



Men with erectile dysfunction (ED) should be screened for cardiovascular risk factors – Cost-benefit considerations in Swiss men

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Summary: *Background:* Current evidence indicates that erectile dysfunction (ED) is an independent risk factor for future cardiovascular events. This study aimed to estimate the cost-effectiveness of screening and subsequent preventive treatment for cardiovascular risk factors among men newly diagnosed with ED from the Swiss healthcare system perspective. *Methods:* Based on known data on ED and cardiovascular disease (CVD) prevalence and incidence costs and effects of a screening intervention for cardiovascular risk including corresponding cardiovascular prevention in men with ED were calculated for the Swiss population over a period of 10 years. *Results:* Screening and cardiovascular prevention over a period of 10 years in Swiss men with ED of all seriousness degrees, moderate and severe ED only, or severe ED only can probably avoid 41,564, 35,627, or 21,206 acute CVD events, respectively. Number needed to screen (NNS) to prevent one acute CVD event is 30, 23, and 10, respectively. Costs for the screening intervention are expected to be covered at the seventh, the fifth, and the first year, respectively. *Conclusion:* Screening and intervention for cardiovascular risk factors in men suffering from ED is a cost-effective tool not only to strengthen prevention and early detection of cardiovascular diseases but also to avoid future cardiovascular events.

Keywords: Erectile dysfunction, cardiovascular disease, cardiovascular risk factors, cost analysis, secondary prevention

Abbreviations

CAD	Coronary artery disease
CHF	Swiss franc
CVD	Cardiovascular disease
DRG	Diagnosis-related group
ED	Erectile dysfunction
HDL	High density lipoprotein
ICD	International Classification of Disease
IIEF-15	International Index of Erectile Function-15
LDL	Low-density lipoprotein
NNS	Number needed to screen
QALYs	Quality adjusted life years

Introduction

Atherosclerotic cardiovascular diseases (CVD) and its various complications like myocardial infarction, stroke, peripheral artery disease are the major causes of death and the third most common reason for hospitalization in Switzerland. In 2020, 26.9% of deaths were due to cardiovascular diseases [1]. Though declining in incidence and mortality rates, CVD significantly increase the burden of disease in Switzerland [2, 3, 4] and they belong to the five most costly non-communicable major diseases in the country [5].

Leading international and national health organizations demand prevention and early detection of CVD as a public

Table I. Patients with erectile dysfunction and cardiovascular disease in Switzerland

Population	Basis for calculation	Number (Swiss population)
Swiss population 2020*		8,670,300
Men	49.6%	4,300,469
20–79 years	74.7%	3,212,450
20–39 years	26.3%	1,131,023
40–64 years	34.9%	1,500,864
65–79 years	13.5%	580,563
Prevalence ED (30–80 years) [13]		624,201
30–39 years	2.3% (n=1,131,023)	26,014
40–69 years	9.5%–34.4% (~19.2%) (n=1,500,864)	288,166
70–80 years	53.4% (n=580,563)	310,021
Incidence rate ED at the age of 40 – 69 years [14]	25.9/1000 man-year (n=3,212,450)	83,203/year
Total ED cases over a period of 10 years [55]	624,201 + (83,202 × 9)	1,373,019
Severe ED cases [20]	19% of all ED cases	260,874
Moderate ED cases [20]	48% of all ED cases	659,049
Prevalence CVD Switzerland 2015 [22]	3601–5600/100,000 persons	115,680–179,897
Incidence CVD in men, Switzerland 2017 [23]	1,463/100,000	46,998/year
Total CVD cases in men over a period of 10 years [55]	179,897 + (46,998 × 9) (Assumption: higher prevalence in men)	602,879
CVD-related ED cases [21] over a period of 10 years	49% of CVD cases (7% mild ED, 17% moderate ED, 25% severe ED)	All ED: 295,410 Mod. + sev. ED: 253,209 Severe ED: 150,720

Notes. * Swiss federal statistical office (BFS), <https://www.bfs.admin.ch> (accessed March 25, 2022). CVD: cardiovascular disease; ED: erectile dysfunction.

health priority [2, 6]. The crucial key for a successful implementation of these strategies is the individual identification and treatment of modifiable risk factors [7]. Current evidence identified that 9 out of 10 common risk factors accounted for >90% of the risk of myocardial infarction and stroke, respectively, and established the focus in prevention of these common CVDs [8, 9]. Implementation of lifestyle changes and lowering blood pressure, blood glucose, and introducing lipid-lowering therapies has been shown to reduce morbidity and mortality [10, 11, 12].

