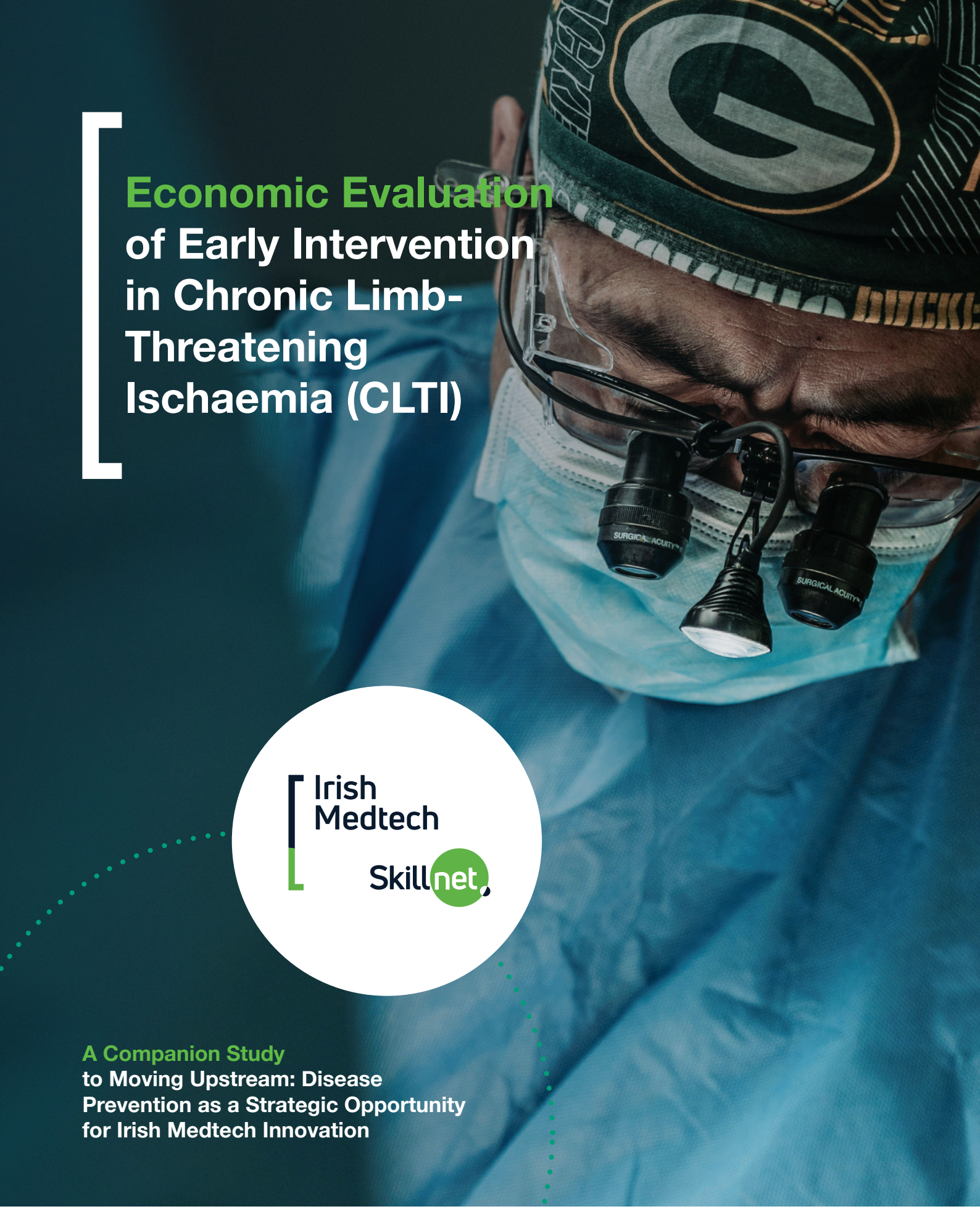

Economic Evaluation of Early Intervention in Chronic Limb-Threatening Ischaemia (CLTI)

Irish Medtech Skillnet

A Companion Study
to Moving Upstream: Disease Prevention as a Strategic Opportunity for Irish Medtech Innovation

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This companion study was developed by the WiFOR Institute in partnership with Irish Medtech Skillnet, Skillnet Ireland, and industry collaborators.

It provides the economic and clinical evidence base underpinning Moving Upstream: Disease Prevention as a Strategic Opportunity for Irish Medtech Innovation. The findings illustrate how earlier intervention in Chronic Limb-Threatening Ischaemia (CLTI) demonstrates both the health and economic value of prevention-focused medtech in the Irish context.

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ACEi	angiotensin-converting enzyme inhibitors
ARB	angiotensin II receptor blockers
CLTI	Chronic Limb-Threatening Ischaemia
CVD	cardiovascular disease
DAPT	Dual Antiplatelet Therapy
DPI	Dual Pathway Inhibition
DRG	Diagnosis Related Group
DSA	deterministic sensitivity analysis
GDP	gross domestic products
HCA	human-capital approach
HTA	health technology assessment
PAD	peripheral artery disease
PPP	Purchasing Power Parities
PSA	probabilistic sensitivity analysis
QALYs	Quality-Adjusted Life Years
R&D	research and development
RTW	Return to Work
SD	standard deviation
SE	standard error
SMEs	small and medium-sized enterprises

Executive Summary

This report serves as a Companion Guide to Moving Upstream: Disease Prevention as a Strategic Opportunity for Irish Medtech Innovation, jointly developed by Irish Medtech Skillnet, Skillnet Ireland, and the WiFOR Institute. While Moving Upstream outlines the strategic, policy, and skills dimensions of prevention-focused medtech innovation, this companion report provides the detailed economic analysis underpinning that case. Using Chronic Limb-Threatening Ischaemia (CLTI) as an exemplar, it demonstrates how early intervention can deliver measurable returns for patients, the healthcare system, and the wider economy.

Ireland is well known for its strength in medtech manufacturing and exports. However, as global healthcare systems increasingly focus on value, outcomes, and evidence, there is growing interest in how Ireland's medtech sector can expand beyond manufacturing into new areas like research, innovation, and value-based healthcare. The focus of investment in the sector must shift towards innovation, specifically, innovation that is patient-centred, driven by clinical need, and prioritised to maximise patient outcomes while delivering clear health economic value. This approach is essential to ensure that innovation genuinely serves patients, clinicians, healthcare providers, and payers. Ultimately, the sustainability and long-term impact of the medtech sector depend on its ability to address the needs of both patients and healthcare professionals in a meaningful and measurable way. To stay competitive, companies must build new skills, especially in strategic market understanding, in upstream marketing that understands health economics, system-level planning, and how diseases impact healthcare resources, budgets, society, and patients.

Moreover, health systems are under pressure due to rising healthcare costs, lack of trained clinical staff and aging population demographics. New technologies, especially those being introduced for the first time, must show both clinical benefit and cost-effectiveness to be accepted and reimbursed. In this context, health economic modelling becomes a valuable tool for medtech companies, enabling them to speak the language of decision-makers and investors and better position their technologies in an increasingly data-driven market. Before evaluating individual innovations, however, it is crucial to first understand the scale and nature of the problem they are intended to solve. Health economic modelling that quantifies the clinical and economic impact of a disease provides a foundation for identifying unmet needs, setting priorities for research, and guiding innovation strategies. This is usually the first step before assessing the value or impact of new technologies, as it highlights where targeted interventions could make the biggest difference for patients and health systems.

This report provides a practical framework for medtech companies in Ireland to support that shift. It shows how economic burden modelling, a method for measuring the costs of diseases, can help guide strategic decisions, highlight where innovation is most needed, and strengthen a company's business case for investment or market access. Germany is used as a reference point in the report. It has successfully moved from being mostly manufacturing-focused to becoming a leader in medtech innovation, research, and global health policy. Ireland now has the opportunity to do the same. Furthermore, Germany was chosen because of good documentation of the health care system and the availability of reliable databases. This data driven approach is what is first needed in order to measure the need and innovate solutions to implement and control outcomes.

To demonstrate the value of this framework, the report includes a detailed analysis of Chronic Limb-Threatening Ischaemia (CLTI) in Germany as an exemplar case study. CLTI is a severe form of peripheral artery disease that can lead to amputation, disability, and death. The findings suggested that the disease causes a major loss in quality of life, measured as nearly 160,000 Quality-Adjusted Life Years (QALYs) lost across the entire patient population over a lifetime. Furthermore, the total economic burden of CLTI in Germany is estimated to be approximatey €9 billion. This includes €5 billion in direct healthcare costs, mainly from surgeries and other non-surgical interventions, hospital stays, and follow-up care, and nearly €4 billion in productivity losses, especially from unpaid work, which often impacts women more heavily. An additional €1.6 billion is linked to complications defined as non-healing ulcers. Amputation and hospital-based revascularisation emerged as the most significant cost drivers, particularly among older and diabetic patients. These findings point to a clear need for earlier intervention and improved care strategies, particularly in high-risk populations, to reduce avoidable complications and healthcare costs.

Although this report focuses on CLTI, the same approach should be employed to identify and to study other high-impact conditions such as cardiovascular disease, diabetes, or cancer. The key message is that understanding the economic burden of a disease enables Mmdtech companies to identify where their products can make the biggest difference to patients and to communicate that value to healthcare systems, investors, and partners.

While the current analysis focuses on quantifying the present economic burden of CLTI, it also lays the foundation for identifying future opportunities. Understanding where the system bears the greatest cost today can help guide future research towards evaluating the impact of new treatment strategies, preventive interventions, and medical innovations. However, determining the extent to which these innovations could reduce the cost burden requires a different type of analysis—one that measures the societal value of specific interventions. This represents a logical next step. By

building on this baseline burden analysis, future studies can assess how targeted innovations may lead to meaningful improvements in patient outcomes and long-term savings for the healthcare system.

In summary, this report provides a clear example of how Irish Medtech companies can use health economic insights to support long-term planning, innovation, and global competitiveness. As the medtech industry evolves, the ability to demonstrate value with data will be essential, not just for success in Ireland, but to compete and lead in the global market.

