

# BURDEN OF CARDIOVASCULAR DISEASE AND POTENTIAL IMPACT OF PCSK9i IN THE PREVENTION OF CARDIOVASCULAR EVENTS IN SWITZERLAND

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## INTRODUCTION

- Cardiovascular disease (CVD) is responsible for approximately one third of the global mortality every year, accounting for 18 million deaths globally and over 21,000 deaths in Switzerland in 2015<sup>1,2</sup>.
- In addition to its large mortality burden, there are significant morbidity consequences after patients have experienced a non-fatal cardiovascular (CV) event, leading to a reduced quality of life for an extensive period after the event and, consequently, a decrease in productivity (both paid and unpaid-work), economic activity and increased need for informal care<sup>3,4</sup>.
- In October 2019, a reimbursement recommendation was issued in Switzerland for Evolocumab, a proprotein convertase subtilisin/kexin type 9 inhibitor antibody (PCSK9i), for the treatment of a very high-risk population of ASCVD patients with LDL-C  $\geq 2.6$  mmol/l. Evolocumab, one of two available PCSK9i, has marketing authorization in Switzerland to reduce risk of CV events.
- As the burden extends well beyond the patients and the health care system, it is crucial to take a holistic perspective when assessing the social and economic impact of CVD.

## OBJECTIVES

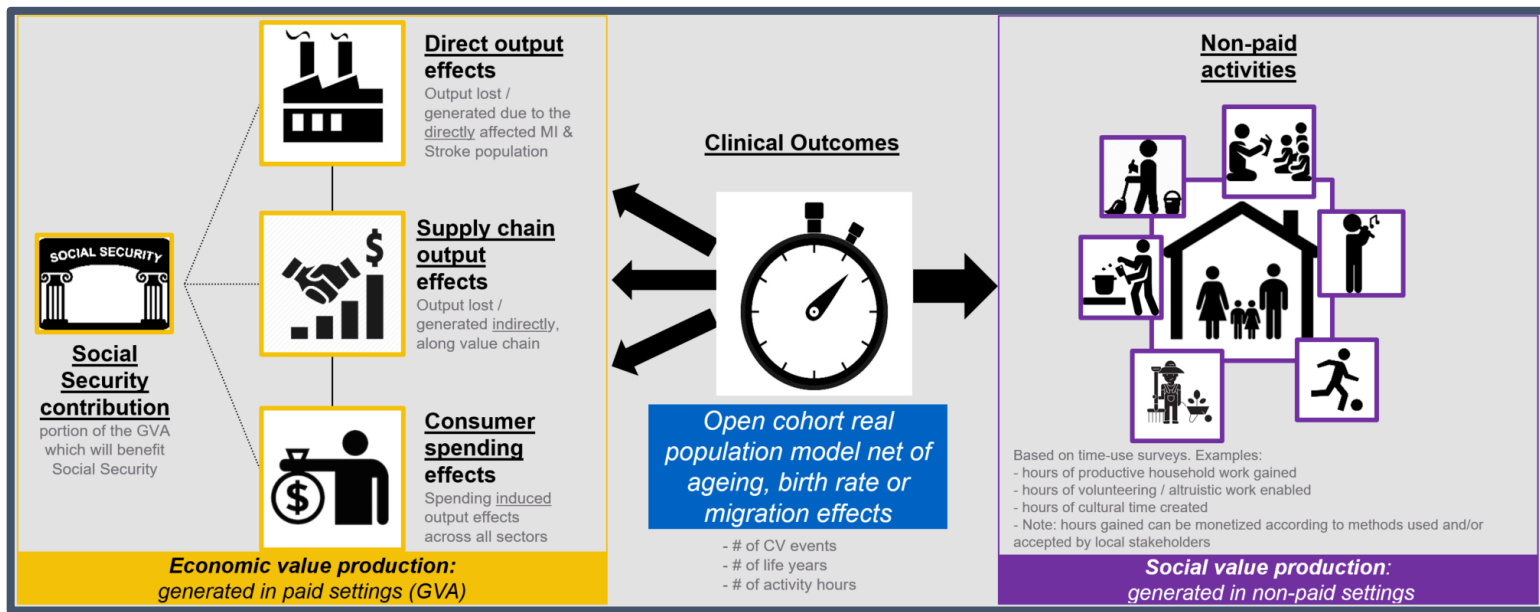
The objective of this study was

- to assess the impact of CVD from an expanded public health and macro-economic perspective in Switzerland, and
- to understand how the potential broader economic and social value of preventing CV events and deaths by using PCSK9i compares to the cost of utilizing this novel technology.