Although frequently misinterpreted as a lifestyle-limiting condition, erectile dysfunction (ED) may be a medically highly relevant disease even in younger men [13].

ED is defined as the consistent or recurrent inability to attain and/or maintain penile erection sufficient for sexual satisfaction, including satisfactory sexual performance [14]. Against common belief, nine out of ten patients with ED have primary organic ED, whereas ED is of primary psychogenic nature in about 10 percent of patients [15]. Among the different pathogenic mechanisms of ED, vascular etiology is the most common organic cause [16, 17, 18].

Due to the shared risk factor background, the co-prevalence of ED and CVD is high. In addition, presence of ED has been associated with increased major cardiovascular adverse events [19]. The penile arteries have a smaller diameter when compared with coronary arteries. This may explain why ED can be an early manifestation of CVD [20]. Montorsi and coworkers described ED as “the tip of the iceberg” of preclinical cardiovascular disorders [21]. Therefore, screening, diagnosing, and treating ED patients may be expected to impact vascular health thereby

leading to a reduction of future cardiac and cerebrovascular events.

The aim of this analysis was to perform a Swiss-based cost analysis for screening and treatment of patients with ED aged >18 years with regard to the occurrence and the possible therapy costs of cardiovascular events in the future 20 years. Considering the perspective of the Swiss health-care system, our hypothesis was that ED screening is economically reasonable through a reduction of subsequent cardiovascular events.

Methods

Study design

This study considered current data on prevalence and incidence of CVD-associated ED adapted to the Swiss population. Costs and effects of a screening intervention for cardiovascular risk including cardiovascular medication and annual diagnostic follow-ups in men who are expected to turn out to be at cardiovascular risk were calculated over a period of 10 years. Separately, aiming at an economical break-even result, additional costs of symptomatic treatment of ED with endovascular intervention were calculated.

Men with ED and CVD

Total number of Swiss men with ED over a period of 10 years was calculated from data on ED prevalence [13], ED

Table II. Number of acute cardiovascular disease events in patients with erectile dysfunction in Switzerland that can be prevented over a period of 10 years*

	All ED n=1,373,019	Severe and moderate ED n=919,923	Severe ED n=260,874
CVD cases to be detected and prevented (ED cases that occur prior to CVD symptoms: 67% of CVD-related ED cases) [21]	197,925	169,650	100,982
CVD events that can be avoided with prevention (21% reduction in major vascular events) [27]	41,564	35,627	21,206
Non-fatal MI (324/100,000 men [†])	19,502	16,715	9,949
Non-fatal stroke (292/100,000 men [†])	17,613	15,098	10,042
Death from MI or stroke (Lethality 10.8% with MI and 10.6% with stroke [‡])	4,449	3,814	1,215
Men to be screened for CVD disease: (ED cases without known CVD)	1,275,534	822,438	211,136
Number needed to screen to avoid one CVD event (NNS=1/[events avoided/number screened]) [55]	NNS=1/0.033=30	NNS=1/0.043=23	NNS=1/0.10=10

Notes. *Based on assumptions and calculations in Table I. [†]Swiss Health Observatory, <https://ind.obsan.admin.ch/de/indicator/obsan/myokardinfarkt>, <https://ind.obsan.admin.ch/indicator/obsan/hirnschlag> (accessed April 10, 2022). [‡]Eurostat. Standardized death rates-diseases of the circulatory system: Switzerland, https://appsso.eurostat.ec.europa.eu/nui/show.do?dataset=hlth_cd_asdr2&lang=en (accessed April 10, 2022). CVD: cardiovascular disease; ED: erectile dysfunction; MI: myocardial infarction, NNS: number needed to screen.

incidence [14], and percentage distribution of ED seriousness degrees [20] using data on the Swiss population from the Swiss federal statistical office ([BFS] <https://www.bfs.admin.ch> [accessed March 25, 2022]) (Table I).

Total number of Swiss men with CVD over a period of 10 years was calculated from data on age-standardized CVD prevalence based on estimations from the 10 most common causes of CVD-related death [22] and age-standardized CVD incidence using data from the BFS. CVD incidence included International Classification of Disease (ICD) codes ICD-10 (I00-I99), ICD-9 (390.0–459.9), and ICD-8 (3900–4589) [23] (Table II).

