularly screened [20, 87]. Furthermore, false positive results have been associated with unnecessary complementary investigations, overtreatment and increased psychological burden. These observations lead to two major recommendations: systematic screening for breast cancer with mammography is not recommended, and currently undergoing systematic screening programmes should be limited in time [20]. As there is a marked difference between US and Swiss recommendations, physicians need to clearly explain to the patients what are the potential harms and benefits of breast cancer screening. The decision to proceed to breast cancer screening or to interrupt a screening program should be then done in a physician-patient decision-sharing context.

### *Prostate cancer*

Prostate cancer is the third most common cancer among men. Its incidence increases with age, especially after fifty years. Deaths associated with prostate cancer are rare before the age of sixty years. In fact, 70% of deaths occur after 75 years of age [88].

Controversies regarding screening for prostate cancer with Prostate-Specific-Antigen (PSA) lead to major changes in recommendations worldwide. The SMB and the Swiss Academy of Medical Sciences declared in 2011 that systematic screening for prostate cancer with PSA-measurement was not recommended anymore because of the limited effect of screening on global mortality and specific mortality, and the potential associated dangers related to biopsy and treatment [20]. Nevertheless, the Swiss Society of Urology recommended individualising PSA-based screening for prostate cancer, and serial measurements in the following years [89]. The USPSTF also reviewed their guidelines and currently recommends against systematic prostate cancer screening based on PSA measurement (Grade D) [90].

The members of the USPSTF based their recommendations on the fact that false-positive results are common (13% cumulative risk for at least one false-positive result after four PSA measurements) and that biopsy due to a false positive result may occur in 5.5% of cases [91]. Furthermore, it has been reported that biopsy-related complications are often encountered (50% have persistent haemospermia, 22% haematuria, 3% fever), and likewise treatment-associated harms [92]. Studies have shown that radical prostatectomy is associated with a 30% increased absolute risk for erectile dysfunction and 20% for urinary incontinence in comparison with a non-invasive attitude after 1 to 10 years. Radiation therapy is also associated with an increased risk to develop erectile dysfunction (17% increase in absolute risk) and bowel dysfunction after 1 to 10 years [93, 94].

In conclusion, PSA-based screening for prostate cancer should not be performed systematically any more. Clinicians should individualise their decision to screen for prostate cancer and clearly inform their patients on the benefits and potential harms associated with an eventual false-positive result [20]. In our opinion, the patient must be engaged in explicit and informed decision making with their physician before initiating or continuing prostate cancer screening.

### Hidden agenda

When patients request a check-up, physicians may assume it is for detection of asymptomatic disease. However, a prospective study has shown that the majority of patients requiring a check-up were motivated by specific symptoms and health concerns and did not consist of “asymptomatic” patients who primarily scheduled a consultation for preventive issues [95]. Patients disclosed their symptoms and concerns once they were talking directly with the physician. However, one in three patients had one or more hidden agendas leading to the check-up [95]. When patients’ expectations are not met, patient satisfaction is likely to be decreased, which can lead to reduced adherence to therapy, increased health care utilisation, more frequent malpractice litigation, and switching doctors or health plans [96–100]. Being alert to behavioural and verbal cues is important in order to recognise and identify hidden agendas and to improve the physician-patient relationship.

### Do check-up examinations make sense?

Opponents of check-up consultations state that head-to-toe examination, accompanied by comprehensive multiphasic investigation and laboratory screening is outdated. They report that time needed to conduct a PHE is twice the time needed for a regular medical consultation. They deplore that unnecessary investigations, which are not based on evidence, are ordered for healthy individuals [101]. Furthermore, potentially harmful examinations, such as whole-body CT scanning, are promoted especially when it comes to exclusive PHEs for managers [102]. The opponents argue that some preventive care services should be performed during regular physician consultations regarding case-findings or during acute care visits [101]. They claim that preventive measures have a more powerful effect when performed at the occasion of an acute or chronic office visit rather than at a special check-up visit [103].

