European Heart Journal Acute Cardiovascular Care

ESC European Society of Cardiology

Original scientific paper

European Heart Journal: Acute Cardiovascular Care
1–9

Article reuse guidelines:
sagepub.com/journals-permissions
DOI: 10.1177/2048872619853959
journals.sagepub.com/home/acc
SAGE

Systematic investment in the delivery of guideline-coherent therapy reduces mortality and overall costs in patients with ST-elevation myocardial infarction: Results from the Stent for Life economic model for Romania, Portugal, Basque Country and Kemerovo region

Bastian Wein[1], Anna Bashkireva[2], Alex Au-Yeung[3], Adam Yoculan[4], Dragos Vinereanu[5], Dan Deleanu[6], Helder Pereira[7], Ernesto Pereira[8], Sofia de Mello[9], Jose R Rumoroso[10], Vladimir Ganyukov[11], William Wijns[12] and Christoph K Naber[13]

Abstract

Aims: The Stent for Life initiative aims at the reduction of mortality in patients with ST-elevation myocardial infarction by enhancing timely access to primary percutaneous coronary intervention. To assess the associated health and socioeconomic impact, the Stent for Life economic project was launched and applied to four model regions: Romania, Portugal, the Basque Country in Spain, and the Kemerovo region in the Russian Federation.

Methods and results: The Stent for Life economic model is based on a decision tree that incorporates primary percutaneous coronary intervention rates and mortality. Healthcare costs and indirect costs caused by loss of productivity were estimated. A baseline scenario simulating the status quo was compared to the Stent for Life scenario which integrated changes initiated by the Stent for Life programme. In the four model regions, primary percutaneous coronary intervention numbers rose substantially between 29–303%, while ST-elevation myocardial infarction mortality was reduced between 3–10%. Healthcare costs increased by 8% to 70%. Indirect cost savings ranged from 2–7%. Net societal costs were reduced in all model regions by 2–4%.

Conclusion: The joint effort of the Stent for Life initiative and their local partners successfully saves lives. Moreover, the increase in healthcare costs was outweighed by indirect cost savings, leading to a net cost reduction in all four model

[1]Heart and Vascular Center Oberallgaeu-Kempten, Germany (Member of the SANA Hospital Network) and Contilia Heart and Vascular Center, Elisabeth-Hospital Essen, Germany
[2]Siberian Association for Interventional Cardiologists, Russian Federation
[3]Department of Health Economics, Policy & Payments, Medtronic Inc., Santa Rosa, USA, Medtronic Inc., USA
[4]CRDN Finance, Medtronic Inc., Santa Rosa, USA
[5]Carol Davila University of Medicine and Pharmacy, University and Emergency Hospital Bucharest, Romania
[6]Department of Invasive Cardiology, Emergency Institute for Cardiovascular Diseases 'Prof. C. C. Iliescu' Bucharest, Romania
[7]Department of Cardiology, Hospital Garcia de Orta, Almada, Portugal
[8]Department of Interventional Cardiology, Hospital Garcia de Orta, Almada, Portugal
[9]Universidade NOVA de Lisboa, Escola Nacional de Saúde Pública/ NOVA National of Public Health (ENSP/NNSPH), Lisboa, Portugal
[10]Servicio de Hemidinamica y Cardiolgia Intervencionista, Hospital Quironsalud Bizkaia, Spain
[11]Scientific Research Institute for Complex Issues of Cardiovascular Diseases, Kemerovo, Russia
[12]The Lambe Institute for Translational Medicine and Curam, National University of Ireland Galway, Ireland
[13]Department of Medicine I, Hospital Wilhelmshaven, Germany

Corresponding author:
Christoph K Naber, Department of Medicine I, Hospital Wilhelmshaven, Friedrich-Paffrath-Straße 100, 26389 Wilhelmshaven, Germany
Email: christoph.k.naber@europcr.com

regions. These findings demonstrate that systematic investments to improve the access of ST-elevation myocardial infarction patients to guideline-coherent therapy is beneficial, not only for the individual, but also for the society at large.

Keywords

Stent for Life, Stent – Save a Life, ST-elevation myocardial infarction, costs, savings, primary percutaneous intervention, net benefit

Date received: 15 August 2018; accepted: 9 May 2019

Introduction

Ischaemic heart disease including ST-elevation myocardial infarction (STEMI) is the leading cause of death worldwide, and results in significant socioeconomic costs due to substantial health expenditure as well as loss of labour productivity.[1,2] Guidelines on the management of STEMI emphasise the importance of timely access to reperfusion to reduce morbidity and mortality in this population.[3] Whenever feasible, primary percutaneous intervention (pPCI) of the occluded coronary artery is the preferred approach. Notwithstanding the clear scientific evidence, reperfusion strategies vary widely across Europe, which led to the constitution of the multi-organisational 'Stent for Life' (SFL) initiative.[4–6] This initiative supports national cardiac societies and stakeholders in the development of systems of care, enhancing timely access to pPCI for all patients with STEMI, initially in Europe, by now worldwide. Results of this successful collaboration with the development of country or region specific multimodal action plans, their implementation and outcomes in a wide variety of different healthcare settings in emerging as well as developed countries, were published previously.[7–11] Whereas the scientific evidence to display the clinical benefits of a pPCI strategy in STEMI patients is sound, the health and socioeconomic impact remains difficult to grasp. Therefore the 'SFL economic model' was developed. We report the clinical results, the attributed costs and the socioeconomic impact of four regions in which the SFL contributed to the enhancement of guideline-coherent therapy in patients with STEMI.