1. Introduction

1.1 The role of economic modelling in shaping medtech innovation strategy

Healthcare costs are rising rapidly across the world, putting increasing pressure on national health budgets. As a result, health systems are being forced to make difficult choices about how to allocate limited resources. In this environment, payers are turning more often to health technology assessment (HTA) methods. These are used to assess the value of new health interventions—not only in terms of clinical benefit, but also in terms of cost-effectiveness, broader economic impact, and long-term value for the healthcare system. [1,2]

This focus on value is especially important for new and innovative health technologies entering the market. These products often face challenges when trying to secure reimbursement or timely market access, especially if there is not enough data to show that they offer both clinical benefits and wider economic value. [3,4]

At the same time, the medtech industry must continue to evolve. To establish itself as a global leader in medtech innovation, Ireland must ensure that both the industry and the research community become more familiar with these value assessment approaches. Ireland is already well known for its strength in medtech manufacturing and exports. [5] However, there is growing recognition that future competitiveness in the global market will depend on the ability to engage in higher-value activities, such as strategic market research, technical research and development (R&D), strategic financial planning, and a deep understanding how to assess and evaluate as well as gain access to markets.

Ireland's medtech sector includes a wide range of companies, with about 60% made up of small and medium-sized enterprises (SMEs). These SMEs are often very innovative, though some may have limited access to the structured processes or tools needed to fully develop value-based business cases. This is essential and for gaining approval from health systems. Even larger multinational companies, despite having more internal resources, are also under pressure to demonstrate the economic value of their products in health systems that are becoming more focused on evidence and value.

As this shift continues, Ireland's medtech sector will need to move beyond its current strengths in manufacturing and develop new capabilities. These include skills in health economics, outcomes research, data analysis, strategic planning, and communication with stakeholders. Building these capabilities will be essential for companies to stay competitive and grow sustainably in global healthcare markets.

1.2 The importance of measuring the health and economic consequences of a disease

Analyses of health and economic consequences of a disease play a critical role in quantifying the societal and economic impact of health conditions, but their value extends beyond policy or academic insight. For medtech companies, studies that evaluate the health and economic consequences of disease represent a powerful tool to guide strategic decisions, inform investment priorities, and enhance alignment with healthcare system needs. Moreover, understanding the health and economic impact of a disease is crucial for shaping strategies in research, market access, and commercial planning. By identifying high-burden conditions, such insights help direct R&D investments towards areas with the greatest unmet needs. They also support reimbursement discussions by providing payers and investors with real-world evidence on the costs of disease and the potential economic value of new interventions. In addition, this knowledge enables companies to refine their go-to-market strategies, ensuring that new technologies align with healthcare system priorities and cost-efficiency goals. Ultimately, by leveraging these insights, medtech companies can drive more targeted innovation, support efficient healthcare delivery, and improve engagement with key stakeholders.

The analyses of health and economic consequences of a disease offer a clearer view of where health interventions can have the most meaningful impact. This includes identifying the patient populations and therapeutic areas where unmet need is greatest and where innovative solutions can deliver both clinical and economic value. These insights not only support long-term planning by helping companies prioritise areas of high relevance but also play a crucial role in informing healthcare policymakers. Demonstrating that higher upfront investment in effective technologies can lead to reduced long-term healthcare expenditure strengthens the case for reimbursement. Importantly, this perspective encourages a shift in mindset—viewing healthcare not merely as a cost, but as a strategic investment and an opportunity for societal and economic growth. Convincing decision-makers of this potential is essential to unlocking opportunities for the medtech sector and ensuring that promising innovations reach the market with sustainable funding support.

Developing analyses of health and economic consequences of a disease requires a multidisciplinary skill set. Epidemiological expertise is essential to understanding disease burden and progression, while knowledge of health economics enables accurate estimation of costs, including hospital care, medical procedures, productivity loss, and quality of life impacts. Familiarity with economic modelling approaches, such as cost-of-illness and cost-effectiveness analysis, allows companies to quantify the wider implications of a disease and to support stronger value-based arguments for their innovations. Analytical and statistical competencies are equally important. Proficiency in tools such as Excel, R, or Python facilitates the handling of complex datasets and enables dynamic scenario modelling.
A solid understanding of clinical care pathways, complications, and treatment variation ensures that models remain relevant and reflective of real-world care.

In practice, studies of health and economic consequences of a disease draw from a wide range of evidence sources—including systematic literature reviews, clinical trial data, and real-world datasets. Analysts must apply critical thinking and problem-solving to adapt models to data limitations and ensure outputs are both rigorous and applicable. Strong communication and project coordination skills are also vital to ensure findings are clearly presented and actionable for decision-makers across different functions.

1.3 Case Study: Chronic Limb-Threatening Ischaemia (CLTI)

In this report, we present a detailed case study examining the health and economic burden of CLTI in Germany, a high-impact condition that offers valuable insights for medtech companies developing solutions in vascular care. CLTI serves as a practical example of how health and economic consequences of disease analyses can be used to identify unmet clinical need, quantify value, and support product planning, positioning, and engagement with healthcare systems. Germany was selected due to relatively strong data availability.

Ireland is recognised globally as a leading hub for medtech innovation, manufacturing, and export. The sector employs over 50,000 people across more than 450 companies, highlighting its strong presence in Ireland. Separately, Ireland ranks among the top five global medtech exporters, underlining its importance as a key player in the international market. Its strength lies not only in advanced manufacturing but increasingly in the development and commercialisation of cutting-edge technologies across a range of therapeutic areas.

Ireland has a strong concentration of companies developing technologies for vascular and cardiovascular disease. Based on current data, approximately 48 companies are active in these areas, including firms focused on peripheral artery disease (PAD), coronary interventions, and atrial fibrillation management. These activities sit within Ireland's broader medtech sector, which employs over 35,000 professionals nationwide. This industrial base underscores the strategic relevance of CLTI as a case study—both for its clinical burden and its alignment with Ireland's industrial strengths in vascular and endovascular innovation.

While this report focuses on CLTI, similar health and economic consequences of disease analyses can be conducted for other conditions, providing valuable insights into their societal and economic impact. Such studies help stakeholders across

the healthcare and medtech industries make informed decisions about resource allocation, research priorities, and the development of innovative healthcare solutions.

CLTI is the most advanced stage of PAD, a condition affecting over 230 million people globally. PAD is characterised by a circulatory disorder that causes reduced blood flow through the arteries. This usually leads to reduced blood flow to the extremities manifesting itself as thigh or calf pain during walking or exertion. Severity ranges from asymptomatic to CLTI. CLTI is developed in approximately 11% of the PAD patients and is defined as the most severe stage of PAD7 and is typified by rest pain of the lower limbs, gangrene or ulceration.[8] CLTI leads to a significant increase in the risk of amputation[9] and revascularisation as the most common intervention to prevent limb loss.[8] Further, hospitalisation for sufferers is common and several patients are re-admitted within 6 months. They usually have a shorter life expectancy, with a mortality rate of over 50% after 5 years. [9]

Statistics show that around 1.8 million people in Germany are affected by PAD, and the trend is rising. [10] This is explained by the link between diabetes as a predictor and the likelihood of CLTI and the underlying increase in diabetes risk worldwide. [11,12] In addition to the suffering of patients due to pain, comorbidities, and decreased quality of life, CLTI causes a significant economic burden, not only through direct health costs but also through indirect costs such as loss of productivity. [13]

Disease management can be the key to improving the substantial morbidity, mortality, and economic burden associated with CLTI. The management strategies need to be economically evaluated to provide a holistic understanding of the health and economic consequences.

This case study models the full economic burden of CLTI, not only to highlight the magnitude of the problem, but also to demonstrate how medtech companies can use similar approaches to understand opportunity spaces, shape value propositions, and engage stakeholders more strategically.

2. Aim and Objectives

The primary aim of this case study is to demonstrate how health economic modelling can be used as a strategic tool by medtech companies to evaluate disease burden, identify areas of unmet clinical need, and support data-driven decision-making for global market opportunities. CLTI has been selected as a sample condition to illustrate this approach, given its rising clinical relevance, alignment with Ireland's vascular medtech strengths, and the availability of sufficient data in Germany to build a robust model.

The objective is to showcase a scalable, transferable methodology that can be applied across other disease areas. The model quantifies the direct healthcare costs associated with CLTI interventions (including amputation and revascularisation), as well as the indirect costs related to productivity losses and unpaid care. It also incorporates estimates of lost quality of life, expressed as QALYs, to provide a comprehensive view of the condition's economic burden.

The project was developed with the following objectives:

- To illustrate how modelling the health and economic consequences of disease g can be used to support strategic planning, innovation targeting, and upstream market analysis within medtech companies.
- To quantify the long-term costs and consequences of CLTI as a case study, using Germany as a pilot setting due to its available data.
- To provide a replicable framework that can be adapted by Irish Medtech companies seeking to assess other therapeutic areas of relevance to their portfolio or capabilities.

3. Methods

3.1 Overview of methodology

To assess the economic burden of CLTI, it is crucial to consider both the health impact, and the direct and indirect economic burden. The health and socioeconomic footprint represent complementary viewpoints of our analysis. Our methodology consisted of three consecutive steps summarised in Figure 1. We started by estimating the health footprint, i.e., the potential number of vascular treatment procedures. Next, we calculated the socioeconomic footprint by incorporating both direct and indirect costs.

Direct Costs refer to the actual expenses incurred for medical care and treatment of CLTI. Direct costs may include costs associated with hospitalisations, outpatient visits, surgical procedures (such as revascularisation and amputation), medications, and rehabilitation services. By analysing direct costs, we captured the financial impact on the healthcare system due to the need for intensive and ongoing management of CLTI patients.

Indirect Costs refer to the broader economic impact of CLTI beyond the healthcare system. These costs primarily relate to lost productivity due to disability, premature mortality, and time lost from work by patients and caregivers. For indirect costs, the monetised impaired or lost time in paid and unpaid work activities was evaluated.

3.2 Health footprint

To quantify the health footprint, we implemented a Markov model, one of the most common decision-analytic modelling techniques informing evidence on economic evaluations. Generally, Markov models may be used to model chronic diseases. These models consist of different health/disease states, probabilities of transitioning between these states and a pre-determined cycle length. An individual can only transition between different states or remain in the same state at the end of each cycle. When conceptualizing a Markov model, the states and cycle length should be carefully chosen to align with the clinical pattern of the chosen disease, i.e., illustrate pertinent clinical events. In the current study, the Markov model consists of three treatment-dependent states and one death state. Therefore, the model assesses treatment pathways rather than disease course, e.g., disease progression.

