Economic Evaluation Study

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Simulated versus physical bench tests

The economic evaluation of the InSilc platform for designing, developing, and assessing vascular scaffolds

Pierpaolo Mincarone, PhD[a,*], Antonella Bodini, PhD[b], Saverio Sabina, MSc[c], Riccardo Colella, PhD[c], Maria Rosaria Tumolo, MSc[a], Martin Fawdry, Eng[d], Dimitrios I. Fotiadis, PhD[e,f], Carlo Giacomo Leo, PhD[c]

Abstract

Background: In silico medicine allows for pre-clinical and clinical simulated assessment of medical technologies and the building of patient-specific models to support medical decisions and forecast personal health status. While there is increasing trust in the potential central role of in silico medicine, there is a need to recognize its degree of reliability and evaluate its economic impact. An in silico platform has been developed within a Horizon 2020-funded project (In-Silc) for simulations functional to designing, developing, and assessing drug-eluting bioresorbable vascular scaffolds.

The main purpose of this study was to compare the costs of 2 alternative strategies: the adoption of In-Silc platform versus the performance of only physical bench tests.

Methods: A case study was provided by a medical device company. The values of the model parameters were principally set by the project partners, with use of interviews and semi-structured questionnaires, and, when not available, through literature searches or derived by statistical techniques. An economic model was built to represent the 2 scenarios.

Results: The InSilc strategy is superior to the adoption of physical bench tests only. Ceteris paribus, the costs are 424,355€ for the former versus 857,811€ for the latter.

Conclusions: In silico medicine tools can decrease the cost of the research and development of medical devices such as bioresorbable vascular scaffolds. Further studies are needed to explore the impact of such solutions on the innovation capacity of companies and the consequent potential advantages for target patients and the healthcare system.

Abbreviations: BVS = bioresorbable vascular scaffolds, CAD = computer aided design.

Keywords: bioresorbable vascular scaffolds, costs and cost analysis, in silico medicine, in silico testing, stents

1. Introduction

Computer modeling, simulation, and visualization of biological and medical processes applied in the diagnosis, treatment, or prevention of a disease is commonly referred to as in silico medicine.[1] In silico medicine allows the building of virtual patient-specific models to support medical decisions, perform virtual pre-clinical and clinical assessments of medical technologies, forecast personal health status,[2] and to serve as an efficient

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[a] *National Research Council, Institute for Research on Population and Social Policies, Research Unit of Brindisi, Brindisi,* [b] *National Research Council, Institute for Applied Mathematics and Information Technologies "Enrico Magenes", Branch of Milan, Milan,* [c] *National Research Council, Institute of Clinical Physiology, Branch of Lecce, Lecce, Italy,* [d] *Boston Scientific Ltd., Galway, Ireland,* [e] *Unit of Medical Technology and Intelligent Information Systems, Department of Materials Science and Engineering, University of Ioannina,* [f] *Institute of Molecular Biology and Biotechnology of the Foundation for Research and Technology Hellas, Department of Biomedical Research, Ioannina, Greece.*

[*] *Correspondence: Pierpaolo Mincarone, National Research Council, Institute for Research on Population and Social Policies, Research Unit of Brindisi, Brindisi, Italy. c/o ASL Brindisi – P.zza Di Summa – 72100 Brindisi, Italy (e-mail: pierpaolo.mincarone@irpps.cnr.it).*

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tool for technical[3,4] and nontechnical[5] training in healthcare. Due to this broad applicability, the interest around in silico medicine is growing and its global market is expected to increase rapidly and, with specific reference to drug discovery, it is anticipated to grow from $2.09 billion in 2018 to $7.92 billion by 2029.[6]