## METHODS

- The burden of CVD is defined in the form of CV events and their associated direct medical costs. However, the broader value that PCSK9i can bring is usually not fully accounted for. The current study addresses this gap by translating the clinical outcomes predicted by a model into the economic and social value that could be generated in paid and unpaid-settings by using PCSK9i (Figure 1).

Figure 1. Analytic Framework Overview



## Epidemiological methods

- The epidemiological part of the model consisted of a simplified three health state Markov open cohort model (Alive, CV death and Non-CV death) that allows the entry of new patients in the model to fully assess the impact of CVD from a population health perspective. The model applies a one-year cycle length.

## Broader economic and social impact

- The productivity time loss in paid and unpaid-settings due to non-fatal CV events was estimated based on the study by Kotseva et al<sup>9</sup>. For the estimation of time loss due to fatal CV events, the human capital approach was used by taking into account the sum of all the wages of the patient during absence from work.
- To monetize the value of the paid working time loss due to CVD, the model goes beyond presenteeism and absenteeism by using the gross value added (GVA) of the country. GVA can be used to measure the full contribution of a therapy as it accounts for the total effect on the economy resulting from a CV event by considering not only the direct effect on the economy but also the downstream induced and indirect effects along the supply chain and consumer spending.
- The analysis takes a conservative approach by focusing on the salary proportion of the GVA as this is the primary component impacted; however, it might also be argued that all GVA components should be considered to estimate the full impact on the economy.
- Unpaid activities are crucial in the estimation of the social value of CVD due to the substantial amount of time that Swiss people dedicate to socially and culturally valuable activities. Following a conservative approach, the “third person criterion” was applied to exclude leisure time from the estimation or productivity loss in unpaid-settings. Unpaid hours were then monetized using a nominal value of 23.30 CHF based on methodology already applied in Switzerland<sup>12</sup>.

## Inputs

- The baseline risk of the general population was calibrated to predict the number of CV events observed during 2017 in Switzerland<sup>4</sup>. The baseline risk of the PCSK9i reimbursed population was estimated from a study conducted in Switzerland by Nanchen et al.<sup>6</sup>
- The treatment effect was based on the relationship between LDL-C lowering and reduced rate of CV events as observed in the CTTC meta-analysis<sup>7</sup>.
- Direct medical costs of MI and IS relevant to the national health-care system were calculated based on two studies conducted by the Winterthur Institute of Health Economics (WIG).<sup>10,11</sup>
- The price of PCSK9i was based on the current list price of Evolocumab of 4,912.96 CHF per year (ex-factory price, excluding margins and value-added tax (VAT)).
- The model inputs are based on data from 2017 but similar inputs and outcomes are expected in the following years. Results are presented for a one-year time horizon.

## RESULTS

### Burden of disease

- A total of 78,026 fatal and non-fatal CV events were predicted in Switzerland resulting in costs to the health care system of more than 3.3 billion CHF at a one-year time horizon (Table 1). These results are consistent with the study conducted in Switzerland by Wieser et al.<sup>13</sup>

Table 1. Predicted health impact of CVD

	Number of CV events	Direct health-care costs (CHF in million)
Non-fatal MI	12,568	884.27
Non-fatal IS	9,750	1,798.50
oASCVD	34,976	420.56
CV death	20,732	209.87
<b>Total CV events</b>	<b>78,026</b>	<b>3,313.19</b>

### Socio-economic impact of CVD

- The socio-economic impact of paid-work hours lost resulting from these events was 6.1 billion CHF in terms of GVA lost to the economy (Table 2).
- The caregiver- and unpaid-work lost due to CVD was estimated to be almost 0.5 billion hours, which were valued at 11.3 billion CHF (Table 3).
- Fatal events have the most significant impact on the total burden of CVD, which is expected as each fatal event leads to many years of loss productivity and unpaid activity as the model uses the human capital approach.