3.3 Definition of the patient population

To approximate the patient population for CLTI in Germany, a multi-step approach was undertaken, focusing on both the prevalence of PAD and the subsequent development of CLTI within this population. The patient population was initially defined by estimating the prevalence of PAD, which serves as a preclinical indicator to CLTI. To approximate the prevalence of CLTI in relation to PAD, we used German evidence reported in Rammos et al.14 They reported the prevalence of PAD in Germany for the years 2009 to 2018 according to Rutherford categories. The Rutherford categories 4 to 6, which reflect CLTI14,15 were used. Moreover, we considered the incidence of CLTI among PAD patients in Germany. The incidence rates were derived from multiple sources, [16,17] which suggest that 5-10% of PAD patients develop CLTI over a 5-year period. For our model, we used an average incidence rate of 7.5%. In this analysis, we considered only three incident cohorts. This choice was made to minimise the potential influence of

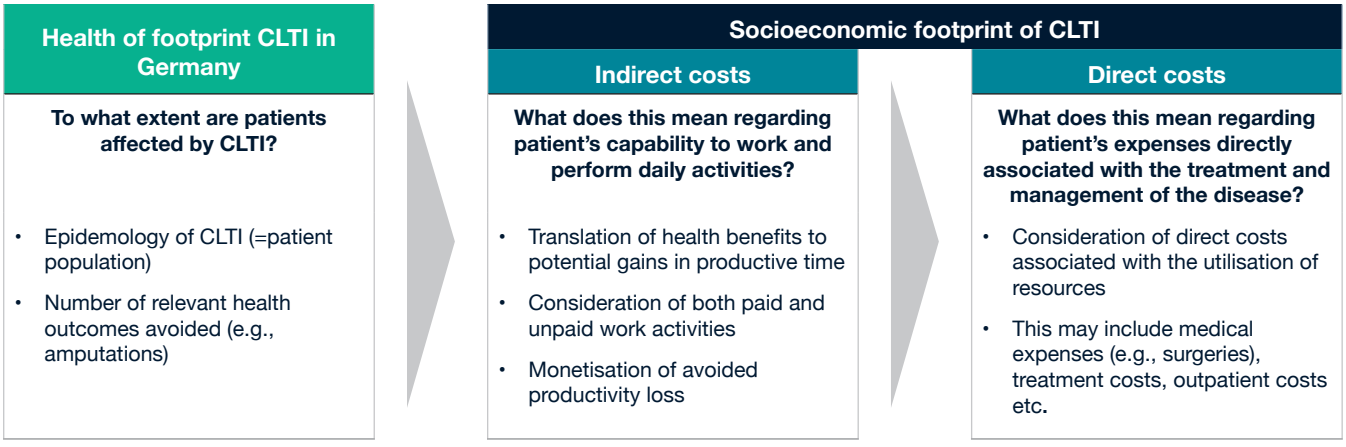


Figure 1: Overview of the model

long-term changes, such as shifts in socioeconomic factors (e.g. costs associated with limb procedures, income levels) or changes in clinical practices (e.g., new treatment methods, or technologies). By focusing on a limited number of cohorts, the model avoids the complexities and uncertainties that may arise from these long-term changes. Moreover, the model accounted for changes in the incidence of CLTI by incorporating population growth rates. This means that as the population size changes over time, the model adjusts the incidence of CLTI accordingly. Population growth rates ensure that the number of new cases reflects the evolving demographic structure of the population, making the model more accurate in predicting future incidence trends. The described modelling approach was applied to five age groups: 18-39, 40-49, 50-59, 60-69, and 70+ years. The analysis incorporates age-specific rates from a real-world German study to account for the higher prevalence of CLTI among older populations. By factoring in age distribution, we ensured the model accurately reflects the increased risk of CLTI in older age groups. In this model, it was assumed that each age group starts at its midpoint, meaning that the calculations for each group were based on the average age within that range. For example, for the 40-49 age group, the midpoint of 44.5 years is used.

Gender distribution (per diabetes subgroup)		
	With diabetes (%)	Without diabetes (%)
Females	52	48
Males	54	46

Table 1: Diabetes status per gender

The patient population was further categorized by age, gender, and diabetes status. For age and gender categorisation, we used the subgroup distribution data reported in the study by Makowski et al. (2022)

Table 1).15 To evaluate the impact of diabetes on the outcomes of CLTI, we conducted a methodological approach that involved several steps. First, we derived data to determine the overall probabilities of key CLTI outcomes, such as amputation and revascularisation, within the CLTI population. This provided a baseline understanding of the likelihood of these outcomes occurring in patients with CLTI. Next, we identified the proportion of CLTI patients who also have diabetes (Table 1).[15] Following this, we reviewed the literature to identify the increased risk of CLTI outcomes in diabetic patients compared to non-diabetic patients. We specifically looked at measures such as relative risk, hazard ratios, and odds ratios to understand the extent to which diabetes might exacerbate the risk of adverse outcomes in CLTI patients. Using the multiplicative property of probabilities, we combined the overall probability of each CLTI outcome with the increased risk associated with diabetes. This allowed us to calculate diabetes-specific probabilities for each CLTI outcome, providing a better understanding of how diabetes impacts the risk profile of patients with CLTI.

We identified a study from Germany18 that reported a statistically significant 42% increased risk of amputation (major and minor) in patients with diabetes compared to those without diabetes. Based on this finding, we adjusted the probability of amputation to reflect the increased risk in the diabetic population subgroup. For other parameters in the model, our literature review indicated no statistically significant impact of diabetes, so no adjustments were made for these.[18,19]

3.4 Description of the health states

For this analysis, we simulated the progression and treatment outcomes of patients diagnosed with CLTI over their lifetime (up to the average life expectancy in the country) due to the chronic nature of the disease, using a six-month cycle length. While many CLTI-specific models employ a one-year cycle, we opted for a shorter cycle to enhance accuracy and minimise potential technical biases that may arise due to the complexity of multiple health states. Outpatient treatments included conservative management or endovascular revascularisation.[20] Surgical revascularisation was excluded from the outpatient setting, as previous research has indicated that this procedure requires inpatient admission due to its complexity and the need for close postoperative monitoring.[21] Moreover, although outpatient endovascular procedures are less prevalent in Germany due to limited incentives under the current reimbursement system, this pathway was included to ensure the model's adaptability and relevance across different healthcare contexts. In countries such as Switzerland, outpatient endovascular treatment is more incentivized and frequently practiced, making it a relevant treatment pathway in those settings. By incorporating outpatient endovascular revascularisation, we aimed to create a model that supports comparative analyses across European countries with varying healthcare policies.

Furthermore, evidence from a study examining endovascular revascularisation in Germany indicated that while the majority of these procedures are conducted in an inpatient setting, outpatient options are available.[22] Overall, including this pathway allowed the model to reflect the range of treatment settings, even where outpatient endovascular procedures are less common.

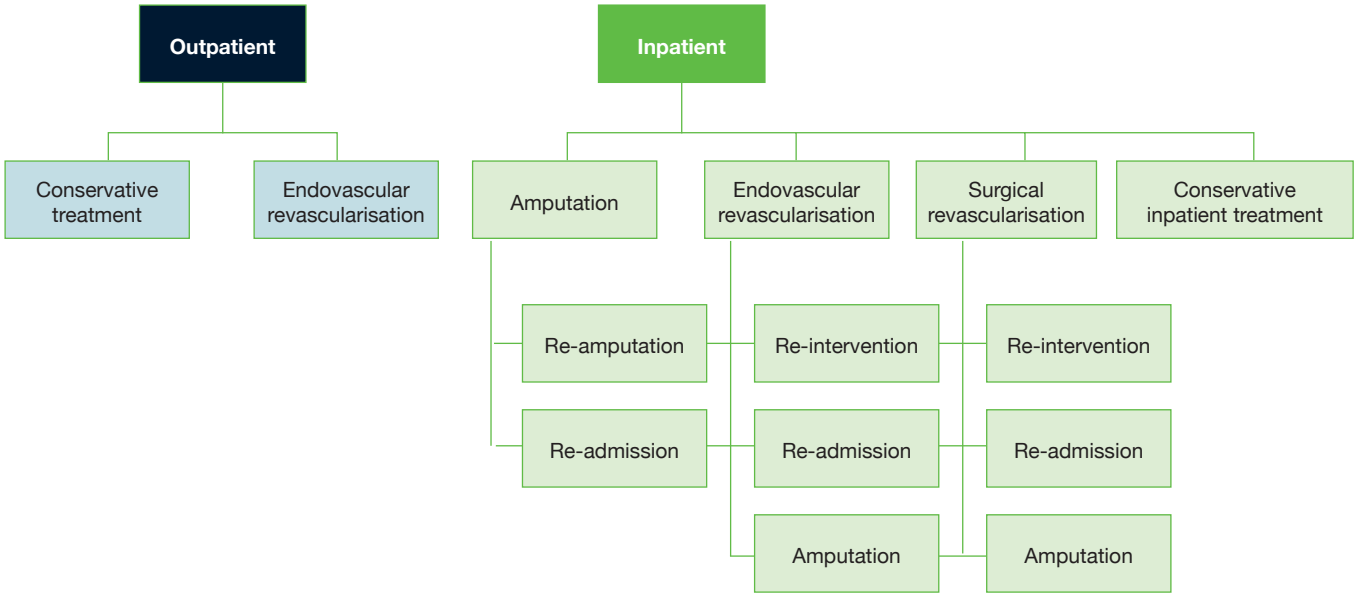


Figure 2: Overview of outpatient and inpatient treatment options

The inpatient treatment pathways involved amputation,[15,23] surgical revascularisation,[15,20] endovascular revascularisation,[15,20] or conservative treatment.[5]

For patients undergoing amputation, the model incorporated the possibility of re-admission24 (e.g., due to post-procedure complications)[25] and re-amputation [26,6], reflecting the common complications associated with this intervention. In the revascularisation pathways (in the inpatient setting), the model distinguished between endovascular and surgical procedures due to their differences in practice and clinical outcomes. Patients who experience unsuccessful revascularisation or develop complications can require hospital re-admission (e.g., due to post procedure complications) [27] or re-intervention.[28,7] In the case of patients treated with outpatient revascularisation, we assumed they have less severe disease, and thus no further interventions were considered in this group. Patients who stabilise after these events continue to receive ongoing medical care, including rehabilitation and condition (and/or comorbidities) management, to reflect the long-term nature of recovery following CLTI- related procedures.