Within the Horizon 2020 framework programme, the European Union has funded projects to develop this research topic, among them In silico trials for drug-eluting bioresorbable vascular scaffolds (BVS) development and evaluation (InSilc). This is a project with the ambition to develop an in silico platform for simulations in designing, developing, and assessing drug-eluting BVSs.[7] The InSilc project was planned to design and develop in-silico clinical trials and integrate in-silico models for obtaining quick and informed answers to several "What if" scenarios. The InSilc platform includes multiscale models to predict acute, short-, long-term performances of the scaffold. The platform can be used for the simulation of the mechanical performance of the stent, its deployment, the fluid dynamics (in the micro and macro scale), the drug-delivery, the BVS degradation, and the myocardial perfusion. Moreover, the platform has the ambition to support organizations involved in the development of BVSs. Even if welcomed with the greatest enthusiasm for its expected superiority over previous generations' drug-eluting stents and bare metal stents, BVSs have been proven to require a delicate mixture of technologies to overcome the safety issues that emerged after clinical studies.[8] BVS research and development is one of the processes where in silico simulations could provide a great help to increase the safety of patients, speed up the time to market, and reduce overall costs.

The first step of BVS development process is the execution of bench tests to evaluate their mechanical and physical properties.

The main purpose of this study was to compare the costs of 2 alternative strategies to perform bench tests: the adoption of a platform for designing, developing, and assessing BVSs (InSilc strategy) versus the performance of only physical bench tests.

2. Methods

The current study was reported according to the Consolidated Health Economic Evaluation Reporting Guidelines (CHEERS).[9] Ethical approval was not necessary as no human data were considered.

2.1. Information sources

A detailed process analysis was performed in cooperation with partners of the InSilc project to model the investigated alternatives. Model parameters were principally requested from project partners by using interviews and semi-structured questionnaires. Among them, Boston Scientific Limited (BSL), a company that develops coronary vascular scaffolds, provided a case study to derive data of processes and costs. Due to the confidentiality that characterizes some of the data on the BVS development process we adopted statistical models to fill in the information gap.

2.2. Setting and location

Bench tests are used to evaluate a device's mechanical and physical properties. These tests can provide insight to help guide safe delivery, deployment, and key product performance properties, such as crossing profile, recoil, post-dilatation overexpansion, and radial strength of the scaffold and stent.[10] Since vascular scaffolds have to be compliant with the specificities of the stenotic area to be treated, several configurations in terms of length and diameter are tested for each model design. Bench tests can determine the evolutionary process of a stent design, providing input for a subsequent updated or refined version. The bench tests follow recognized standards, such as ISO 25539-1 (Cardiovascular implants—Endovascular devices—Part 1: Endovascular prostheses)[11] or ISO 25539-2 (Cardiovascular implants—Endovascular devices—Part 2: Vascular stents),[12] and are needed to achieve regulatory certification for placement on the market.[13] The application of in silico medicine solutions in this scenario, that is, simulated bench tests, may help companies save time and costs (e.g., reduction in tested and destroyed samples) during the development phase even if, to date, they cannot replace physical tests when executed for regulatory purposes.

The perspective was that of a medical device company.

2.3. The economic model

The InSilc platform is currently able to perform 16 tests, a subset of the total suite of bench tests required by ISO 25539-1[11] and ISO 25539-2.[12] In practice, these tests do not follow a pre-specified order, but are driven by specific questions arising during the stent development process. Some tests are executed more often than others, as they are connected to critical design aspects. We supposed that their demand follows the frequency of occurrence that we derived from the project partners' experiences. Tests were ordered following the supposed occurrence and, when their results came from a single computer simulation, were grouped accordingly (see Table S1, Supplemental Digital Content, http://links.lww.com/MD2/A251).

The stent development process usually requires the design of several sub-versions that evolve as long as new evidence is obtained from bench tests. Based on internal interviews, 10 sub-versions are typically produced, with an attrition rate of 70% and, if the tests of a specific sub-version are interrupted because of failure, the subsequent sub-version has a higher probability of passing more tests.

A detailed reconstruction of the tests performed by each sub-version in the case study was not possible from the available data. For this reason, an ad hoc simulation model was built with the following assumptions:

a) The tests are executed consecutively.
b) In both strategies, the first tests to be performed are those included in the InSilc platform (in fact, due to their quicker execution, in silico tests allow the stent developers to promptly obtain an overall idea of performance with respect to physical tests).
c) InSilc virtual tests are executed in consideration of the grouping reported previously and have been considered as 10 macro tests (see Group in Table S1, Supplemental Digital Content, http://links.lww.com/MD2/A251). In contrast those tests, when executed as physical tests, are considered independent and distinct.
d) Each sub-version is an improvement of the previous one, with a higher probability of passing more tests before being abandoned for failure (unless it is the one that passes all the tests). The number of passed tests grows slightly in passing

from one initial sub-version to the next, but then grows significantly in more advanced sub-versions.