Methods

Economic model

The economic model was developed by the Health Economic Working Group of the SFL initiative to demonstrate the financial, economic and clinical benefit of timely STEMI admissions and increased numbers of patients treated with pPCI. It was designed to allow applicability to a wide variety of different countries and regions, emerging as well as developed countries, with their corresponding healthcare settings. The model was adapted for each country or region of interest, and real world data, e.g. from local registries, provided by the local stakeholders were used. To evaluate the economic impact of the SFL initiative, the model compares the results and outcomes of the SFL initiative against a baseline scenario which simulates the continuation of the status quo without increase in pPCI numbers and consecutive improvement in outcomes.[9] The decision tree model constructed is presented in Figure 1.[12] The following variables were used: population of the catchment area, STEMI incidence, admission rates within 12 h, the distribution of reperfusion strategies and their corresponding outcomes (see Supplementary Material Table S-1 for details). The results display the clinical impact as well as outcomes and are the basis for the subsequent health and socioeconomic evaluations.

The impact on healthcare resources is quantified by determining the costs directly attributable to the healthcare sector.[13] The first cost category is represented by the fixed costs, meaning that these costs are to be spent irrespective of the number of future STEMI patients to be treated. Those costs mainly result from the investments into the essential infrastructure enhancing timely access to – and provision of – 24/7 pPCI capacities. Examples for those costs in earlier projects were investments to build and equip new catheterization laboratories, train or hire interventional cardiologists, investments in a telemedicine infrastructure with, for example, retrofitting of emergency ambulances with telemedicine-suitable ECG machines or spending on public awareness campaigns. The second cost category is represented by the, so-called, direct variable costs which depend on the number of patients treated. These costs accrue from the reimbursement of healthcare providers for the index hospitalisation, as well as follow-up costs due to readmissions, use of other medical services or medication costs. They are modelled from a third-party payer perspective. The variable costs are determined for each reperfusion strategy. All costs besides the initial fixed costs are discounted with country-specific discount rates and given in US dollars (USD) to allow comparability between countries.

The impact on the loss of productivity due to reduction of morbidity and mortality is quantified using a human capital approach.[14] To allow applicability, comparability and scaling over different countries and regions the per capita gross domestic product (GDP), as determined by the World Bank, was used as a measure of an individual's productivity, instead of a wage-based value. Loss of productivity per individual due to mortality or disabling morbidity

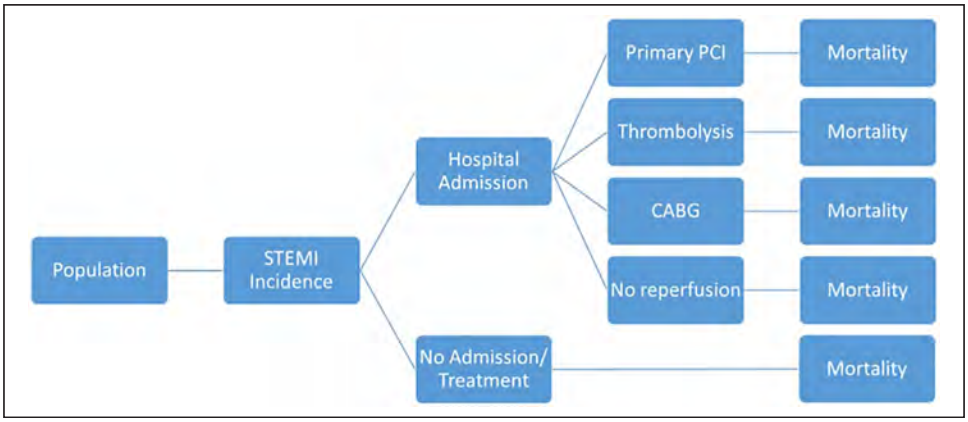

Figure 1. Decision tree model to quantify the impact of the Stent for Life (SFL) initiative.
CABG: coronary artery bypass graft; PCI: percutaneous coronary intervention; STEMI: ST-elevation myocardial infarction.

was estimated by multiplying the difference between retirement age and mean age at time of death or disablement with the annual per capita GDP. The percentage of persons dropping out of the labour market was assumed to be 8% for patients admitted to hospital and 12% for those without hospital treatment. For the quantification of the loss of productivity due to morbidity per individual, the time period of being temporarily absent of work until full recovery was estimated. For the model, it was estimated that a return to work after the STEMI event was after one month with pPCI therapy and three months without pPCI. As to thrombolysis, time to full recovery was adjusted based on differences of readmission rates after pPCI and thrombolysis, respectively. Readmission rates were derived from the derived from the Primary Angioplasty vs Immediate Thrombolysis in Acute Myocardial Infarction (PRAGUE-2) and the Swedish Early Decision (SWEDES) trials, respectively.[15,16] The proportion of a year not being able to work multiplied by the per capita GDP then gives the indirect costs per individual caused by STEMI morbidity.