To accurately model mortality within the CLTI cohort, we used a combination of sources to derive the overall probability of death. First, general population mortality probabilities were obtained from German life tables[29] to provide a baseline. Then, CLTI-specific mortality rates were integrated to account for the increased risk associated with the condition.[30] Additionally, the model incorporated the probability of death following each intervention.[28,31–33] These distinct probabilities were then calibrated to ensure that the overall mortality risk reflected both the general population's life expectancy and the specific risks associated with CLTI and its treatments. This approach allowed for a refined estimation of mortality, tailored to reflect both disease progression and the effects of various interventions. Moreover, we considered the average life expectancy in Germany which has been reported [80]. 5 years,[34] representing the upper age limit in our analysis. Figure 2 provides an overview of the health states assessed.

The model results are presented as undiscounted values (i.e. without adjusting for the time value of money) to provide a straightforward view of the total burden of the disease over time. This can be particularly useful for understanding the full extent of the disease burden, especially in public health discussions where immediate costs and future impacts are considered equally. Nevertheless, we also present the discounted values with a 3% discount rate, which is the rate that is recommended in the German context.[35]

3.5 Direct cost components included in the analysis

All direct cost components were sourced primarily from the German Diagnosis Related Group (DRG) system and relevant literature. In cases where German-specific cost data was unavailable, we utilised evidence from other European countries, such as France and Belgium. To ensure the accuracy of these estimates within the German context, we adjusted the values using Purchasing Power Parities (PPP), [36] which allowed for cross-country cost comparison. Additionally, historical cost data from previous years were inflated to reflect 2024 values. For the year 2024, we assumed a similar inflation rate as 2023 as updated estimates are currently not available.

[5] Patients who did not receive amputation or revascularisation.

[6] Evidence was carefully selected from the literature to ensure that there is no overlap between the probabilities of re-admission and re-amputation.

[7] Evidence was carefully selected from the literature to ensure that there is no overlap between the probabilities of re-admission and re-intervention.

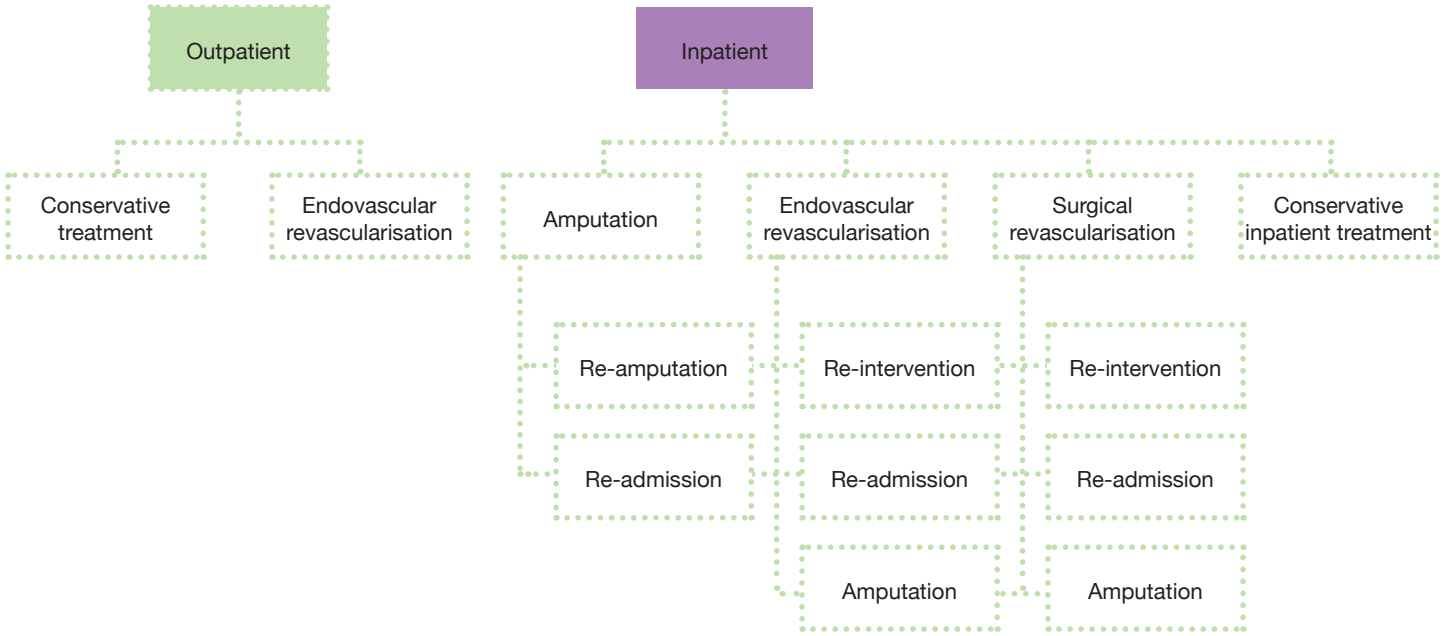


Figure 3: Overview of the different cost elements related to CLTI

The model included the direct costs related to amputation, with specific figures for both amputation and re-amputation procedures obtained from the German DRG system (€10,782.12).[8] Additionally, long-term follow-up costs associated with post-amputation care were integrated, based on estimates from Hoffmann et al. (2013).[38] These follow-up expenses included medical care, rehabilitation, outpatient services, non-physician care, and long-term care, such as nursing home stays and professional caregiving. The six-month cost for these follow-up services was estimated at €6,151.38 We assumed that these costs were incurred throughout the patient's lifetime, reflecting the chronic nature of care required for amputees.

The model incorporated the direct costs of revascularisation, including both endovascular and surgical procedures, as well as the costs of re-intervention procedures, to fully capture the economic impact of these interventions in patients with CLTI. For inpatient care, the average direct cost of endovascular revascularisation was estimated at €7,100.74 while surgical revascularisation incurred an average cost of €9,644.36. To estimate long-term care costs following revascularisation, we utilised data from a cohort study of patients covered by a French health insurance. France was selected as a proxy country for Germany, as previous research has identified it as an appropriate comparator for similar cost structures in long-term care. [39] The long-term care costs after revascularisation included a wide range of healthcare services, such as physician visits, care provided by other healthcare professionals (including nursing care, and physiotherapists), biological testing, and transportation services, ambulances, light medical vehicles, taxis, mobile emergency medical services, and mobile emergency units). The six-month cost for these follow-up services was estimated at €2,625. Aligning with previous research,[39] the same input values were applied to outpatient-related costs. Moreover, the same value was applied to patients likely presenting with a less severe stage of CLTI and treated in an outpatient setting. These patients, not requiring amputation or revascularisation, reflect a population for whom more conservative treatment approaches are appropriate.

For the costs of re-admission, we relied on a study conducted in Belgium reporting the respective costs following limb procedures. Belgium was considered an appropriate proxy country for Germany, as both are high-income countries in Europe with similar healthcare expenditures relative to their respective gross domestic products (GDP). This alignment in healthcare spending patterns makes Belgium a suitable reference point for estimating re-admission costs in the German context.[40] The cost of re-admission after adjusting for PPP and inflation was estimated to be €16,071.[9]

Additionally, in the model, the use of key medications was considered. As an input, we used literature based on real world evidence, which accounts for patient adherence. As such, it should be noted that the reported parameters do not reflect perfect adherence to clinical guidelines. For female patients, it was estimated that 50.8% will receive statins, 67.7% use anti-thrombotic medications, and 80.4% are treated with angiotensin-converting enzyme inhibitors (ACEi) or angiotensin II receptor blockers (ARB).[15] For male patients, 61.8% are expected to receive statins, 73.5% receive anti-

[8] The DRG include all operating costs (personal costs, material costs for drugs, implants and other medical supplies as well as infrastructure costs)[37]

[9] It has been reported that the most frequent reasons for re-admission among CLTI and PAD patients are procedure-related complications, wound-related complications, and sepsis. To ensure accuracy and avoid double counting costs with those reported fore- admission, we have considered only complication-related costs under re-admission expenses. This approach maintains a clear distinction between procedure-specific costs and those driven by complications.

thrombotic medications, and 77.3% are treated with ACEi or ARB therapies.[15] These percentages reflect typical observed treatment patterns for managing cardiovascular risk factors and preventing further disease progression in CLTI patients.[15] Ideally, these percentages would approach 100% for full adherence to clinical guidelines; however, as they are based on observed real-world treatment patterns, they reflect actual usage rates, including potential issues with compliance. We further identified relevant six-month costs in the literature. Specifically, the six-month statin, anti-thrombotic medications and ACEi costs were estimated at €69.91, €85.26, and €77.03 respectively. [41–43]

Overall, the analysis centers on the economic burden associated with different procedures for CLTI rather than on their cost-effectiveness. By examining the costs linked to vascular procedures, we provide insights into the financial impact of these interventions without making comparative claims about their cost-effectiveness.

3.6 Ulceration

In modelling the economic burden of CLTI, we treated ulceration costs as a separate category to accurately capture the financial impact of unhealed wounds. This approach allowed us to assess the economic burden of ulceration distinctly, avoiding potential double-counting with other health states or interventions. It is important to note that ulcer types vary and may include arterial, neuropathic, and neuro-ischemic ulcers. However, due to limited data on the incidence rates and specific costs associated with each ulcer type, further differentiation was not feasible in this analysis.