Costs and effects

Costs comprises costs of medical examination of men with ED including laboratory tests and angiological investigation (Table III) as well as costs of medication with statin and acetylsalicylic acid and costs of annual diagnostic follow-ups in case of established cardiovascular risk (Table IV). An angiological investigation is an expensive however essential tool to define patients with systemic atherosclerotic disease and to initiate preventive therapies. Total estimated costs of screening and prevention will depend on the size of the population screened (Table V). In severe ED, endovascular intervention incurs 7132.80 CHF per procedure according to diagnosis-related group (DRG) classification F59G in case of single obstruction unilateral stenting and 9139 CHF per procedure according to DRG F59F in case of need for multiplex stents. Effects of the screening intervention are acute CVD events likely to be avoided, quality adjusted life years (QALYs) gained, and cost savings from prevention of acute CVD events including non-fatal myocardial infarction, non-fatal stroke, and cardiovascular death. Health state utility value estimates to calculate QALYs were 0.79 in men with no CVD events and 0.69 or 0.64 after non-fatal myocardial infarction or ischemic stroke, respectively [24]. Costs of acute CVD events and subsequent annual

Table III. Costs of investigations for CVD in ED patients

Test	Costs in CHF*
Physical examination and consultation	41.41
Laboratory tests	
Hemogram	14.60
Lipid panel	32.40
Sodium, Potassium	5.30
Kreatinin	2.50
HbA1c	17.80
Thyroid levels	28.40
Additional fee, laboratory test	24.00
Angiological investigation [†]	793.59
Total	960.00

Notes. *Prizes from 2022. [†]Angiological investigation includes assessment of the vascular status by means of sonography and oscillometric measurement as well as sonographic functional tests. CHF: Swiss Francs; CVD: cardiovascular disease; ED: erectile dysfunction.

Table IV. Costs of medical therapy for secondary CVD prevention

Medication	Costs in CHF
Statin therapy*	409.20/year
First follow-up (visit, diagnostic test) [†]	161.71
Annual follow-up (visit, diagnostic test) [†]	178.46/year
Acetylsalicylic acid*	77.40/year

Notes. *<https://compendium.ch/search?q=Acetylsalicylsäure&type=ProductActiveSubstanceGroup>, <https://compendium.ch/search?q=Atorvastatin>, accessed April 9, 2022. [†]Prizes from the year 2019, Swiss Federal Office of Public Health (FOPH), Health Technology Assessment report (HTA). CHF: Swiss Francs; CVD: cardiovascular disease.

costs were adopted from previous cost-effectiveness studies [25, 26] (Table VI). Costs were reported in Swiss franc (CHF) and adjusted for inflation using the inflation rate from the Swiss Federal Statistical Office, accessed from the OECD website (<https://data.oecd.org/price/inflation-cpi.htm>, accessed on April 8, 2022). The annual inflation rate in Switzerland was recorded at 2.4%. Costs and effects were

Table V. Costs of investigation and medical therapy for CVD in men with ED over a period of 10 years*

	All ED (Costs in CHF)	Severe and moderate ED (Costs in CHF)	Severe ED (Costs in CHF)
Investigation for CVD	1,173,225,013	764,598,041	196,504,983
Medical therapy for secondary prevention of CVD			
Statin and acetylsalicylic acid	93,435,897	80,032,428	48,204,804
First follow-up	31,028,914	26,597,483	15,831,460
Annual follow-up	152,733,066	130,913,777	77,924,756
Total	1,450,422,890	1,002,141,729	338,466,003

Notes. *Adjusted for inflation of 2.4% (<https://data.oecd.org/price/inflation-cpi.htm#indicator-chart>, accessed April 11, 2022) and considering a discount rate of 3%. CHF: Swiss Francs; CVD: cardiovascular disease; ED: erectile dysfunction.