The burden of a disease is defined as the result of the negative influence of a disease on the general health of a population.[17] To quantify the impact of the SFL initiative on the burden of disease with increased numbers of pPCI, years of life lost (YLL) were calculated for each reperfusion strategy. YLL are those years between actual death due to a STEMI and the statistical life expectancy in years.[18] To calculate it on a population level, the population, STEMI incidence, STEMI mortality, mean age at STEMI presentation and region-specific life expectancy were used. Incorporating the value of a statistical life year and multiplying it by YLL gives a monetary estimation of the change of the burden of STEMI in the different reperfusion strategies.[19] For the burden of disease from morbidity, disability weights to indicate the loss of perfect health due to the disease were used. For a STEMI patient treated with pPCI, we found the disability weight to be 24%, and for thrombolysis 27%.[20]

The basis for the quantification of the health and socioeconomic impact of the SFL initiative are the expected or observed clinical outcomes with increased numbers of timely STEMI admissions, increased numbers of pPCI, and the reduction in mortality and morbidity. Those outcomes are then compared to a baseline scenario, assuming that the SFL initiative did not take place and that treatment patterns, morbidity and mortality remain unchanged. The difference of direct healthcare costs including fixed costs and the savings in indirect costs over the region-specific observation period gave the quantified net societal benefit of a treatment strategy in general. Subtracting the net benefit of the baseline scenario from the net benefit of the SFL initiative scenario, finally, gives the incremental benefit as a measure of the quantified socioeconomic impact of the SFL initiative.

Furthermore, the impact of the SFL initiative on the reduction of the burden of disease caused by STEMIs is quantified by the difference in years of life lost times the value of a statistical life year between the baseline and SFL scenario.

See the Supplementary Material Table S1 for details on the input variables and Supplementary Material Table S2 for details on the output metrics of the SFL economic model and how they were calculated.

Model regions

The four model regions for which the results are presented are Romania, Portugal, the Basque Country, Spain and the Kemerovo region in the Russian Federation.

The annual STEMI incidence in the 19.7 m Romanian citizens is estimated at 1040 patients per million people. In 2010, pPCI was provided by 10 hospitals and 35 interventional cardiologists. Beside the efforts to increase pPCI reimbursement, access to pPCI facilities, public awareness and the training of a sufficient number of interventional cardiologists were major challenges.[7,10] The data for the health economic model were provided by the Romanian

ST-Elevation Myocardial Infarction (RO-STEMI) registry and the health authorities.[7]

In 2011, Portugal, had a population of 10.6 m citizens. In 2011, 24/7 pPCI services were provided by 18 PCI centres. As only 23% of STEMI patients were admitted to hospital a special focus was put on raising public awareness, beside efforts to overcome barriers in access to pPCI centres.[10] Input data came from the Portuguese Registry of Acute Coronary Syndromes (ProACS) and the database of the central administration of the health system (ACSS).[21]

The STEMI network of the Basque Country covers 0.6 m citizens. One hospital with five interventional cardiologists provides 24/7 pPCI services for 950 STEMIs per million population per year.[9,10] Clinical and cost data came from regional hospital registries and health authorities.

A total of 2.7 m citizens live in the Kemerovo region, located in north-east of the Russian Federation. In 2011, the Siberian STEMI incidence was around 1140 cases per million population, but up to 84% did not receive pPCI or reperfusion therapy at all. One pPCI centre provided 24/7 services. In 2012, the principles of the SFL initiative were implemented with convincing results. For this region, input parameters came from local registries and health authorities.

Results

The SFL economic model was adapted for four model regions (Romania, Portugal, Basque County, Kemerovo) to evaluate its applicability as well as the health and socioeconomic changes initiated by the SFL initiative and their partners in charge. Preliminary findings were reported previously.[7,9,10] Table 1 presents the results in detail, whereas Figure 2 displays the increase in the numbers of pPCI per million population in the four model regions. Figures 3(a)–(d) display the development of the incremental direct, indirect and net costs, respectively as well as the cumulated net cost savings and the lives saved in the SFL scenario compared to the baseline scenario.

For Romania, the model included the whole country and assessed changes between the years 2009–2014. Based on the developed programme the number of pPCIs was increased from 136 to 434 per million population, while mortality was reduced by 10%. This was mainly achieved by opening new catheterization laboratories, quadrupling the number of interventional cardiologists, increasing the reimbursement of the pPCI procedures, and introducing telemedicine facilities on more than 800 ambulances. This resulted in an increase of timely hospital admissions (<12 h after symptom onset) for up to 60% of all STEMI patients and pPCI rates of 60% of all timely admitted patients. All these changes led to an increase of direct healthcare costs by 23% over the observation period compared to the baseline scenario, including the substantial investments of 26.5 m USD. The 6% decrease in loss of productivity, amounted to a net cost reductions of 40 m USD.