To integrate the economic burden associated with ulcers, the model population was stratified by treatment type—revascularisation, amputation, and conservative management—with rates of non-healing ulcers sourced from the literature.[44,45] We focussed specifically on patients presenting with ulcers, using cost estimates derived from a German study.[46]

3.7 Productivity related costs

A key channel through which a disease can impact macroeconomic performance or output is productivity losses.[47] Methodologically, paid work productivity losses (productivity impairment) are estimated using the human-capital approach (HCA). The HCA considers human beings as assets and values poor health leading to work impairment as lost production to an economy.[48,49]

Table 2: Productivity and activity impairment rates
In this analysis, the calculations for indirect costs associated with CLTI were derived from data that focus on the impact of PAD on work productivity, particularly examining absenteeism, presenteeism, and activity restriction (Table 2). Although the study primarily focused on PAD, it is assumed that CLTI shares similar pathways affecting quality of life and work productivity. Given the more severe nature of CLTI, it is likely that work and activity impairments in CLTI patients could be more significant, thus the analysis is likely to underestimate the true impact. Nevertheless, the specific study represented the best available evidence to approximate the indirect costs in the specific patient population. For this analysis, the adjusted mean percentages for absenteeism, presenteeism, and overall activity impairment reported for PAD patients were used as proxies for CLTI patients. This approach assumed that the indirect costs related to work productivity and activity restriction for CLTI patients are at least comparable to those for PAD patients, if not higher, due to the increased severity of the disease. The evidence on the impairment rates were referred to EU5 (Germany, Italy, Spain, UK, France) countries.[50]

We calculated productivity losses associated with absenteeism and presenteeism for all living patients with CLTI. For amputated and revascularised patients we further applied Return to Work (RTW) rates after the respective procedure (Table 2).[51,52] In order to quantify losses due to poor health to the German economy, we first determined the working time of an average German employed person stratified by age and gender.[53] To quantify the productivity losses associated with CLTI, the model adjusted the employment rates of the general population to reflect those specific to patients with PAD. This adjustment was necessary to avoid the assumption that CLTI

Gender distribution (per diabetes subgroup)		
	Productivity and activity impairment rates for PAD/CLTI patients (%) and Return to Work (RTW) rates	References
Absenteeism	7.68	Marrett et al. (2013) [50]
Presenteeism	23.37	Marrett et al. (2013) [50]
Activity restriction	38.27	Marrett et al. (2013) [50]
RTW after amputation	66.00	Fisher et al. (2003) [51]
RTW after revascularization	79.00	Pfund et al. (2001) [52]

Table 2: Productivity and activity impairment rates

patients would have the same employment rates as the general population, which would likely lead to an overestimation of productivity losses. Since CLTI is a severe form of PAD, it often affects patients' physical capabilities, resulting in a reduced ability to work. Thus, by aligning the employment rates with PAD-related figures, this model more accurately captured the true economic burden associated with lost productivity due to CLTI. Specifically, we utilised evidence from Marrett et al 50 who reported that approximately 32% of patients with PAD were engaged in paid employment. This approach allowed us to more accurately estimate the productivity losses for specific subgroups within our population, capturing the variation in employment across different demographic groups. Generally, our monetization approach was based on average patient statistics across the population, a method commonly used in other economic evaluations.

Appendix 1. shows the socioeconomic inputs by age and gender used to determine the average working time of a German inhabitant. Appendix 2. demonstrates the calculations performed for evaluating productivity losses.

3.8 Estimating the loss in active time

To fully capture the social impact of health conditions, it is crucial to account for productivity losses in both paid and unpaid work. Individuals who are not in active employment also contribute to a nation's prosperity through domestic work or other voluntary activities. This value added, which is not typically considered in GDP, was included in our calculations, and referred to as "unpaid" work. While the traditional approach focuses mainly on paid work activities (i.e., a job for which a person receives monetary compensation), this analysis also considered unpaid work activities. Unpaid work activities are performed by all employed, unemployed, and retired population and contribute significantly to a nation's wealth. Unpaid work, which includes household tasks, caregiving, and volunteer activities, plays a significant role in maintaining the well-being of individuals and communities. Neglecting this aspect results in an underestimation of the economic health and economic consequences of a diseases, especially for older populations typically not engaged in formal employment.

Productivity losses related to unpaid work are particularly relevant for CLTI, since many of the CLTI patients are older adults who may no longer be formally employed but still contribute significantly through unpaid work (Figure 4). As such, only focusing on paid work as an indication of productivity would result in an underestimation of the social impact of CLTI and its clinical complications, such as amputation. Moreover, unpaid work is often done by females. Thus, incorporating the productive value of unpaid work in economic analyses also reduces gender bias.

To differentiate between leisure time and time spent on unpaid work activities, the third-person criterion is used.[54,55] Following this criterion, the time spent on unpaid work activities which can be replaced by another (third) person is included in our analysis. Concretely, in our model we consider the time spent on the following unpaid work activities:

- Unpaid domestic work for own household
- Unpaid care work for household members
- Unpaid work as support to other households and voluntary work

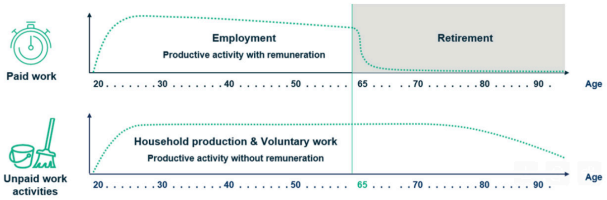


Figure 4: Contribution of individuals in terms of paid and unpaid work over their lives

3.9 Estimating losses in quality of life

CLTI and its treatment pathways also affect the quality of life of patients, which results in an additional social burden. Losses in QALYs were used to describe the impact of CLTI and its treatment pathways on the quality of life of patients. QALYs combine information about life years and the quality of those life years, by describing the quality of life in terms of a preference-based adjustment to a health state.[56]
A literature review was used to identify relevant QALY values for living with CLTI, living after a surgical or endovascular interventions, and living with an amputation.[57,58] An overview of these values, with references from the original studies which present the elicitation of these values, can be found in Table 3.[59–61] QALY losses due to a loss in quality of life were calculated by subtracting the QALY value of living in a certain CLTI health state from normative QALY values per age group in Germany. [62,63] The societal burden in terms of QALY lost per age group was calculated by summing all QALY losses of all the patients in their respective age groups over the time horizon.

Normative values by age group were derived from Janssen et al.[62] These values were adjusted into values that are relevant for the age groups in our report. For this, the average of two age groups were taken to calculate the normative QALY value relevant for our report. To illustrate, the average between the QALY values of the age groups 35-44 and 45-54 in the report of Janssen et al.[62] were used to calculate the QALY value for the age group 40-49. For the age group [18-39] in our report, first

the QALY values of the age groups 25-34 and 35-44 from Janssen et al. were averaged, and this number was again averaged with the QALY value of the age group 18-24. Finally, for individuals aged 80 and above, we used the same QALY value as the 75+ age group from Janssen et al.[62]

	QALY* value	Reference
CLTI patients	0.56	Pisa et al. (2012) [59]
Amputation	0.47	Busschbach et al. (1999) [60]
Surgical or endovascular interventions	0.55	Forbes et al. (2012) [6]

Table 3: Used Quality Adjusted Life Year values for different health states
QALY*: Quality Adjusted Life Year

3.10 Sensitivity analysis

A probabilistic sensitivity analysis (PSA) was conducted to quantify the level of confidence in the direct economic burden (being the biggest driver), of the analysis in relation to the uncertainty in cost inputs parameters. The purpose of a PSA was to evaluate model uncertainty. Usually, input parameters derived from clinical trials or real-world evidence are associated with uncertainty.[64,65] Health economic models involve the base case analysis, where the mean value of each parameter is used in the analysis. In the PSA a statistical distribution is specified for each selected input parameter. The distributions chosen for each input and the relevant distribution parameter calculation were based on Briggs et al.[64] recommendations. In case that no data was available for standard error (SE), we assume a conventional 10% as SE.[66] Moreover, a deterministic sensitivity analysis (DSA) was conducted to identify the most influential economic and health-related parameters by varying each selected parameter individually to its upper and lower bounds. Parameters were adjusted by ±20%, a commonly used range in health economics modelling.

3.11 Assumptions and limitations

In developing the economic burden model for CLTI, various assumptions and simplifications were made. Economic models, by their nature, simplify the complexities of real-world systems. In this model, average estimates were used for key parameters, including costs, and transition probabilities, due to limited availability of data in the literature. These averages may not fully capture the variability seen in real-world populations, where patients differ in terms of age, comorbidities, disease severity, and treatment responses. While the model relied on aggregated data, it may overlook individual variabilities that can affect patient outcomes. Additionally, as this study focused on the health and economic consequences of a disease, our emphasis was on treatment pathways rather than the detailed clinical progression of CLTI. Nevertheless, our modelling approach aligned closely with methodologies used in prior economic evaluations of CLTI. [39,67,68]

The modelling approach used can influence the outcomes of the analysis. This model uses a six-month cycle length, applying a half-cycle correction to ensure accuracy in capturing the timing of key events such as amputations. However, different approaches—such as Markov models, decision trees, or microsimulation—can produce varying results, each with its own strengths and limitations. This model simplifies the pathway through health states for greater usability.

In the absence of access to real-world, or health claims data, the model drew heavily on the identified literature to estimate healthcare costs, transition probabilities, and outcomes. However, there are inherent gaps and biases in real-world datasets. Health outcomes and complication rates may be underreported, and the data may be sourced from specific regions or healthcare systems that do not represent the broader population. Additionally, cost variations exist across different regions or institutions, even within the same country, due to differences in local practices, available resources, or reimbursement structures. Additionally, the literature search indicated limited publicly available evidence with regards to the epidemiology of CLTI. Thus, we relied on the best available evidence to approximate the patient population. Where gaps in country-specific data were encountered, the model relied on proxy countries or applied validated adjustment techniques to approximate the missing values. While these methods ensured that the model remains relevant despite the lack of ideal evidence, they also introduced an element of uncertainty into the results. Additionally, external factors—such as advancements in medical practice, the introduction of new therapies, changes in healthcare policy, or unforeseen events like pandemics—were not fully predictable, yet they can have a significant impact on real-world outcomes. These externalities are challenging to integrate into the model, which may limit its predictive accuracy in evolving healthcare landscapes.

An additional limitation of this analysis lies in the categorisation of ulceration costs as a single entity. Ulcers in CLTI patients can vary significantly, with distinct types such as arterial, neuropathic, and neuro-ischemic ulcers, each presenting unique healing trajectories and resource demands. Differentiating between these ulcer types with separate calculations might more accurately reflect the costs associated with each specific treatment pathway and outcome. However, due to limitations in data availability, such detailed analysis was not feasible. If more granular data on ulcer types, healing rates, and recurrence by patient subgroup becomes available, the model could be refined to improve cost accuracy and offer a more comprehensive understanding of the economic impact of ulcer-related complications.

Finally, a key limitation of the analysis is the exclusion of informal caregiving costs. CLTI often imposes a heavy burden on family members who provide unpaid care, which can have significant implications for both the caregivers' quality of life and their ability to engage in paid work. Despite the substantial burden of CLTI on the patient population, the disease may affect their informal caregiver as well and therefore decrease their productivity. Informal care is often neglected in health economic evaluations, but it has a significant influence on both direct and indirect health costs and should be recognised for a holistic perspective beyond the patient. On the one hand, the burden caused by unpaid patient care manifests through deteriorations in quality of life and health of carers, and it can result in absences from work and a reduction in paid work.[69] Due to a lack of evidence, this significant part of the burden of CLTI could not be considered in this analysis, potentially underestimating the economic burden. Future studies should seek to quantify this aspect in order to capture the full scope of CLTI's economic burden.