Table VI. Healthcare costs of acute CVD events over a period of 10 years*

CVD	Per CVD [25, 26] (Costs in CHF)	All ED (Costs in CHF)	Severe and moderate ED (Costs in CHF)	Severe ED (Costs in CHF)
Non-fatal MI 1 st year	16,923	319,533,515	274,628,709	158,560,961
Annual costs post-MI	1,734	147,472,935	125,291,423	74,653,562
Non-fatal stroke 1 st year	19,828	338,956,949	290,556,478	193,255,317
Annual costs post stroke	11,967	913,006,551	781,855,735	520,028,802
CVD death [26]	8,511	36,751,521	31,506,029	10,036,662
Total		1,755,721,471	1,503,838,374	956,535,304

Notes. *Adjusted for inflation of 2.4% (<https://data.oecd.org/price/inflation-cpi.htm#indicator-chart>, accessed April 11, 2022), and considering a discount rate of 3%. CHF: Swiss Francs; CVD: cardiovascular disease; ED: erectile dysfunction.

discounted with an annual rate of 3% over a period of 10 years ($\text{discount factor}_{n \text{ years}} = 1 / (1 + \text{discount rate})^n$).

Results

Cardiovascular risk associated with ED

Based on previously published data on prevalence [22] and incidence [23], we anticipated a total of 602,879 CVD events over a period of 10 years in Switzerland. From findings of Montorsi et al. [21] we assume a proportion of 49% of all CVD cases to be associated with ED, resulting in 295,410 ED-associated CVD events in Switzerland over a period of 10 years (Table I).

Effects of screening and cardiovascular prevention

A share of 67% of ED-associated CVD events occur only after men's awareness of ED [21], which is equivalent to 197,925 CVD events over a period of 10 years. Provided the cardiovascular risk is recognized at the time of ED diagnosis, and secondary prevention is conducted accordingly, we assume that 21% of acute CVD events may be prevented [27]. If screening for CVD risk includes men with all ED seriousness degrees (1,275,534 men), men with moderate or severe ED (822,438 men), or only men with severe ED (211,136 men), a total of 41,564 CVD events, 35,627 (85.7% of all anticipated) CVD events, or 21,206

(51.0% of all anticipated) CVD events, respectively can be prevented over a period of 10 years. The number of men needed to be screened to prevent one acute CVD event is estimated at 30, 23, and 10, respectively (Table II, Figures 1 and 2). Prevented acute CVD events correspond to 44,591, 38,225, and 19,009 QALYs gained over a period of 10 years, respectively.

Costs of screening and cardiovascular medication

Ten-year costs of screening and prevention of cardiovascular risk in men with moderate and severe ED are estimated at 69.1% (1,002,141,729 CHF), and of men with severe ED only at 23.3% (338,466,003 CHF) of the costs incurred with screening of men with ED of all seriousness degrees (1,450,422,890 CHF) (Table IV, Figure 2).

Cost effectiveness

Incremental cost-effectiveness ratios (ICER), independent of cost savings, were CHF 32,527/QALY with screening/prevention of men with all ED seriousness degrees, CHF 26,217/QALY with screening/prevention of men with moderate or severe ED, and CHF 17,806/QALY with screening of only men with severe ED. Due to cost savings from prevention of acute CVD events, the screening intervention is expected to turn out to be economical at the seventh, the fifth, and the first year with screening/preventing