e) If a sub-version successfully passes all InSilc platform virtual tests, it continues to be tested using the suite of physical bench tests not covered by InSilc. Sub-versions that successfully pass all these physical tests have to execute confirmatory physical tests (the ones previously simulated through InSilc) for regulatory purposes.
f) Each test is executed for the same number of configurations for each sub-version (data derived from the case study).
g) Ten sub-versions have been considered out of which 2 or 3 pass the bench testing phase (in line with the previously reported average 70% attrition rate of the bench testing phase). This is possible because, based on the adopted evolutionary approach, the industry does not necessarily stop its research at the first model passing all the bench tests, but can further refine the model.
h) Based on the qualitative judgement expressed in a semi-structured questionnaire by the project partners (engineers and experts in bioinformatics) involved in module validation, the InSilc simulations are considered perfect mimics of real tests.

According to model assumption d), the number of tests performed by each sub-version was considered to follow an exponential growth. In order to recognize both the non-numerical nature of increasingly labeled sub-versions and the non-deterministic degree of subsequent improvements, a random noise was added to the exponential growth. For each sub-version, the number of passed tests as determined by a suitable exponential function was randomly modified by adding a random integer value from the arbitrary interval –3 to 3. With reference to the number of tests passed by the first sub-version, it was assumed that at least one test is always passed. Moreover, that number was assumed to be a Poisson random variable, with a number of expected performed tests equal to 6, hereafter denoted by Po(6). This means that in 95% of cases, the number of tests performed by the first sub-version was ≤ 10.

One thousand simulations were carried out to consider the process variability. For each simulation:

1. the number N_1 of performed tests by sub-version 1 was extracted from the Po(6) distribution;
2. the exponential function $f(\blacksquare|N_1)$ passing through the points (1, N_1) and (8,69) was determined (69 was an arbitrary chosen number as any other would have not substantially changed the analysis); and
3. for each sub-version k, the number of performed tests was computed as $f_r(k|N_1)+n_k$ where $f_r(k|N_1)$ is the rounded value of $(f|kN_1)$ and n_k is an integer value randomly chosen between –3 and 3 according to the uniform discrete distribution. For $k=8$, the value $f_r(8|N_1)+n_g$ was censored to 69.

A few instances of the simulation process are shown in Fig. 1.

The simulated number of performed tests was used to feed the economic model.

Starting with the data of the considered case study, a detailed reconstruction of the costs of the physical bench tests included in the InSilc platform was carried out. In each simulated scenario, the cost of performing the tests not simulated by the InSilc platform was equal for the 2 compared strategies and therefore was not considered.

The time needed to perform physical bench tests included in the InSilc platform is one of the elements needed to perform the economic evaluation. The time needed to test a single device was derived by the case study and is reported, together with the number of devices and tested configurations, in Table S2, Supplemental Digital Content, http://links.lww.com/MD2/A252.

In the calculation of resources, we assumed that: the technicians were already fully trained and the test methods were already validated; the fixturing and equipment were calibrated and maintained; and the costs of consumables, such as sheaths, guidewires, and overheads, were estimated as 20% of the direct costs.

Parameters for calculations are reported in Table S3, Supplemental Digital Content, http://links.lww.com/MD2/A253. The number of the tested devices and the total time a person needed to perform each bench test were estimated, starting with the case study.

The cost of each single test is reported in Table S4, Supplemental Digital Content, http://links.lww.com/MD2/A254.

With respect to the price structure of the InSilc platform, the following components were defined within the InSilc project: the price for creating a model of the stent to be tested and the price for executing the bench tests. In the former case, there are 3 possibilities with different prices: it is necessary to derive the stent model from a real physical stent (5000€), a computer aided design (CAD) representation exists (1000€), or only refinements of a previously modeled stent are needed in terms of modified length and/or diameter (100€). In the latter case, several prices were defined for the different tests. The detailed definition of prices is reported in Table S5, Supplemental Digital Content, http://links.lww.com/MD2/A255. A side-by-side comparison of the real (costs) and in silico tests (prices) is proposed in Table 1.