For Portugal, the economic model also included the entire country, measuring data from 2010–2013. At the start of the SFL initiative in 2010, the number of pPCIs in STEMI patients was 264 per million population and was increased to 340 per million population by 2013. The public awareness campaign contributed with a 22% increase of timely admissions. The net result of these improvements was a reduction of mortality of 414 lives and nearly 45.6 m USD savings in labour productivity losses. This was achieved by increasing the number of trained interventional cardiologists, while the overall number of catheterization laboratories was actually reduced. Compared to the baseline scenario, direct healthcare costs attributable to the increased pPCI numbers rose by 8%. The burden of disease decreased by almost 150 m USD.

For Spain, the Basque Country region was selected as model region, as the data pool was the most consistent compared to other areas. Over the course of the SFL initiative, the initial number of pPCIs per million population was estimated at 254 in 2012 and grew to 341 by 2015, mainly driven by a 15% increase in timely admissions and a 7% higher pPCI rate. Significant reductions in mortality of 3% as well as cost savings of 3 m USD were achieved in an area of less than 0.7 m people, without building new catheterization laboratories or training additional interventional cardiologists. Nevertheless direct healthcare costs were increased by 10%. But still, a net cost reduction was achieved with a 2% decrease in labour productivity losses.

For Russia, we focused on the Kemerovo region starting from 2011, at the onset of the SFL initiative, until 2015. The increase of pPCI numbers from 78 to 315 per million population, saved 387 lives and decreased mortality by 9%. During this period, there were substantial investments of 1.8 m USD to build one catheterization laboratory, train four interventional cardiologists and improve the emergency medical services transportation system. This lead to an increase in direct healthcare costs of 70% from 10 to 17 m USD over four years. However, the productivity savings due to higher rates of pPCI more than offset these investments and higher healthcare costs, resulting in net cost savings of almost 4.8 m USD per year and a 10% reduction in burden of disease.

Discussion

The collected data, clinical outcomes and results of the SFL economic model clearly demonstrate the significant reduction in mortality in patients with STEMI, as well as labour productivity losses and the burden of disease achieved by the joint efforts of the SFL initiative and their local partners. These benefits resulted from an increase in the number of STEMI patients treated with pPCI, mostly driven by increased pPCI capacities. But as shown for the Basque Country, other interventions are at least as important to enhance timely access to pPCI.

Table 1. Comparison of measures and outcomes before and after the Stent for Life (SFL) initiative in four model regions and comparison of the cumulated numbers of the baseline scenario simulating the status quo and the SFL scenario integrating attributable changes.

	Romania 2009–2014			Portugal 2010–2013			Basque Country, Spain 2012–2015			Kemerovo Region, Russian Federation 2011–2015		
Comparison of changes before and after the SFL initiative												
	Pre-SFL	Post-SFL	Δ in %	Pre-SFL	Post-SFL	Δ in %	Pre-SFL	Post-SFL	Δ in %	Pre-SFL	Post-SFL	Δ in %
Primary PCI per m population	136	434	219	264	340	29	254	341	34	78	315	303
Catheterization laboratories	10	16	100	32	28	−13	1	1	0	1	2	100
Interventional cardiologists	22	92	318	73	79	8	5	5	0	10	14	40
Timely hospital admission rates	55%	60%	9	32%	39%	22	34%	39%	15	48%	62%	44
Primary PCI as treatment strategy rates	20%	60%	300	75%	88%	17	91%	97%	6	12%	39%	225
Comparison of the cumulated numbers of the baseline- and the SFL scenario												
	Baseline scenario	SFL scenario	Δ in %	Baseline scenario	SFL scenario	Δ in %	Baseline scenario	SFL scenario	Δ in %	Baseline scenario	SFL scenario	Δ in %
Mortality by STEMI	21,841	19,645	−10	10,553	10,139	−4	620	601	−3	4132	3745	−9
Direct costs in m USD	184	227	23	98	106	8	10	11	10	10	17	70
Labour productivity loss in m USD	1422	1338	−6	1905	1852	−3	162	158	−2	159	148	−7
Net costs in m USD	1606	1565	−3	2003	1958	−2	172	169	−2	169	164	−3
Burden of disease in m USD	6248	5587	−11	3724	3575	−4	289	280	−3	620	558	−10

m: million; PCI: percutaneous coronary intervention; STEMI: ST-elevation myocardial infarction; USD: US dollars.
Pre-SFL: baseline scenario before the start of the SFL initiative; post-SFL: results after the SFL programme; Δ: percentage difference between values; timely hospital admission rates: rate of patients with STEMI being admitted to a hospital <12 h after symptom onset of the STEMI population; primary PCI as treatment strategy rates – percentage of all timely admitted hospitals undergoing primary PCI as first treatment; direct costs include variable and fixed costs over the observation period; net societal costs of STEMI: sum of direct costs and labour productivity losses.