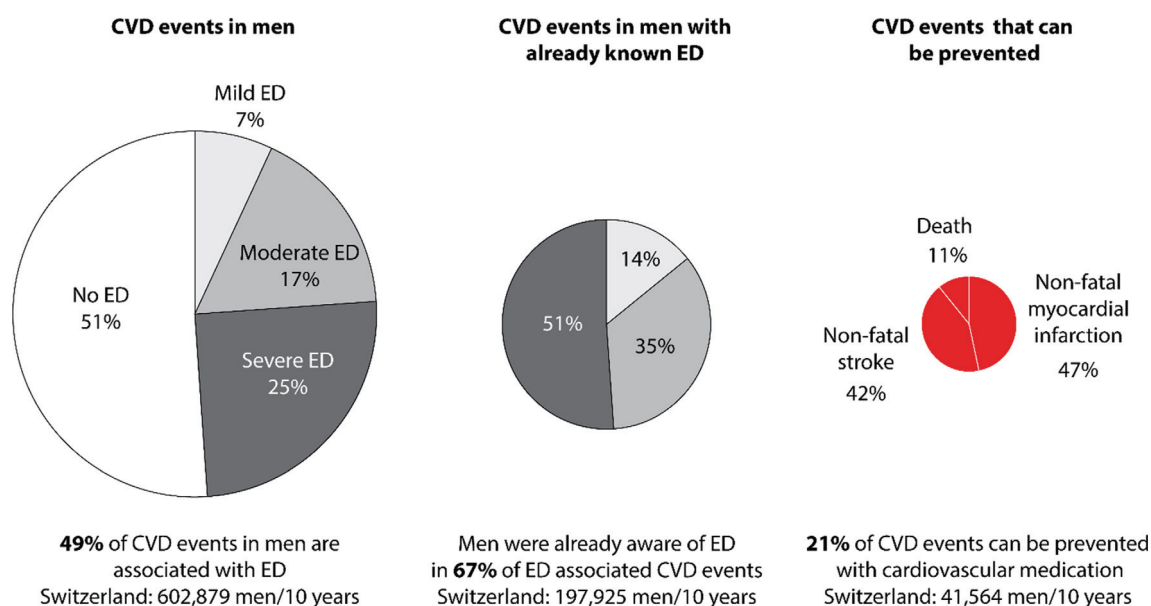


Figure 1. Pie chart shows proportions and numbers of cardiovascular events associated with ED, and CVD events that can be prevented with medication as soon as the cardiovascular risk is identified through screening of ED patients. Proportions are based on previous study results [21, 27] and on data from the Swiss Health Observatory (Table II). Notes. CVD: cardiovascular disease; ED: erectile dysfunction.

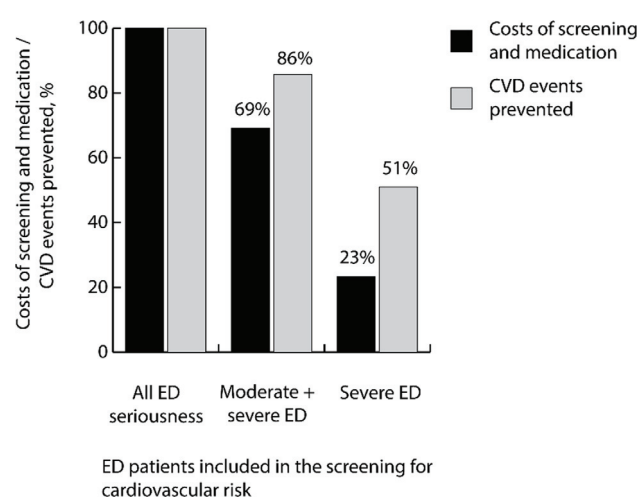


Figure 2. Comparison of costs of screening/medication and number of CVD events that can be prevented over a period of 10 years between screening of all men with ED (set at 100%) and screening with restricted inclusion criteria regarding ED seriousness degree. Notes. CVD: cardiovascular disease; ED: erectile dysfunction.

of men with ED of all seriousness degrees, of only moderate and severe ED, or of only severe ED, respectively (Figure 3).

Covering costs of endovascular interventions

Cost savings from prevention of CVD events can cover costs of endovascular interventions for symptomatic ED treatment depending on the size of the population to be screened and the complexity and number of interventions (Figure 4). In case of screening and prevention that includes men with moderate and severe ED in Switzerland over a period of 10 years, it can be expected, that costs of

endovascular interventions with single or multiple stents in 48% (72,551) or 38% (56,624) of men with severe CVD-associated ED, respectively will be covered to achieve an economical break-even result. In case of screening that includes only men with severe ED, cost savings from prevention can cover costs of single or multiple stent implantations in 59% (89,379) or 46% (69,759) of men with severe CVD-associated ED, respectively.

Discussion

This paper presents a health economic analysis of the screening and intervention for cardiovascular risk factors in men suffering from ED in the Swiss setting. In our analysis, the estimated cost-effectiveness compared favorably for screening intervention in those patients by achieving an avoidance of over 40.000 acute CVD events with a NNS of 30 men with all ED seriousness degrees, of 23 men and 10 men with moderate to severe and severe ED, respectively.

Accordingly, incremental cost-effectiveness ratios (ICER) with screening and prevention in men with ED, independent of cost savings, were around CHF 33,000/QALY in all seriousness degrees, CHF 26,000/QALY in moderate/severe and CHF 18,000/QALY in severe ED. Furthermore, these cost savings can cover the costs for minimal invasive treatment options helping to improve organic ED and reconstitute sexual health.