Table 2. Economic loss (in paid-work settings) of CV events

	Hours lost (in million)	Production losses (CHF in million)
Non-fatal MI	2.48	163.87
Non-fatal IS	1.03	68.24
CV Death	100.03	5,897.59
<b>Total CV events (w/o non-fatal oASCVD)</b>	<b>103.55</b>	<b>6,129.69</b>

Table 3. Caregiver and unpaid-time loss

	Caregiver and unpaid hours lost (in million)	Monetary loss (CHF in million)
<b>Total CV events (w/o non-fatal oASCVD)</b>	<b>485.12</b>	<b>11,301.28</b>

## ABBREVIATIONS AND FOOTNOTES

CHF, Swiss francs; CV, cardiovascular; CVD, cardiovascular disease; MI, myocardial infarction; oASCVD, other atherosclerotic CV disease; IS, ischemic stroke; SoC, standard of care; w/o, without

\*Other atherosclerotic CV disease: all non-fatal CV disease other than MI and IS; i.e. peripheral vascular disease, atrial fibrillation, other pulmonary disease, diseases of pericardium, valve disorders, tachycardia, ill-defined heart disease, other aneurysms and other disorders of arteries/veins.

## RESULTS (cont'd)

### Potential socio-economic impact from utilizing PCSK9i

- In the PCSK9i reimbursed population of 28,100 patients, 1,624 out of a total of 4,424 (i.e. 37%) major adverse cardiovascular events (MACE) could be avoided, which would result in healthcare cost savings of 95.2 million CHF (Table 4).
- In addition to the implications on the health-care system, PCSK9i usage was predicted to result in a significant impact on the GVA of the country leading to savings of more than 49 million CHF in paid-work settings as well as over 188 million CHF in unpaid-work settings (Figure 3). Since the average age of patients being treated with PCSK9i is 64 years, the impact in paid-work is lower than on unpaid-work settings as patients are close to retirement age.
- On average, for every 1 CHF invested in PCSK9i, 2.41 CHF was returned to society on avoided medical costs and monetary value of paid and unpaid-work (net return-on-investment: 1.41 CHF) (Table 5).

Table 4. Potential health impact and health-care cost from utilizing PCSK9i

	CV events with SoC treatment	Health-care costs of CV events with SoC treatment (CHF in million)	CV events avoided with PCSK9i	Health-care cost savings due to CV events avoided (CHF in million)
Non-fatal MI	1,303	81.30	481	30.09
Non-fatal IS	1,019	154.01	378	57.36
CV death	2,102	21.28	764	7.74
<b>Total CV events (w/o non-fatal oASCVD)</b>	<b>4,424</b>	<b>256.59</b>	<b>1,624</b>	<b>95.20</b>

Figure 3. Predicted number of hours gained and associated monetary savings in paid and unpaid-settings