4. Results

Overall, the number of patients older than 18 years with CLTI in Germany was estimated to be 308,594 patients in 2024. The following figure illustrates (Figure 5) the distribution of the population by age and gender. For patients with diabetes, the prevalence increases with age, reaching a peak in the 70-79 age group, where there were 31,466 male patients and 22,858 female patients. A significant number of patients was also found in older ages (>60 years). In contrast, the number of younger patients (≤39 years) with diabetes was very low, with only 155 female and 113 male patients in this category.

For patients without diabetes, the distribution followed a similar pattern, with the highest number of patients in the 70-79 age group, where there were 26,804 male and 21,100 female patients. As with the diabetic cohort, the number of patients aged ≤39 was relatively small, with 132 males and 104 females in this category.
In both graphs, the number of male patients generally exceeded the number of female patients across most age groups. The largest gender difference was observed in the older age groups, particularly in the 70-79 range.

With regards to the incident population, the number of incident cases in 2024 were estimated at 27,282 patients with CLTI. Considering the population growth estimates, the incidence of 2025 and 2026 were estimated to 27,503 and 27,726 respectively.

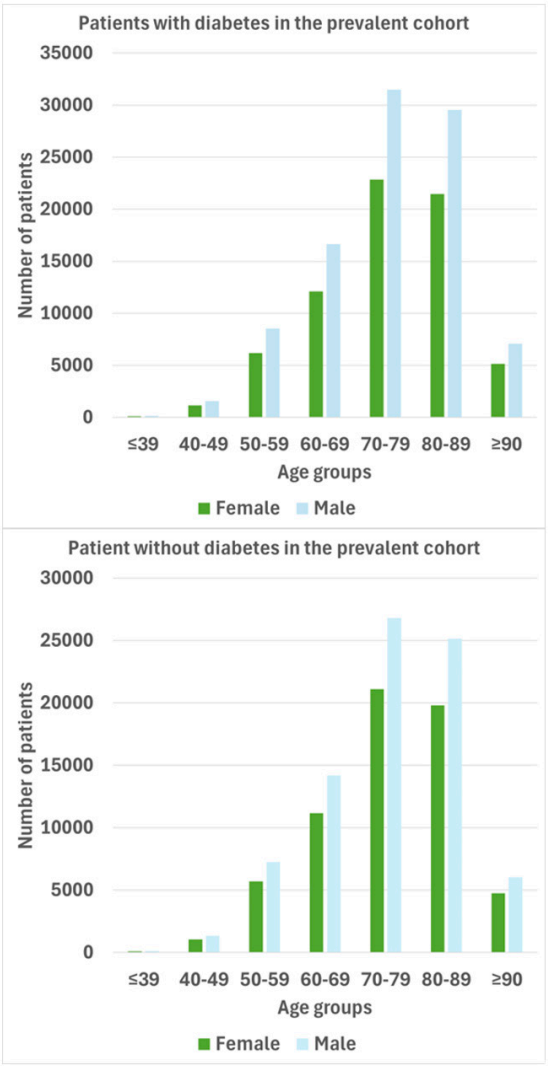


Figure 5: Age and gender distribution in the prevalent population

This study assessed the occurrence of amputations within the CLTI patient population. A total of 34,157 amputations were estimated over the lifetime horizon. Of these, 20,395 occurred in patients with diabetes and 13,762 in patients without diabetes. Most amputations were observed in the age group 70 years old and above (more than 50%). Gender-specific analysis showed that approximately 60% of amputations were performed on male patients, while almost 40% occurred in female patients. The incidence of re-amputations following primary amputations was also examined. A total of 2,874 re-amputations were estimated. Among patients with diabetes, 1,707 experienced re-amputation, compared to 1,167 among those without diabetes. Additionally, following amputations a total of 16,821 re-admissions were estimated.

Figure 6 illustrates the number of amputation events across different age and gender subgroups, comparing individuals with diabetes to those without. The data highlights that amputation events are more frequent in the diabetes population, with a sharp increase observed in older age groups, particularly in males aged 70 years and above. Males experienced a higher incidence of amputations than females in both populations. The difference between males and females can be attributed to the higher number of males in the patient population, but also the fact that males are more likely to receive amputation
compared to females.

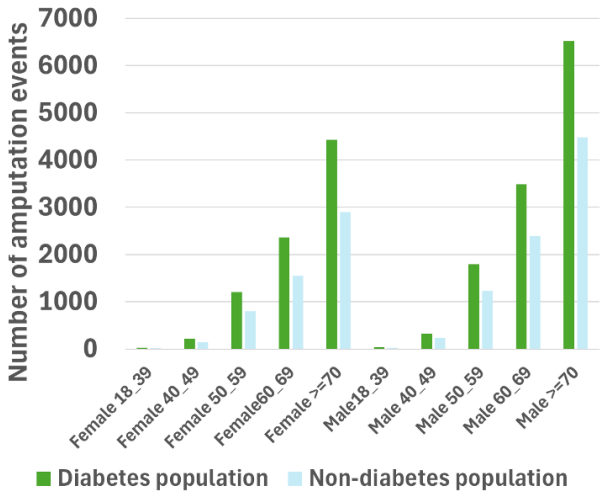


Figure 6: Number of amputation events by age and gender subgroups in diabetes and non-diabetes populations.

Endovascular revascularisation, a common treatment modality for CLTI, was performed on 94,712 patients over the lifetime horizon. Of these, 49,958 procedures were carried out in patients with diabetes, while 44,754 occurred in patients without diabetes. An additional 38,154 surgical revascularisations procedures were performed. Furthermore, 3,728 and 719 patients underwent re-interventions after their initial endovascular and surgical procedure respectively. Re-admissions following surgical and endovascular interventions were recorded in 33,912 and 17,225 patients receiving endovascular and surgical revascularisation respectively
over lifetime.

Figure 7 illustrates the number of endovascular revascularisation events across various age and gender subgroups, comparing individuals with diabetes to those without. The data showed that revascularisation events increase with age in both populations, with a notably higher frequency in the non-diabetes population, particularly in males aged 70 years and above. Males tended to experience more revascularisation events than females across all age groups, with the largest difference observed in the oldest age group (≥70 years).

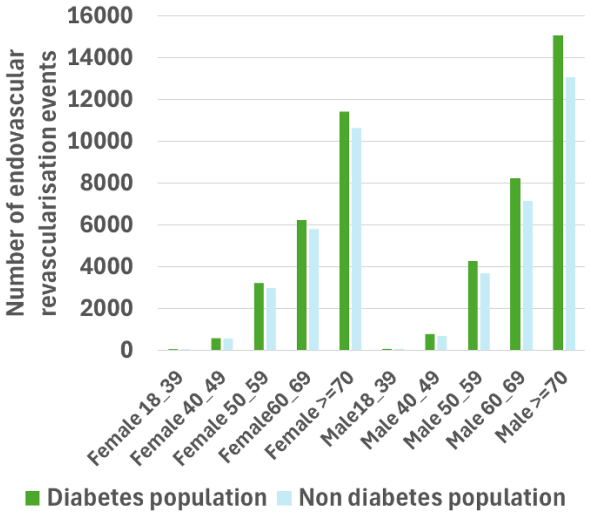


Figure 7: Number of endovascular revascularisation events by age and gender subgroups in diabetes and non-diabetes population

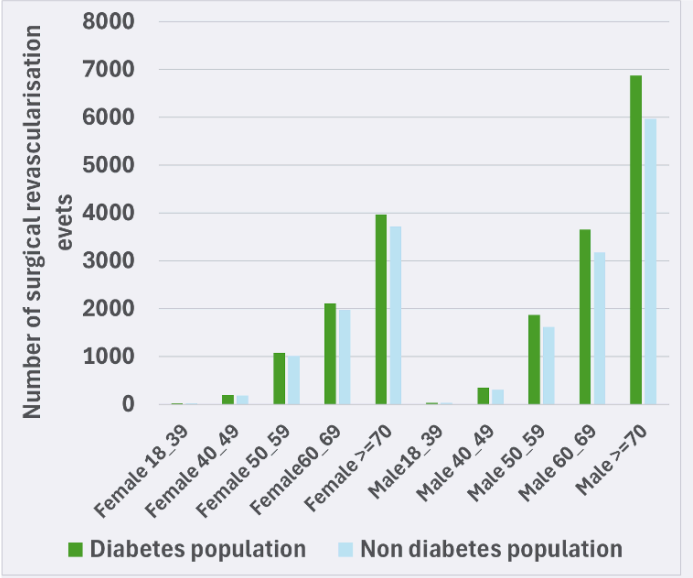


Figure 8: Number of surgical revascularisation events by age and gender subgroups in diabetes and non-diabetes population

Figure 8 displays the number of surgical revascularisation events across distinct age and gender subgroups, comparing individuals with and without diabetes. Similar to endovascular revascularisation, the data showed that surgical revascularisations became more frequent with increasing age, with a marked rise observed in both populations, particularly among males aged 70 years and older. The diabetes population experienced a slightly higher number of events in most subgroups, especially in the oldest male group. Males generally had more surgical revascularisations than females across all age groups in both populations, with the largest difference seen in the ≥70 age group.

The total economic burden of CLTI was substantial, amounting to €8.99 billion over a lifetime horizon. This included direct healthcare costs of €5.12 billion, along with drug costs of €188.13 million. Notably, productivity losses represented a significant portion of the overall costs, with unpaid work-related productivity losses being particularly impactful, totaling € 2.9 billion. These losses, which often arise from the inability of older patients to engage in unpaid work, underscore the need to account for this aspect especially in an ageing population. Paid productivity losses, while smaller, still contributed €975.46 million over lifetime. The data emphasises the broad economic consequences of CLTI, extending beyond healthcare to include considerable unpaid work disruptions (Figure 9). Appendix 3 presents the discounted results.