Diseases of the heart and the vascular system significantly increase the burden of disease in Switzerland with premature deaths and rising costs in the health sector. Knowledge and detection of risk factors that precede CVD are invaluable in identifying individuals who are more

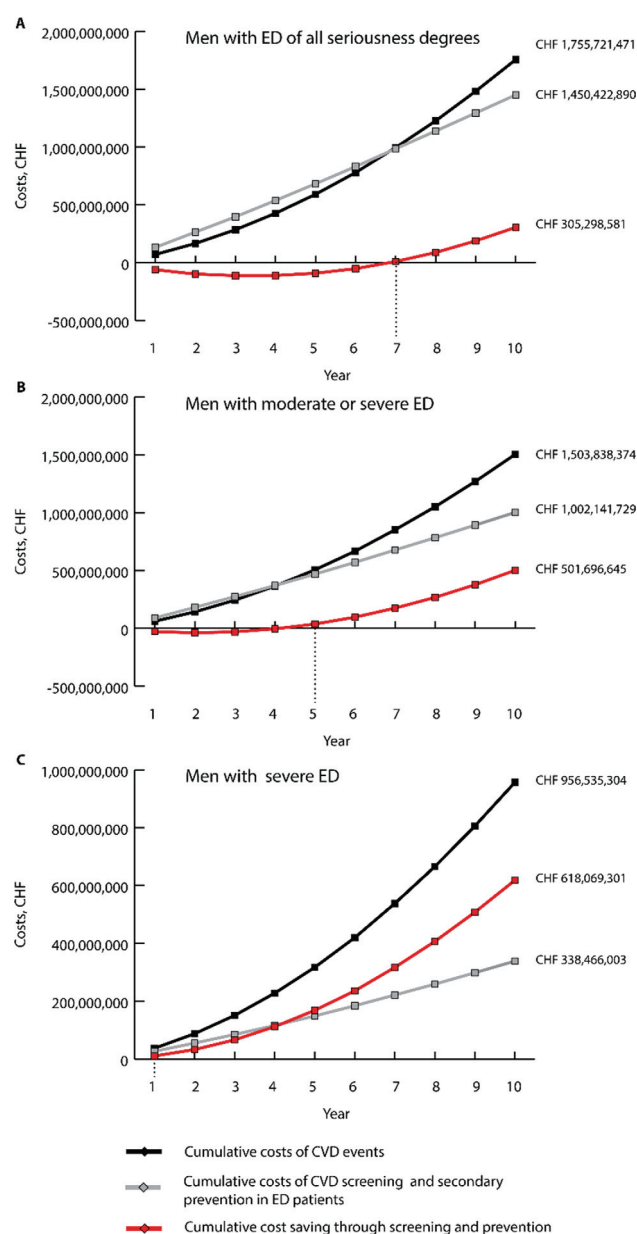


Figure 3. Cumulative costs of CVD events, screening and secondary prevention, and cost savings by CVD screening of patients with mild to severe (A), moderate and severe (B), and severe (C) erectile dysfunction and medication in case of increased cardiovascular risk over a period of 10 years. The calculation considered an inflation rate of 2.4% and a discount rate of 3%. Dashed line shows time when screening and secondary prevention turned out to be economical. Notes. CHF: Swiss Francs; CVD: cardiovascular disease; ED: erectile dysfunction.

likely to develop CVD so that interventional strategies can be used to address the risk factors and modulate their effects on CVD risk. The National Strategy for cardiovascular disease, stroke, and diabetes 2017–2024 accordingly set claims to strengthen prevention and early detection [2]. Several meta-analyses showed evidence that ED is a strong predictor of ischemic heart disease associated with an increased risk of CVD, stroke, and all-cause mortality [28, 29]. The risks to develop CV events in men with ED were described to be as high as 43% for CVD, 59% for CHD, 34% for stroke and 33% for all-cause mortality [29].

Therefore, the importance of preventing CV events in men suffering from ED is unchallenged and demanded for more than 10 years by the Third Princeton Consensus Panel [30] and reinforced with the current guidelines of the American Urology Association [31]. Both provide recommendations for the evaluation and management of cardiovascular risk in men with ED and no known CVD.