When a CAD representation of the stent was available, all the InSilc virtual tests were lower in price, in comparison to the corresponding physical tests. On the contrary, if it is necessary to build a stent model from a physical stent, the first virtual test has to bear the greater cost of a full stent modeling and is more expensive to perform (5000€ instead of 1000€). In the latter case, physical tests were more convenient up to the third test.

We also stressed the InSilc scenario model by considering an increase in the price of the platform up to a break-even point. The price increment was proportionally applied to all the price components:

(1) price for creating a model in the absence of a CAD representation of the stent (increment × 5000€);
(2) price for creating a model starting from a CAD representation of the stent (increment × 1000€);
(3) price for refining a previously existing model with changes to length and/or diameter (increment × 100€); and
(4) price for executing a bench test (increment × P_i, where i refers to the i-th test and P_i is the price of such a test, as defined in Table 1).
(5) Finally, a sensitivity analysis was performed by considering an attrition rate of 60% and 80% (instead of 70%) and, at the same time, by varying the InSilc price (i.e., the increment parameter was varied from 100% to 500%).

3. Results

The results of the comparison between the 2 strategies are reported in Table 2. The InSilc strategy was investigated with and without the availability of a CAD model of the assessed stent model.

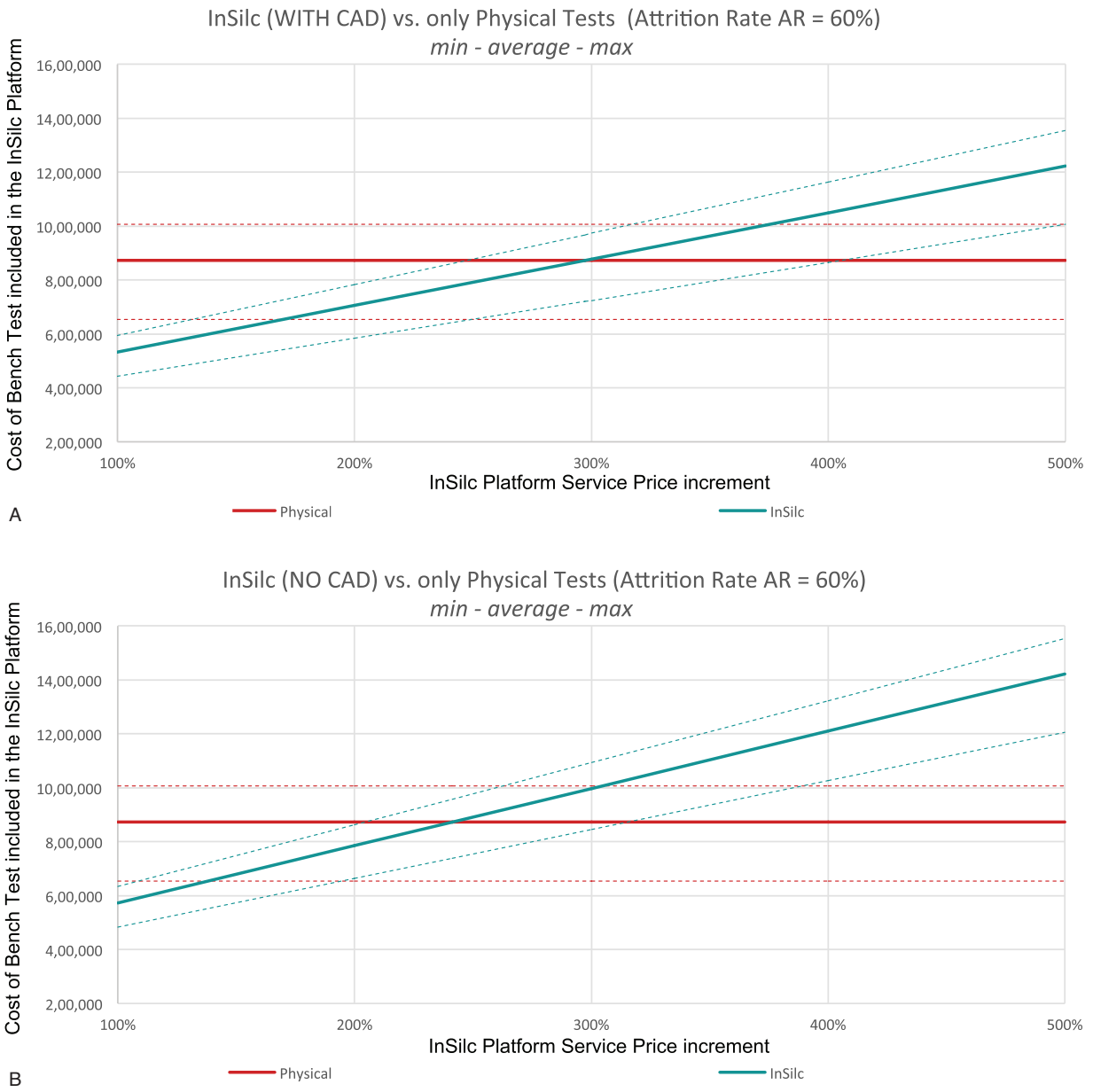

Figure 1. Number of performed bench tests for each sub-version in 5 out of 1000 simulations. The number of performed tests by sub-version 1 came from the Po (6) distribution; the number of performed tests for the first 8 versions increases according to an exponential curve. Deviations from this curve are due to a uniform random noise cut to 69 for the eighth version.

The InSilc strategy was found to always be superior to the one adopting only physical bench tests. Ceteris paribus, the costs are 424,355€ for the former (464,355 without a CAD model) versus 857,811€ for the latter. When considering the increment in the price of the InSilc platform, a break-even point was identified for increment = 355% and increment = 287%, respectively, with and without the CAD model (see Fig. 2A and B, respectively).