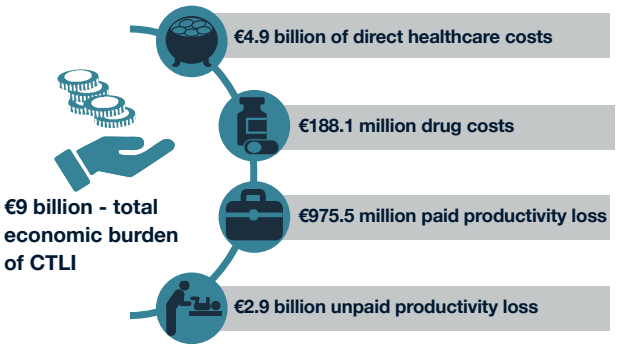


Figure 9: Direct and indirect economic burden of CLTI

Figure 10 illustrates the total economic burden of CLTI stratified by age group and gender. The economic burden increased with age for both males and females, with the highest costs observed in the 70–79 age group. Males consistently show a higher economic burden across all age groups, particularly in the 60–69 and 70–79 age ranges, where the gap between genders is most pronounced.

The distribution of direct costs (excluding drug costs) between the diabetes and non-diabetes populations is illustrated in Figure 11. The diabetes population accounted for € 2.66 billion of the total direct costs, while the non-diabetes population comprised €2.27 billion. Given that the total direct costs amount to €4.93 billion, the diabetes population contributes a larger share, emphasizing the economic impact of CLTI among individuals with diabetes. The total costs for key interventions related to CLTI were evaluated, including both the overall economic burden and the average cost per procedure.

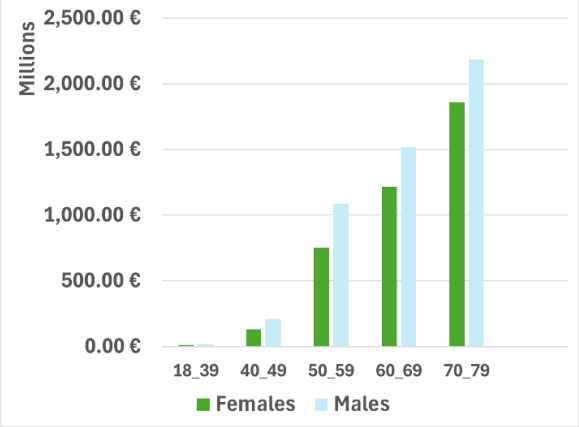


Figure 10: Total economic burden of CLTI stratified by age group and gender

The total cost of amputations amounted to €1.22 billion, with an average cost of €35,608.30 per procedure. Endovascular revascularisations resulted in a total cost of €1.92 billion, with an average cost of €20,282.73 per procedure. Surgical revascularisations had a total cost of €910.82 million, with the average cost per procedure being €23,872.43. These figures reflect the substantial financial impact of these procedures in managing CLTI.

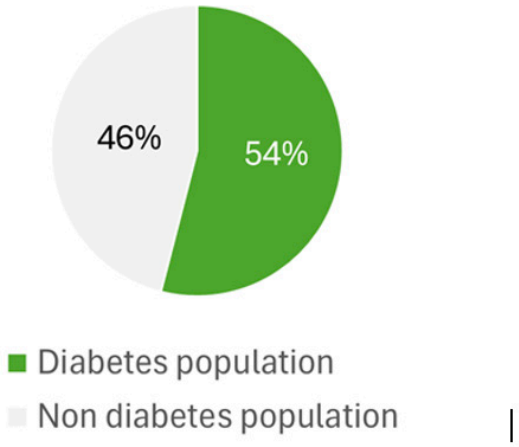


Figure 11: Distribution of the total direct costs (excluding pharmaceutical costs) between diabetes subgroups

The total cost of ulceration calculated as unhealed ulcers amounted to €1,64 billion (Figure 12). Ulceration represents a significant complication for patients with CLTI, contributing to an increased economic burden. However, as mentioned in the above section, to avoid the risk of double counting with other cost categories, such as re-admission, we have refrained from including ulceration-related costs in the overall total for the model. This approach ensures the integrity of the economic analysis by maintaining distinct cost categories and preventing overlap between complication-driven expenses.

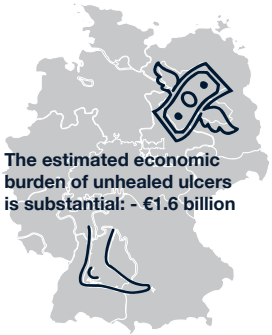


Figure 12: The economic burden of ulcers

Figure 13: Differences in productivity losses between males and females in both paid and unpaid employment due to CLTI

Figure 13 highlights the differences in productivity losses between males and females in both paid and unpaid employment due to CLTI. Males experienced significantly higher losses in paid employment, with a total of €693.57 million, compared €281.88 million for females over a lifetime horizon. However, the trend reversed in unpaid work, where females face higher losses, amounting to €1.51 billion, compared to €1.39 billion for males over a lifetime. This reflects the disproportionate burden of unpaid work on females, emphasising the gender disparity in how productivity losses are distributed, particularly in unpaid labour. This gender-specific working pattern is explained by the employment rates and the working/ activity hours per gender. Males have higher employment rates and weekly working hours as opposed to females. On the contrary, females spend more time on unpaid work activities (in terms to weekly activity hours) than males.

Additionally, CLTI and its clinical complications also affect the quality of life of patients. Undiscounted, this resulted in a total loss of 157,477 QALYs in the whole patient population over a lifetime. A higher undiscounted QALY loss can be identified in the diabetes group, where 83,649 QALYs were lost, compared to 73,827 QALYs lost in the non-diabetes group. From a gender perspective, males lost 88,335 and females 96,141 undiscounted QALYs, which indicates a slightly higher burden in the male population. Additionally, more undiscounted QALYs were lost in older populations (50+) than the younger population. Patients younger than 50 lost 6,638 QALYs, while patients older than 50 years lost 150,805 QALYs highlighting the greater burden of CLTI in older patient populations.

To assess the uncertainty surrounding the results, we conducted 1,000 Monte Carlo simulations, varying selected economic inputs simultaneously. The PSA produced a mean economic impact of €8.97 billion (Standard Deviation (SD) ± €210.57 million), highlighting the robustness of the model. It is important to note that this figure represents the average outcome across all simulations, not the base case value. The DSA analysis highlights activity impairment (%), return to work after revascularisation (%), and re-admission costs as the three most influential factors impacting the model's cost estimates. Activity impairment has the largest effect, suggesting that productivity loss due to impaired activity levels significantly drives the economic burden of CLTI. The return-to-work rate after revascularisation is the second most impactful, as it affects employment and productivity. Lastly, re-admission costs contribute substantially to costs, reflecting the high financial implications of hospital readmissions in CLTI management.

5. Discussion

5.1 Strategic use of disease burden modelling for innovation and market planning

This report was created to give medtech companies a practical tool for using health economic evidence to support strategic decision-making. Although CLTI is used as an example in this report, the same modelling approach can be applied to many other disease areas and markets. The goal is to shift the perception of these studies—not as purely academic or policy-driven exercises, but as valuable resources to guide innovation and commercial strategy. At the same time, it is crucial to communicate to policymakers and other decision-makers that higher upfront investment in effective treatments should not be viewed as a cost or loss to society. Rather, it represents an opportunity to improve patient outcomes while reducing long-term pressure on healthcare systems—generating both economic and social returns. Before new innovations can be properly evaluated, it is essential to understand the health and economic burden of the disease they are meant to address. This type of modelling provides a foundation for identifying high-impact disease areas, unmet patient needs, and system inefficiencies. It is typically the first step in building a value proposition for new technologies, helping companies prioritise research efforts and plan future product development in a way that aligns with clinical demand and system-level needs.

The structure of this report primarily focuses on the needs of medtech companies, rather than targeting public policy or health system reform. It is not meant to shape health policy directly, but instead to support company planning, innovation, and investment decisions. This reflects how industry is changing: in today's value-driven healthcare environment, companies must be able to demonstrate both clinical and economic value to secure market access and long-term success.

Ireland's medtech sector is at an important juncture. It has a strong foundation in manufacturing and global exports, but staying competitive will require a focused and deliberate expansion into more strategic areas like health economics, market access, and data analytics. These capabilities are critical for companies that want to play a bigger role in shaping healthcare delivery and improving patient outcomes. In developing this report, we also looked at international examples, such as Germany, which has evolved from a manufacturing-based medtech economy into a leader in innovation and healthcare policy. Germany's focus on R&D, structured value assessment, and global market engagement shows how a country can successfully move up the strategic value chain. Ireland could follow a similar path by building health economic expertise internally within companies, strengthening links between industry and academia, and creating the knowledge base needed for long-term, evidence-based growth.

While Ireland itself represents a relatively small domestic market, its medtech sector is globally focused, manufacturing devices and technologies for export to international markets. For that reason, identifying high-burden diseases and emerging healthcare trends globally is critical for Irish companies seeking to align innovation with international demand and long-term strategic value. By applying this approach, Ireland's medtech sector can strengthen its position as a global leader—not only in producing high-quality medical devices, but also in shaping the strategic and clinical direction of medtech solutions worldwide.

Understanding the health and economic consequences of a disease is not just a public health tool—it is a strategic asset. When translated effectively, this data can strengthen business cases, guide R&D, shape market access strategies, and help medtech companies demonstrate value in ways that resonate with payers, investors, and health system stakeholders. This means shifting the conversation around disease burden—from viewing it purely as a societal cost, to recognising it as an opportunity for targeted innovation that can deliver measurable improvements in outcomes and cost savings.

Although CLTI is the focus of this report, the modelling approach presented is flexible and scalable. With robust health and cost data, it can be applied across a wide range of conditions—from oncology to cardiovascular disease to chronic conditions like diabetes. Whether the aim is to build a more targeted pipeline, evaluate new markets, or prepare for payer negotiations, this framework offers a practical and replicable tool for informed, data-driven decision-making. Ultimately, it empowers companies to play a more active role in improving healthcare systems while driving sustainable innovation.

5.2 Evaluating the health and economic consequences of a disease analysis: A Staged Process

Conducting a robust health and economic disease impact analysis involves a series of interconnected stages. Each phase requires specific data inputs and draws on a diverse, multidisciplinary set of skills to ensure the outputs are meaningful and actionable.