However, no significant move towards meeting these demands has been achieved. Based on our presented analysis, we strongly suggest screening and initiation of treatment for cardiovascular risk factors in men suffering from ED without known CVD as a cost-effective tool to ameliorate otherwise inevitable CVD process. The favorable number needed to screen to prevent one CVD event as well as the fact that costs for the screening intervention are expected to be covered as early as the first year in severe ED is another strong argument to strengthen the need for a better awareness of ED and its relevant risk-factor treatment.

The main causal and modifiable CVD risk factors are low-density lipo-protein (LDL), high blood pressure, cigarette smoking, and diabetes mellitus. Overwhelming evidence links CVD and ED, with both conditions having similar risk factors [28, 30, 32].

As the physiology of erection is heavily dependent on vascular structures, many of the known cardiovascular risk factors have been associated with the development of ED [33], resulting in a high prevalence of ED in patients suffering from CV risk factors.

Thirty to 50% of patients with essential hypertension exhibit symptoms of ED [34, 35, 36]. The higher rate of ED in diabetic men is also known with prevalence rates ranging from 35% to 90% [37, 38, 39]. Additionally, diabetic men tend to develop ED 10 to 15 years earlier than the average ED patient [20]. They appear to present with more severe ED and suffer a greater diminishment in health-related quality of life components compared to the general population [40, 41]. Epidemiologic data has confirmed that hyperlipidemia is a strong independent risk factor for the development of ED via endothelial damage and inflammation [42]. High LDL levels and low HDL levels seem to be related to ED [43]. Smoking has been shown to be strongly associated with the degree of ED [44]. Multiple cross-sectional studies established an increased risk of smokers varying from 1.5 to 3.1 fold when compared to nonsmokers [45, 46]. Lifestyle modification like increased physical activity is protective against developing ED [47, 48].

From a different perspective, the most prevalent ED risk factors are cigarette smoking (42%), followed by arterial hypertension (29%) and alcohol consumption (25.1%) [49]. Younger age at first manifestation of ED, cigarette smoking, presence of comorbidities and socioeconomic disadvantage were all associated with higher hazard ratios for subsequent atherosclerotic CV events [50]. The prognostic value of ED for CVD is strongest in middle-aged men younger than 60 [51].