Through a sensitivity analysis, we considered possible variations of the attrition rate and found that the InSilc strategy is always dominant. Ceteris paribus, the costs were 532,631€ (+40,000€ in case CAD models are not available) for the InSilc strategy versus 872,907€ for only physical bench tests, in the case of a 60% attrition rate (better performing design process), and 322,304€ (+40,000€ without CAD) versus 840,013, in the case of an 80% attrition rate (less performing design process). For the 2 scenarios, a break-even point was reached with a price increase of 297% (241% without CAD) and 409% (330% without CAD), respectively, for an attrition rate equal to 60% and 80% (see Figures S1, http://links.lww.com/MD2/A249 and S2, Supplemental Digital Content, http://links.lww.com/MD2/A250).

4. Discussion

This study contributes to the growing body of work on in silico medicine that focuses on the estimation of the costs for the execution of bench tests with or without the adoption of the InSilc platform for designing, developing, and assessing BVSs. As

Table 1

Side-by-side cost/price comparison of real and InSilic bench tests.

Test ID	Group ID	Test	Cost/Price (€)	Cumulative cost/Price (€)				
			Real tests	InSilc tests (CAD)	InSilc tests (No CAD)	Real tests	InSilc tests (CAD)	InSilc tests (No CAD)
1	1	Radial force/compression	2970	2400	6400	2970	2400	6400
2	2	Three-point Bending	3252	2200	2200	6222	4600	8600
3	3	Longitudinal tensile strength	2,748	900	900	8970	5500	9500
4	4	Profile/diameter	14,160	5500	5500	23,130	11,000	15,000
5	4	Foreshortening	4200			27,330		
6	4	Dog boning	9522			36,852		
7	4	Stent-free surface area	1560			38,412		
8	4	Inflation	9948			48,360		
9	4	Recoil	8,154			56,514		
10	5	Crush resistance/crush resistance with parallel plates	2970	600	600	59,484	11,600	15,600
11	6	Local compression	2970	600	600	62,454	12,200	16,200
12	7	Flex/Kink	6258	2000	2000	68,712	14,200	18,200
13	8	Pushability	15,390	3100	3100	84,102	17,300	21,300
14	8	Trackability	11,160			95,262		
15	9	Torquability	4080	1200	1200	99,342	18,500	22,500
16	10	Radial fatigue	1392	700	700	100,734	19,200	23,200

CAD = computer aided design.

reported above, we adopted the point of view of a medical device company in this study.