Supporters of PHEs argue that these kinds of consultations might improve two critical elements of care: relationship building and preventive care [104]. In fact, it might be difficult for busy general practitioners (GPs) to dedicate enough time for preventive care as patients consult their GPs more for specific complaints than for advice on prevention. To fully satisfy the USPSTF recommendations, a patients’ panel of 2,500 individuals would need 1773 hours of a physician’s annual time, representing a total of 7.4 hours per working day only to provide preventive care services [105]. Thus, longer scheduled visits allow the physicians to carry out preventive measures more frequently

and to obtain a more holistic view on their patients by discussing their social networks (patients’ families, works and social lives) [103, 105]. Furthermore, these consultations provide opportunities to screen for less obvious conditions, such as depression [61, 104].

Beyond the discussion whether preventive care should be provided by physicians seeing patients for acute visits or during PHEs, physicians ask for new methods of preventive care delivery, as preventive services currently recommended by the USPSTF require an unreasonable amount of time [105]. They request a clearer focus on which services can be best provided and by whom [105].

### Are check-up examinations harmful?

A recently published Cochrane systematic review concluded that general health examinations were not associated with an increase or decrease in all-cause mortality (RR 0.99, [95%CI, 0.95–1.03]) and disease specific mortality [106]. Data were available from 14 randomised controlled trials involving more than 182,000 patients. A total of 8 trials reported on cardiovascular mortality (RR 1.03, [95% CI, 0.91–1.17]) with substantial heterogeneity, and 8 trials reported on cancer mortality (RR 1.01, [95% CI, 0.92–1.12]) with moderate heterogeneity. Furthermore, no effect was found on hospital admission rates, disability, additional physician visits or absence from work. The review excluded studies which targeted specific diseases or which evaluated specific tests. This could theoretically underestimate the effect of PHEs on particular conditions. Moreover, most trials were old, as the earliest article was published in 1963 and the latest in 1999. During this time span, there have been many changes in medical practice such as risk assessment methods and available preventive drugs. Of the 11,940 deaths that occurred over nine years of follow-up, the number of healthy individuals who died from a condition targeted by the screening intervention, and could therefore have benefited from early detection, was probably quite low compared to those who died of causes that the screening intervention did not target efficiently, such as cancer and unintentional injury [3]. Another limitation is the scant data on the risks and costs of PHEs. There is no data on how frequently PHEs lead to a cascade effect of testing or over-diagnosis [4].

In 2007, a systematic review by Boulware et al. regarding the value of PHE concluded that patients benefit from PHEs through its association with improved delivery of some recommended clinical preventive services and through reduction of patients’ concerns [103]. The authors found no harms associated with PHEs and emphasised that elimination of worry or concerns regarding illness may represent a powerful motivator for action on the patients’ side [103].

Besides, many physicians feel that PHEs strengthen the physician-patient relationship [4, 107, 108]. In fact, in 2005 a survey by Prochazka et al. demonstrated that 94% of GPs believed that a PHE could improve the physician patient relationship [108]. According to Prochazka and Caverly, time spent getting to know a patient is time that pays dividends down the road [4]. They hope that payment system reforms

will incentivise value over volume and eventually translate into more time available to establish a healing relationship. In the meantime, one way for physicians to carve out some time might be to avoid performing non-beneficial examinations and unnecessary tests, and thereby avoiding the time-consuming task of chasing down false-positive and incidental findings [4]. New initiatives, such as “Smart Medicine” or “Choosing Wisely”, have been set up in Switzerland and in the United States, respectively, and should eventually help physicians to promote evidence-based tests performed at PHEs [109, 110].

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**Correspondence:** Lukas Zimmerli, MD, Division of Internal Medicine, Cantonal Hospital Olten, Baslerstrasse 150, CH-4600 Olten, Switzerland, [lukas.zimmerli\[at\]spital.so.ch](mailto:lukas.zimmerli[at]spital.so.ch)

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