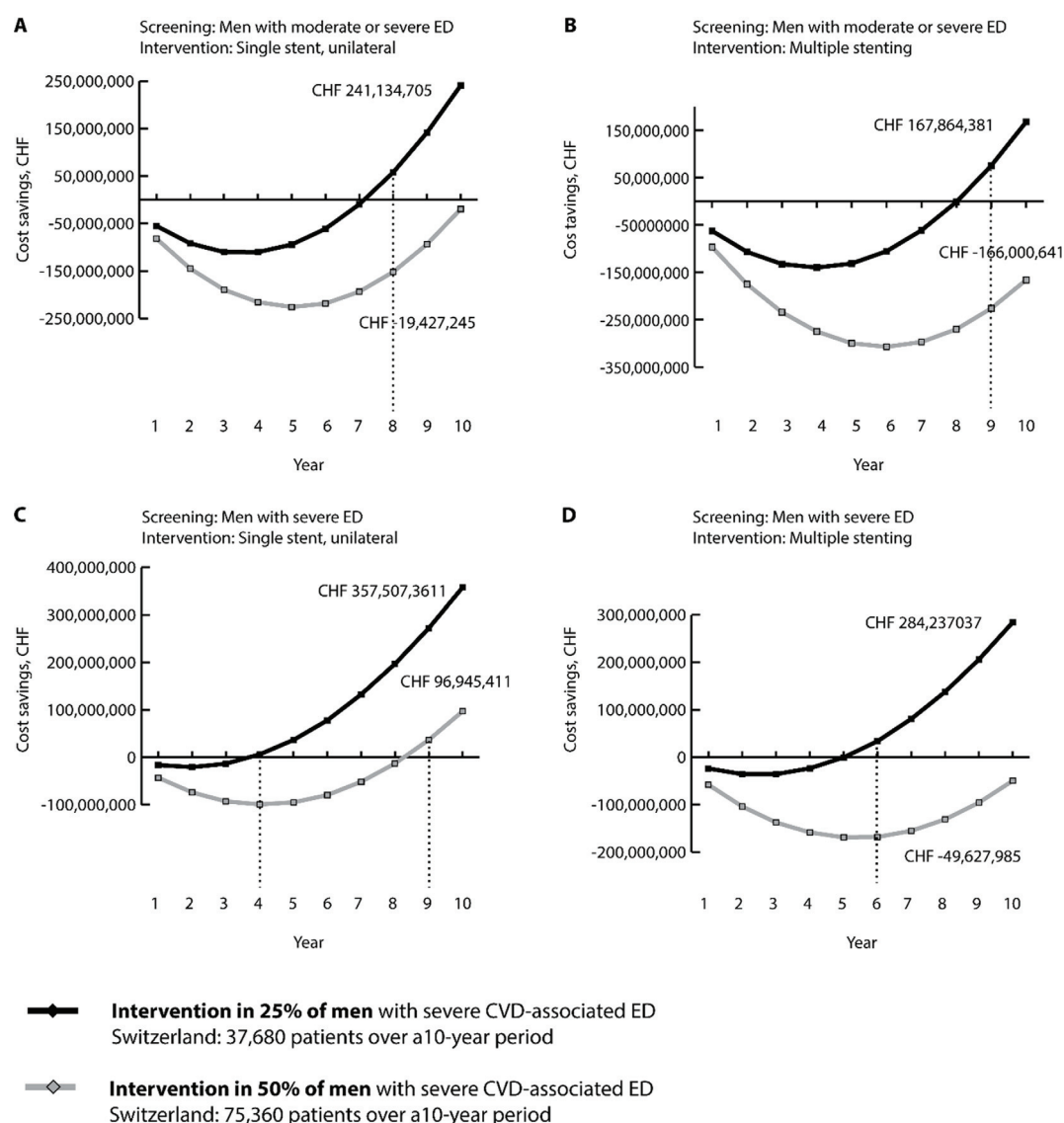


Figure 4. Cumulative cost savings with cardiovascular screening and prevention of men with moderate and severe (A, B) or only men with severe ED (C, D) considering additional costs of endovascular intervention in 25% or 50% of men with severe CVD-associated ED with single (A, C) or multiple (B, D) stenting over a period of 10 years. Costs incurred 7132.8 CHF per procedure according to DRG classification F59G in case of single, unilateral stenting and 9139 CHF per procedure according to DRG F59F in case of multiple stenting. Calculation considered an inflation rate of 2.4% and a discount rate of 3%. Dashed line shows time when screening, secondary prevention, and endovascular intervention turned out to be economical. Notes. CHF: Swiss Francs; CVD: cardiovascular disease; DRG: diagnosis-related group, ED: erectile dysfunction.

As a conclusion of the above associations, we believe that ED can act as an important tool to trigger both patients and physicians to screen for CV risk factors and initiate changes of lifestyle as well as medical treatment if necessary.

Despite their high relevance, sexual problems are seldomly investigated by general practitioners and specialists [52, 53]. Continuing education is necessary to lessen barriers stemming from a lack of awareness about the potential clinical consequences of ED as an important marker disease.

Conservative treatment options for ED are limited. Rare cases of hypogonadism can be treated with hormonal substitution. In case of a mild neurogenic or vascular pathology, vasoactive agents such as PDE-5 Inhibitors may help to improve erection. Early detumescence due to cavernous dysfunction can sometimes successfully be

treated with a penile ring. In addition, patients with ED of vascular etiologies may profit from shock wave treatment.

Minimal-invasive treatment by angioplasty and stent implantation can be discussed in case of arteriogenic ED non-responsive to conservative measures [54]. Our analyses implicate that cost savings from prevention of CVD events can cover costs of endovascular interventions for symptomatic ED treatment. Thus, the positive effects on CVD prevention are accompanied by an economic break even result for a beneficial treatment of ED.

Limitations

Study limitations include the use of modeling and the estimates these were based on, which were sensitive to inputs

(most notably the effects of losing insurance on mortality and of premium increases on becoming uninsured), the assumption that health opportunity cost in QALYs lost per CHF spent is a constant ratio, the variability of health opportunity costs by population and the exclusion of non-health opportunity costs.

Conclusions

In conclusion, the importance of ED as a marker of undiagnosed CVD and substantial risk factor for future CV events is unchallenged. We provide evidence that screening and treatment of CV risk factors are cost effective tools with an estimated reduction of CV events, a gain of Quality-adjusted life-years and short-term coverage of costs for the screening intervention. Interestingly, within the present study, costs for minimal-invasive therapies for patients with severe ED unresponsive to medical treatment alone were covered by the benefits of ED screening.

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