While there is an increasing trust in the possibility of in silico medicine to reduce the costs of the testing process,[14] we do not have knowledge of published economic evaluations of applications similar to ours that can be seen as a first attempt to investigate possible cost reductions driven by computer simulation platforms.

Based on currently available data on both real and simulated processes, our analysis shows that, assuming equal performance of the tests, the recourse to in silico medicine tools, such as the InSilc platform, allows savings in terms of costs (about 50%).

The cost advantages of the InSilc strategy persist within the sensitivity analysis: the platform could remain competitive even with a doubling (or in some simulations even more) of its price. Specifically, as the attrition rate increases, the InSilc platform becomes more preferable. In fact, when attrition rate increases, 2 concomitant effects are registered in the InSilc strategy:

- There is an increase of defective versions, which are only tested virtually with tests also included in the InSilc platform. Cost is 19,200€ or 23,200€, respectively, with or without a CAD representation of the investigated stent, when simulated, in comparison to 100,734€ calculated for real executions (see Table 1).
- There is a reduction in passing sub-versions, that is, the ones that determine an increase of costs for the InSilc strategy due to the need for both virtual and physical testing.

Even if not quantified in our economic analysis, it is worth mentioning that, besides the reported cost saving, the platform gives the possibility to virtually test, in a very short time and with a significantly lower cost, concepts in an initial development phase and before prototype production. This could improve the exploratory phase and increase the innovation capacity of a company, with added consequent potential advantages for target patients.

The findings of our study need to be considered with care for several reasons. Some of the data from the testing process were not available and have been estimated, obviously in agreement with the collaborating industry source. The choice of the order of tests (based on the supposed occurrence from the project partners' experience) when adopting the platform does not rely on an extensive use of the platform and, hence, has been set as the most plausible. The number of sub-versions tested for each bench test comes from a real case study and not from an extensive dataset. The InSilc platform has been considered to perfectly mimic the real bench tests even in the absence of an external validation of the tool, according to the qualitative judgement collected by InSilc partners.

In silico medicine tools may decrease the cost for the development of medical devices such as BVS. The InSilc platform can simulate bench tests at approximately half of the cost of physical tests.

Besides the evaluation of costs reported in our analysis, the platform has the potential of generating substantial positive

Table 2

Descriptive statistics of the costs (€) of the 2 considered strategies.

	Min	1st quartile	Mean	2nd quartile	3rd quartile	Max	Standard deviation
Only real tests	584,004	819,272	857,811	866,142	904,739	1,005,948	66,738
InSilc strategy (no CAD)	367,868	413,268	464,355	493,352	514,752	533,502	51,223
InSilc strategy (CAD)	327,868	373,268	424,355	453,352	474,752	493,502	51,223

CAD = computer aided design.