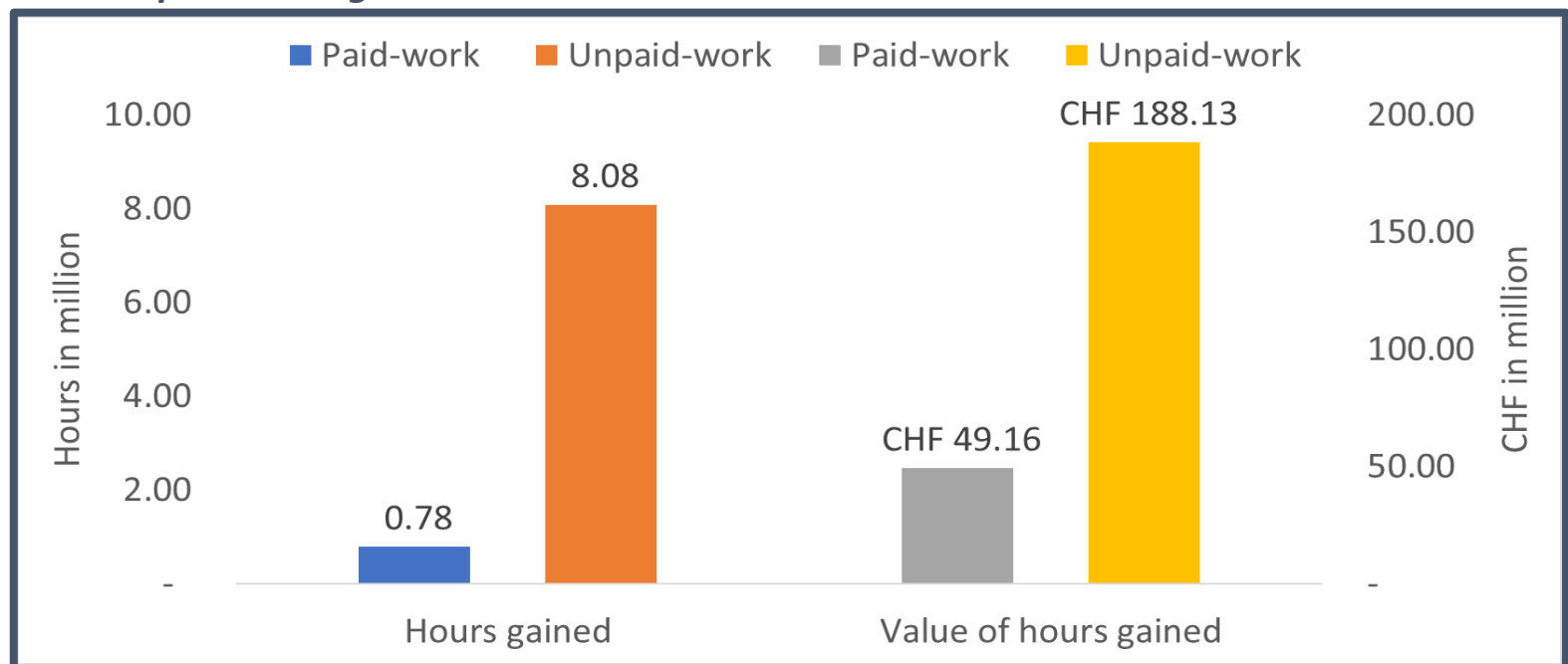


Table 5. Value of investing in PCSK9i in the current reimbursed very high-risk population

	Value-Invest Ratio (value created per CHF invested in PCSK9i)	Value created by PCSK9i (CHF in million)
Avoided direct medical costs	0.69 CHF	95.20
Monetary value of paid-work	0.36 CHF	49.16
Monetary value of unpaid activities	1.36 CHF	188.13
<b>Total return to society</b>	<b>2.41 CHF</b>	<b>332.48</b>
Cost of PCSK9i	1.00 CHF	138.05
<b>Potential net return on investment of PCSK9i</b>	<b>1.41 CHF</b>	<b>194.43</b>

- Sensitivity analyses were also conducted to investigate the robustness of the model and results to a change in assumptions and parameters. The results of the sensitivity analyses indicate that the model takes a conservative approach and that the value-invest ratio stays well above 1 in all the scenarios considered, which means that the value of using PCSK9i exceeds their cost.

## DISCUSSION

- The economic and social impact of CVD in Switzerland in 2017 was estimated to be 21 billion CHF when accounting for the direct impact on the health-care system as well as the substantial economic burden that results for the hours loss in paid and unpaid-settings.
- Treating the current reimbursed population with PCSK9i would result in total savings of 95.20 million CHF in direct medical costs, 49.16 million CHF in indirect costs and 188.13 million CHF in societal costs per year by avoiding approximately 40% of all major adverse cardiovascular events (MACE). This translates into a total positive net return on investment of 194.43 million CHF.
- Even when PCSK9i would be accessible by the entire eligible population (not just very high-risk patients under the current reimbursement), the results reveal a net positive return on investment from a full economic and societal perspective. The results from these analyses showed that for every 1.00 CHF invested in PCSK9i, 1.74 CHF is returned to society. These results indicate that broadening the reimbursed population will create value in excess of the budget required to fund broader patient access.**
- This study shows that the burden of a disease and the value of preventing morbidity and mortality by utilizing medical technology can only be correctly assessed when the full economic and social impacts are accounted for. Methodologies to quantify the broader set of impacts exist and conservative assumptions and modeling parameters can ensure under- rather than over-estimate results in a real population.**
- The model aims to show a plausible set of inputs and assumptions as part of the base-case given the lack of available evidence in some areas, such as the time spent in unpaid activities after retirement, which would be an important area for future research.

## CONCLUSIONS

- PCSK9i show economic and social value in reducing the risk of cardiovascular events (myocardial infarction, stroke and coronary revascularization) through safe and intense LDL-C lowering in addition to statins in patients with established ASCVD.
- Through the potential to prevent MACE, the predicted return-on-investment of PCSK9i is positive from a full economic and social impact perspective.
- The return to society of PCSK9i investment was predicted to be 2.41 CHF per 1.00 CHF invested in the currently reimbursed high-risk population.**
- Even if the reimbursed access were expanded to all eligible Swiss patients (according to Swissmedic label), an economic and social return of 1.74 CHF would be generated for every 1.00 CHF invested in PCSK9i. In other words, the larger the eligible population treated, the more wealth is created.**
- Concerns related to the cost and budget impact of PCSK9i should be weighed up against the possibility of this investment creating a net positive return to society.**
- There is a need to broaden the perspective when assessing the cost of CVD to fully understand the value that PCSK9i can deliver for eligible patients and the overall society.**

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