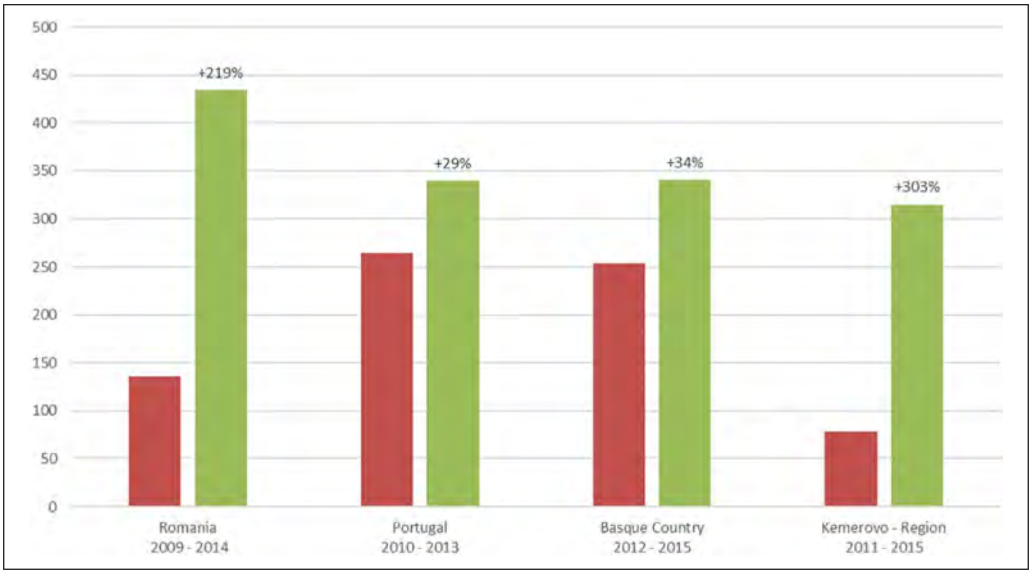

Figure 2. Numbers of primary percutaneous coronary intervention (PCIs) per million population at the start and after the program of the Stent for Life (SFL) initiative and their relative change.
Pre-SFL: at the start of the SFL initiative; Post-SFL: after the SFL initiative.

The SFL economic model is a generic model constructed to be applicable to a wide variety of regions and healthcare settings. The noteworthiness of this model is that it not only evaluates the perspective of the healthcare system as used in cost-utility analysis or health-technology assessments, but also incorporates the socioeconomic perspective, e.g. the reduction of productivity losses or the burden of disease.[22,23] The decision tree model reflects the real-life situation.[3] The data on pPCI rates and outcomes of hospitalised patients mostly came from regional or national STEMI registries. Whereas those data are quite reliable, numbers of untreated and non-hospitalised patients and therefore the real STEMI incidence had to be estimated.

Regarding direct costs, the determination of fixed costs strongly depends on the identification and pricing of essential investments in the infrastructure. The direct variable costs depend on the country specific reimbursements for healthcare services, drugs and devices as well as estimation on the rate of healthcare utilisation. Furthermore, the impact on direct costs could be underestimated as the increase in PCI capacities might have triggered further direct costs, e.g. in patients with non-STEMIs or stable coronary artery disease newly treated with PCI.

The modelling of indirect costs must rely on several assumptions. The used human capital approach compared to the friction cost method rather overestimates indirect costs, but is still the one most widely accepted.[24] Basing measurement of loss of productivity on average annual income is the more commonly used approach, but definitions and capture methods vary. The decision to use the per capita GDP instead arises from the fact that it is published for nearly every country and calculated with a uniform method by the World Bank. Furthermore, it is an indicator of an individual's productivity and not only income and, most importantly, it enhances the applicability of the SFL economic model to different regions.[14,25] The assumptions to calculate years of life lost and costs due to morbidity were chosen conservatively, thus rather underestimating costs as, for example, time back to work varies strongly between countries.[20,26–28]

Altogether, the SFL economic model is a generic model in which the input of local data is preferred, if available. If not, missing input variables are estimated using conservative assumptions. For the four model regions, the model has shown its applicability and the process with data collection, validation, discussion and interpretation of results in collaboration with local experts led to reliable results.

The multimodal approach to enhance pPCI rather than thrombolysis in patients with STEMI developed by the SFL initiative and their local partners, most importantly, saved lives by the reduction of STEMI-associated mortality. In all model regions after this approach, absolute mortality rates were reduced by between 3.1% and 10.1%. This relative risk reduction is lower than that reported in randomised controlled trials comparing pPCI and thrombolysis.[29,30] In comparison to these trials with either pPCI or thrombolysis, our present data reflect a change in the distribution of treatment patterns with an increase of pPCI per million population of between 29% and 303%. The growth rates were higher with lower starting points. To achieve these results a multimodality approach was mandatory. This involved the increase of pPCI capacity by building new catheterization laboratories, training of additional interventional cardiologists, as well as providing new protocols for the accident and emergency services. The results of the Basque Country with increased numbers of pPCI and a reduction in mortality were achieved with the same number of catheterization