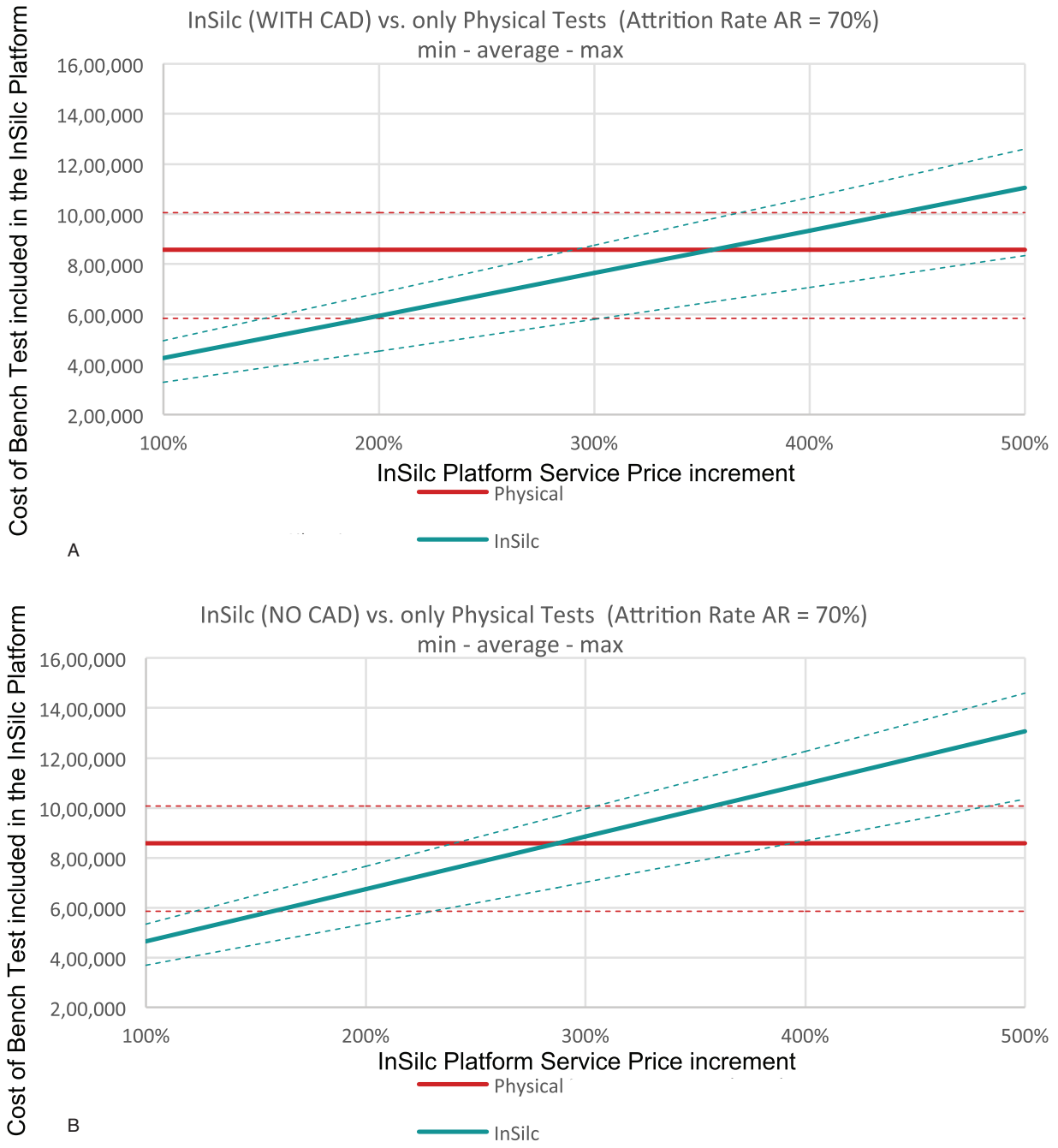

Figure 2. Identification of the break-even point. Figure 2A - Breakeven point when a CAD model of the stent is available in the InSilc strategy; Figure 2B - Breakeven point when a CAD model of the stent is not available

impact from a societal perspective (i.e., an expected reduction in the time-to-market), as well as a payer perspective (i.e., expected reduction of prices due to the Research & Development cost containment). Further analyses are needed to evaluate the impact of such a tool on clinical trials in terms of reducing costs and risks for patients.

Future research directions include the generation of enough evidence for establishing the credibility of the in-silico models and the consequent adaptation of the regulatory framework for allowing the widelspread adoption and penetration of such in-silico approaches throughout the current practise.

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Author contributions

Conceptualization: Pierpaolo Mincarone, Antonella Bodini, Carlo Giacomo Leo.
Data curation: Pierpaolo Mincarone, Antonella Bodini, Carlo Giacomo Leo.
Formal analysis: Pierpaolo Mincarone, Antonella Bodini, Saverio Sabina, Riccardo Colella, Maria Rosaria Tumolo, Martin Fawdry, Dimitrios I. Fotiadis, Carlo Giacomo Leo.
Funding acquisition: Dimitrios I. Fotiadis.
Methodology: Pierpaolo Mincarone, Antonella Bodini, Saverio Sabina, Riccardo Colella, Maria Rosaria Tumolo, Martin Fawdry, Dimitrios I. Fotiadis, Carlo Giacomo Leo.
Project administration: Carlo Giacomo Leo.
Supervision: Carlo Giacomo Leo.
Validation: Pierpaolo Mincarone, Antonella Bodini, Saverio Sabina, Riccardo Colella, Maria Rosaria Tumolo, Martin Fawdry, Dimitrios I. Fotiadis, Carlo Giacomo Leo.
Writing – original draft: Pierpaolo Mincarone, Antonella Bodini, Carlo Giacomo Leo.
Writing – review & editing: Pierpaolo Mincarone, Antonella Bodini, Saverio Sabina, Riccardo Colella, Maria Rosaria Tumolo, Martin Fawdry, Dimitrios I. Fotiadis, Carlo Giacomo Leo.

References

[1] European Commission DG CONNECT. Glossary | Shaping Europe's digital future. Available at: https://ec.europa.eu/digital-single-market/en/glossary. Accessed September 18, 2020.
[2] Insigneo Institute for in silico Medicine. In Silico Medicine: Definition, History, Institutions, Main Achievements - Insigneo. Available at: https://insigneo.org/in-silico-medicine-definition-history-institutions-main-achievements/. Accessed September 18, 2020.
[3] Harder BN. Use of simulation in teaching and learning in health sciences: a systematic review. J Nurs Educ 2010;49:23–8.
[4] McGaghie WC, Issenberg SB, Cohen ER, Barsuk JH, Wayne DB. Does simulation-based medical education with deliberate practice yield better results than traditional clinical education? A meta-analytic comparative review of the evidence. Acad Med 2011;86:706–11.
[5] Cumin D, Boyd MJ, Webster CS, Weller JM. A systematic review of simulation for multidisciplinary team training in operating rooms. Simul Healthc 2013;8:171–9.
[6] BIS Reseach. Global In-Silico Drug Discovery Market: Focus on Products, Technologies, Workflow, End Users, Country Data (17 Countries), and Competitive Landscape – Analysis and Forecast, 2018-2029; 2020. Available at: https://www.researchandmarkets.com/reports/4986909/global-in-silico-drug-discovery-market-focus-on?utm_source=dynamic&utm_medium=GNOM&utm_code=fvw8lw&utm_campaign=1352832+-+Global+In-Silico+Drug+Discovery+Market+2018-2029%3A+Focus+on+Products%2C+Technolog. Accessed October 14, 2020
[7] Karanasiou GS, Rigas GA, Kyriakidis SK, Tachos NS, Sakellarios AI, Fotiadis DI. InSilc: 3D reconstruction and plaque characterization tool. Proceedings of the Annual International Conference of the IEEE Engineering in Medicine and Biology Society, EMBS Vol 2018-July Institute of Electrical and Electronics Engineers Inc 2018;4528–4531.
[8] Cassese S, Byrne RA, Juni P, et al. Midterm clinical outcomes with everolimus-eluting bioresorbable scaffolds versus everolimus-eluting metallic stents for percutaneous coronary interventions: a meta-analysis of randomised trials. EuroIntervention 2018;13:1565–73.
[9] Husereau D, Drummond M, Petrou S, et al. Consolidated health economic evaluation reporting standards (CHEERS)-explanation and elaboration: a report of the ISPOR health economic evaluation publication guidelines good reporting practices task force. Value Heal 2013;16:231–50.
[10] Ormiston J, Motreff P, Darremont O, Webber B, Guerin P, Webster M. Bioresorbable scaffolds on the bench. EuroIntervention 2015;11:V166–9.
[11] International Organization for Standardization [ISO]. ISO 25539-1 - Cardiovascular Implants — Endovascular Devices — Part 1: Endovascular Prostheses; 2017. Available at: https://www.iso.org/standard/66925.html. Accessed September 23, 2020.
[12] International Organization for Standardization [ISO]. ISO 25539-2 - Cardiovascular Implants — Endovascular Devices — Part 2: Vascular Stents; 2012. Available at: https://www.iso.org/standard/60604.html. Accessed September 23, 2020.
[13] Council EP and E. Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices; 2017. Available at: https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:02017R0745-20170505. Accessed November 10, 2020.
[14] Avicenna Alliance. In silico Clinical Trials: How Computer Simulation will Transform the Biomedical Industry; 2015. Available at: https://avicenna-alliance.com/files/user_upload/PDF/Avicenna_Roadmap.pdf. Accessed September 18, 2020.