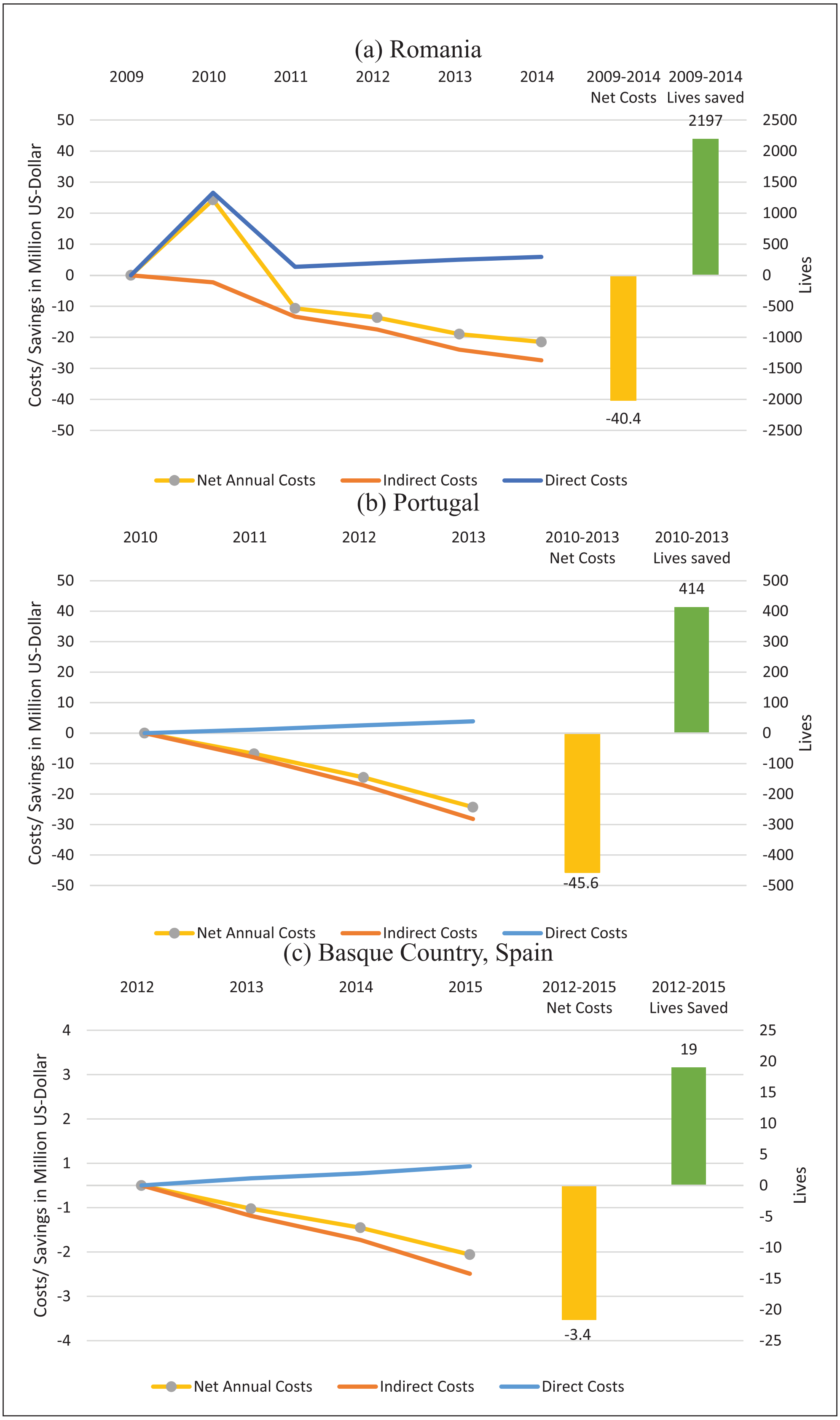

Figure 3. (Continued)

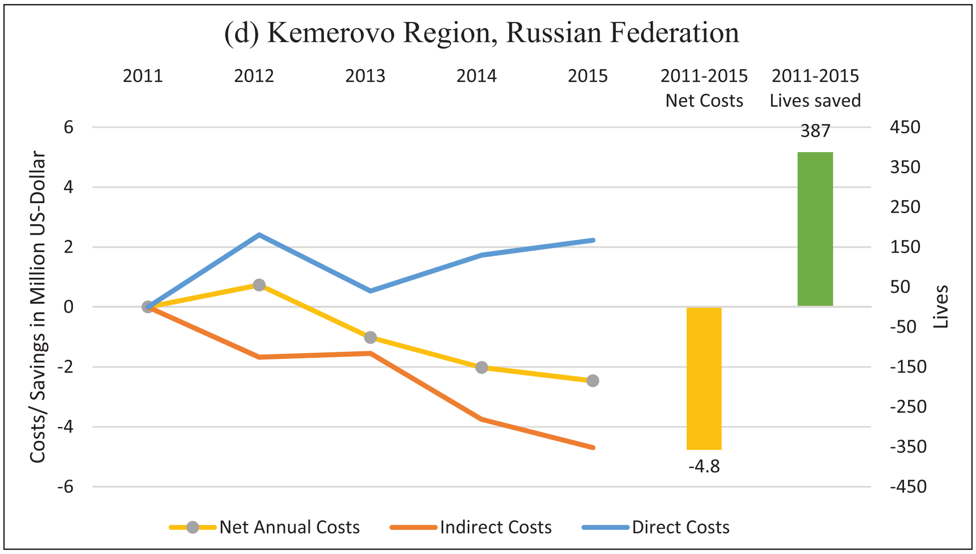

Figure 3. Incremental direct, indirect, annual, and cumulated net costs of the Stent for Life scenario compared to the baseline-scenario, as well as the incremental cumulated number of lives saved for (a) Romania, (b) Portugal, (c) Basque Country, Spain and (d) the Kemerovo region, Russian Federation, respectively.

Costs are displayed in millions of US dollars; positive costs stand for additional spending, negative ones for savings; net costs are the difference between direct and indirect costs per annum and cumulated, respectively; direct costs include variable and fixed costs (e.g. investments) – Portugal and the Basque Country were without substantial fixed costs; Lives saved are the cumulated incremental numbers of lives saved in the Stent for Life scenario compared to the baseline scenario.

laboratories and cardiologists. This demonstrates that the multimodal efforts of the SFL initiative in reducing time to first medical contact by public awareness campaigns and time of first medical contact to balloon by improved pre-hospital processes are at least as important in enhancing pPCI rates, hence giving better outcomes.[31]

Applying the SFL economic model to the four model regions, the increase of pPCI rates led to an increase of direct costs by 8% to 70%, caused by investments in the infrastructure and increased variable costs due to higher treatment costs with pPCI compared to thrombolysis. The relative increase also depended on the pPCI rate starting point. In the same time, the indirect societal costs due to productivity losses decreased substantially by 2.5% to 6.9%. Comparing the cumulated numbers of the baseline scenario and the changes initiated by the SFL programme with an observed increase in direct and reduction in indirect costs, a clear net cost benefit for all four model regions was shown, which is in accordance with published literature.[20,22,23] With a reduction of mortality and morbidity, the burden of disease in the population caused by STEMIs could be reduced.

Limitations

The SFL health economic model, like every model, strongly depends on the quality and validity of the input data. Most of the data were obtained from local STEMI registries and health authorities, but for some, assumptions had to be made based on the expertise of local stakeholders. For all assumptions, as explained above, a conservative approach was used in order not to overestimate the socioeconomic benefits of enhanced pPCI rates in patients with STEMI.

Conclusion

The joint structured and multimodal programme in collaboration with professional societies, health authorities, health service providers and the SFL initiative to enhance pPCI rates in STEMI patients saves lives. The SFL economic model has proved its applicability in four model regions and has demonstrated that socioeconomic savings clearly outweigh the increase of healthcare investments and costs.

Acknowledgements

The authors would like to thank Zuzana Kaifoszova and Isabelle Tran for their support of the project as project managers of the ‘Stent for Life/ Stent – Save a Life’ initiative.

Conflict of interest

The authors declare that there is no conflict of interest. Adam Yoculan and Alex Au-Yeung are Medtronic employees and were involved in the analysis of the data and the design of the health economic model. Although the employees of Medtronic did not have any financial interest in this article, Medtronic, like other companies offering interventional products, may benefit from increased PCI numbers in STEMI, non-STEMI and stable coronary artery disease patients, but there was no biasing influence of Medtronic on the design, input parameters or results of the study, especially as all input parameters were provided by local stakeholders independent from Medtronic.

Funding

The study was funded by the 'Stent for Life/Stent – Save a Life' initiative (www.stentsavealife.com). This initiative is supported by Medtronic, Terumo, Biotronik and Biosensors. The study was furthermore supported by the Science Foundation Ireland Research Professorship Award (Grant Number 15/RP/2765).

References

1. World Health Organization (WHO). The top 10 causes of death, http://www.who.int/mediacentre/factsheets/fs310/en/ (2017, accessed 28 February 2017).
2. Leal J, Luengo-Fernandez R, Gray A, et al. Economic burden of cardiovascular diseases in the enlarged European Union. *Eur Heart J* 2006; 27: 1610–1619.
3. Steg PG, James SK, Atar D, et al. ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. *Eur Heart J* 2012; 33: 2569–2619.
4. Widimsky P, Wijns W, Fajadet J, et al. Reperfusion therapy for ST elevation acute myocardial infarction in Europe: Description of the current situation in 30 countries. *Eur Heart J* 2010; 31: 943–957.
5. Widimsky P, Fajadet J, Danchin N, et al. 'Stent 4 Life' - targeting PCI at all who will benefit the most. *EuroIntervention* 2009; 4: 555–557.
6. Kristensen SD, Laut KG, Fajadet J, et al. Reperfusion therapy for ST elevation acute myocardial infarction 2010/2011: Current status in 37 ESC countries. *Eur Heart J* 2014; 35: 1957–1970.
7. Benedek I, Gyongyosi M and Benedek T. A prospective regional registry of ST-elevation myocardial infarction in Central Romania: Impact of the Stent for Life initiative recommendations on patient outcomes. *Am Heart J* 2013; 166: 457–465.
8. Kaifoszova Z, Kala P, Alexander T, et al. Stent for Life initiative: Leading example in building STEMI systems of care in emerging countries. *EuroIntervention* 2014; 10: T87–T95.
9. Kaifoszova Z, Kala P and Wijns W. The Stent for Life initiative: Quo vadis? *EuroIntervention* 2016; 12: 14–17.
10. Kristensen SD, Fajadet J, Di Mario C, et al. Implementation of primary angioplasty in Europe: Stent for Life initiative progress report. *EuroIntervention* 2012; 8: 35–42.
11. Kristensen SD, Laut KG, Fajadet J, et al. Reperfusion therapy for ST elevation acute myocardial infarction 2010/2011: Current status in 37 ESC countries. *Eur Heart J* 2017; 35: 1957–1970.
12. Philips Z, Ginnelly L, Sculpher M, et al. Review of guidelines for good practice in decision-analytic modelling in health technology assessment. *Health Technol Assess* 2004; 8: iii–iv, ix–xi, 1–158.
13. Johnston K, Buxton MJ, Jones DR, et al. Assessing the costs of healthcare technologies in clinical trials. *Health Technol Assess* 1999; 3: 1–76.
14. Bebrysz M, Wladysiuk M, Fedyna M, et al. Calculating indirect costs - differences caused by various approaches to unit costs. Results of Move to Work Study (M2W). *Value Health* 2014; 17: A773.
15. Widimsky P, Budesinsky T, Vorac D, et al. Long distance transport for primary angioplasty vs immediate thrombolysis in acute myocardial infarction. Final results of the randomized national multicentre trial – PRAGUE-2. *Eur Heart J* 2003; 24: 94–104.
16. Svensson L, Aasa M, Dellborg M, et al. Comparison of very early treatment with either fibrinolysis or percutaneous coronary intervention facilitated with abciximab with respect to ST recovery and infarct-related artery epicardial flow in patients with acute ST-segment elevation myocardial infarction: The Swedish Early Decision (SWEDES) reperfusion trial. *Am Heart J* 2006; 151: 798.e1–7.
17. Murray CJ, Vos T, Lozano R, et al. Disability-adjusted life years (DALYs) for 291 diseases and injuries in 21 regions, 1990–2010: A systematic analysis for the Global Burden of Disease Study 2010. *Lancet* 2012; 380: 2197–2223.
18. Moran AE, Forouzanfar MH, Roth GA, et al. The global burden of ischemic heart disease in 1990 and 2010: The Global Burden of Disease 2010 Study. *Circulation* 2014; 129: 1493–1501.
19. Miller TR. Variations between countries in values of statistical life. *Journal of Transport Economics and Policy* 2000; 34: 169–188.
20. Aasa M, Henriksson M, Dellborg M, et al. Cost and health outcome of primary percutaneous coronary intervention versus thrombolysis in acute ST-segment elevation myocardial infarction-Results of the Swedish Early Decision reperfusion Study (SWEDES) trial. *Am Heart J* 2010; 160: 322–328.
21. Timoteo AT and Mimoso J. Assessment of quality performance measures in patients with acute coronary syndromes: Data from the Portuguese Registry of Acute Coronary Syndromes (ProACS), a nationwide registry. *J Eval Clin Pract* 2018; 24: 439–446.
22. Hartwell D, Colquitt J, Loveman E, et al. Clinical effectiveness and cost-effectiveness of immediate angioplasty for acute myocardial infarction: Systematic review and economic evaluation. *Health Technol Assess (Rockv)* 2005; 9(17): 1–99.
23. Regueiro A, Bosch J, Martin-Yuste V, et al. Cost-effectiveness of a European ST-segment elevation myocardial infarction network: Results from the Catalan Codi Infart network. *BMJ Open* 2015; 5: e009148.
24. Jo C. Cost-of-illness studies: Concepts, scopes, and methods. *Clin Mol Hepatol* 2014; 20: 327–337.
25. World-Bank. GDP per capita (current US$), http://data.worldbank.org/indicator/NY.GDP.PCAP.CD?view=chart(2017, accessed 05 May 2017).
26. Kovoor P, Lee AK, Carrozzi F, et al. Return to full normal activities including work at two weeks after acute myocardial infarction. *Am J Cardiol* 2006; 97: 952–958.
27. Babic Z, Pavlov M, Ostric M, et al. Re-initiating professional working activity after myocardial infarction in primary percutaneous coronary intervention networks era. *Int J Occup Med Environ Health* 2015; 28: 999–1010.
28. Jezewski T, Konopa B, Tarchalski J, et al. Comparison of clinical results and life quality after myocardial infarction therapy with primary percutaneous coronary intervention and fibrinolytic agents. *Pol Arch Med Wewn* 2009; 119: 26–31.
29. Keeley EC, Boura JA and Grines CL. Primary angioplasty versus intravenous thrombolytic therapy for acute myocardial infarction: A quantitative review of 23 randomised trials. *Lancet* 2003; 361: 13–20.
30. Boersma E. Does time matter? A pooled analysis of randomized clinical trials comparing primary percutaneous coronary intervention and in-hospital fibrinolysis in acute myocardial infarction patients. *Eur Heart J* 2006; 27: 779–788.
31. Regueiro A, Rosas A, Kaifoszova Z, et al. Impact of the 'ACT NOW. SAVE A LIFE' public awareness campaign on the performance of a European STEMI network. *Int J Cardiol* 2015; 197: 110–112.