	Objective	Key Deliverables:	Required Skillsets
Stage 1: **Defining the Scope and Health Context**	Identify the condition of interest, population scope, and relevant outcomes to assess.	• Disease definition and clinical classification • Population demographics (e.g. age, gender, geography) • Epidemiological data on prevalence, incidence, and progression	• Knowledge of disease epidemiology to understand disease burden and population-level health trends • Clinical knowledge to ensure alignment with real-world care pathways
Stage 2: **Gathering and Synthesising Evidence**	Collect and curate data from multiple sources, including literature, real-world data, and expert opinion.	• Published literature (systematic reviews, clinical trials) • Health system data (hospital admissions, treatment rates) • Expert input where data gaps exist	• Evidence synthesis and critical appraisal • Familiarity with real-world data sources • Communication and stakeholder engagement (e.g. with clinicians or data holders)
Stage 3: **Economic Modelling and Cost Quantification**	Quantify the direct and indirect costs of the disease using established modelling techniques.	• Unit costs (e.g. procedures, medications, hospital stays) • Productivity loss estimates (e.g. absenteeism, unpaid work) • Utility values (e.g. QALYs, health-related quality of life)	• Health economics, including cost-of-illness and cost-effectiveness analysis • Proficiency in modelling tools (Excel, R, Python, or SAS) • Ability to apply discounting, sensitivity analysis, and scenario testing
Stage 4: **Interpreting Results and Drawing Insights**	Translate complex outputs into clear, decision-relevant insights.	• Estimates of direct and indirect costs • QALYs lost and productivity impacts • Visualisations and contextual benchmarks	• Critical thinking and problem-solving • Data interpretation and health communication • Ability to tailor messages for industry, policy, or payer audiences
Stage 5: **Communicating Findings and Supporting Decision-Making**	Deliver the analysis in a format that supports strategic planning and stakeholder engagement.	• Clear reports or slide decks • Stakeholder presentations or workshops • Tailored recommendations (e.g. market access, R&D focus, investment planning)	• Cross-functional collaboration (e.g. with medical, market access, commercial teams) • Strategic thinking • Strong presentation and storytelling skills

5.3 Why CLTI? Relevance for Ireland's Health and medtech Landscape

While the overarching objective of this report is to provide a replicable framework for health and economic consequences of a disease analysis, CLTI was selected as the focus case due to its strategic relevance to both Ireland's healthcare context and its medtech industry.

CLTI is particularly relevant to Ireland due to its ageing population and the increasing prevalence of PAD, which disproportionately affects older individuals. The economic and societal burden of CLTI is further compounded by the high costs of interventions such as amputations and revascularisations, as well as the productivity losses and other costs associated with disability and caregiving. Additionally, Ireland's strong vascular industry, comprising 48 companies focusing on peripheral vascular conditions, 38 addressing coronary conditions, and 14 specialising in atrial fibrillation, underscores the importance of CLTI as both a commercial and public health priority. Furthermore, the vascular industry in Ireland employs over 35,000 professionals. Understanding the burden of CLTI in Ireland not only provides a clearer picture of its healthcare and economic implications but also supports industry efforts to develop innovative treatments and align public health strategies with the needs of patients and stakeholders.

5.4 Key findings from the case study: demonstrating the magnitude of CLTI health and economic consequences

The results of this case study illustrate the significant health, financial, and societal burden posed by CLTI, reaffirming its relevance as a priority area for data-driven planning and innovation. Germany was selected as the initial focus for this study due to its comparatively stronger data resources, providing a useful basis for constructing this model. However, CLTI is still an area with considerable knowledge gaps, even in Germany. The availability of relatively more data, despite these gaps, allowed us to refine our modelling approach.. Nevertheless, the absence of comprehensive data on CLTI highlights the pressing need for further data collection and investigation to fully understand the disease's economic and healthcare impact. Addressing these data gaps would enhance the accuracy of future analyses and support more effective resource allocation for CLTI management.

In this case study, we considered procedural, and the associated follow-up costs. By applying follow-up over a lifetime horizon, the model captured the full economic impact of CLTI-related interventions beyond the initial surgical intervention. These costs significantly contributed to healthcare costs. Excluding these long-term costs would underestimate the true economic burden of CLTI, as follow-up care represents a substantial and necessary part of the patient's overall care journey. The findings further pointed to the critical role of age and gender in exacerbating the burden of CLTI, as older male patients experienced higher rates of amputation, revascularisation, re-admission, etc. Additionally, diabetes was found to be an important risk factor, particularly with respect to amputation. This is confirmed by previous literature that suggests statistically significant differences in the amputation rates among diabetes and non-diabetes people, while the difference in revascularisation rates or event mortality has not been identified as statistically significant from previous research.[18,19] This is in line with the literature, where amongst other things, diabetes was associated with severe below the knee atherosclerosis with calcification and increased technical difficulties in managing the disease.[70] These risk factors combined result in higher costs and higher losses in quality of life. This might suggest that the risk of amputation in CLTI extends beyond vascular factors alone. Although restoring blood flow through revascularisation is crucial in managing CLTI, it does not fully address other critical complications associated with the disease, particularly in those with diabetes. Diabetic patients often experience neuropathy, which leads to a loss of sensation in the extremities. This might make it difficult for patients to detect injuries or infections in their feet and legs early on, allowing minor wounds to progress into serious complications. Moreover, diabetes weakens the immune system, making patients more vulnerable to infections that can spread rapidly if not managed effectively. This combination of neuropathy, and a compromised immune response means that diabetic patients may face an increased high risk of amputation. Addressing these "beyond vascular" factors is critical in managing the full spectrum of risks associated with CLTI.

Our results demonstrated that the total lifetime economic burden of CLTI is significant, reaching approximately € 9 billion. Direct healthcare costs, amounting to over €5 billion, make up the largest portion, with productivity losses accounting for an additional €2.9 billion in unpaid work disruptions. These findings underscored the broad socioeconomic impact of CLTI, extending beyond healthcare systems to affect unpaid work and productivity. Ulceration represents a particularly burdensome complication within the CLTI population, contributing significantly to healthcare costs and patient morbidity. Our model estimated that the cost associated with non-healing ulcers alone amounts to €1.6 billion. Notably, we treated ulceration costs as a separate category, to prevent double counting with other cost categories such as re-admissions, re-amputations, and re-interventions. Moreover, the study additionally demonstrated the significant CLTI's impact on quality of life, with a total QALY loss of approximately 157 thousand across the lifetime horizon. This burden was higher in diabetic patients, particularly men, and more severe in older patients. These results further highlighted the importance of early intervention strategies aimed at improving quality of life, particularly for older and diabetic populations, where the impact of CLTI is more pronounced.

Our results are further confirmed by the Global health and economic consequences of a disease study that showed that CLTI is a globally relevant health problem due to its high health burden. [71] Additionally, a study by Malyar et al. [72] concluded that PAD results in high direct inpatient healthcare costs in Germany. Despite this considerable health and financial burden, there is a lack of studies that comprehensively assess the broader societal impact of CLTI. [13] To illustrate, a review by Shan et al. [73,] who identified seven of cost-utility analyses published up to August 2012, found that most were confined to the healthcare system's perspective. As a result, the broader social implications of CLTI remain largely unexplored. Nevertheless, an economic analysis for CLTI patients in Germany considering the long-term consequences of the disease and related procedures was not identified.

Moreover, the per-procedure costs calculated in this study, which show higher costs for amputation, followed by surgical revascularisation, and then endovascular revascularisation, are consistent with findings from previous cost-effectiveness studies in the literature. While this analysis was not explicitly designed as a cost-effectiveness study, the cost hierarchy aligns with established research. This typically indicates that endovascular procedures are less costly upfront compared to surgical revascularisation. Meanwhile, amputation appears to be the most expensive due to the high costs of operative care and long-term management. These results provide further validation of the model's cost estimations in reflecting real-world economic burdens associated with different interventions for CLTI.

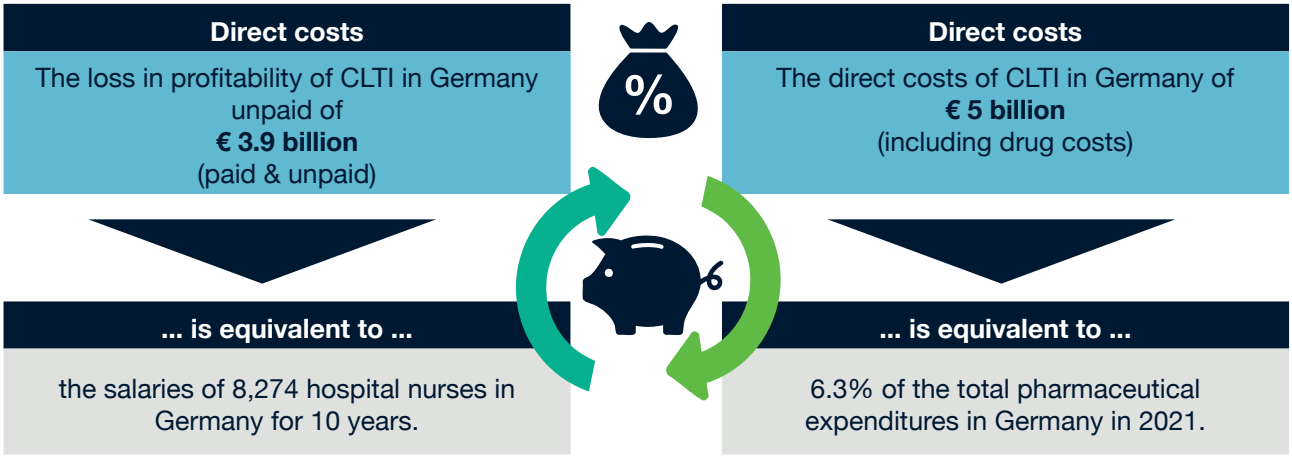


Figure 14: Contextualisation of results

Unpaid productivity losses disproportionately impacted females, who often take on a greater share of household duties, while males tend to experience higher losses in paid employment due to work absences or reduced capacity. The significant role of unpaid work in this economic assessment highlighted the importance of incorporating this factor in economic and health and economic consequences of disease studies of CLTI, especially considering the ageing population. This observation has also been made in previous similar studies in other disease areas. For instance, a study assessing the burden of selected cardiovascular disease (CVD) in Germany estimated that approximately €23.4 billion in productivity losses were attributed to unpaid work, compared to €1.1 billion associated with paid work due to hospitalisation. [74]

Although the focus of the analysis was the socioeconomic impact of disease, it is important to acknowledge that prevention and innovation are key to reducing this burden over time. Revascularisation remains a standard approach for treating patients with CLTI, aiming to restore blood flow in the affected limb. [75] However, even following revascularisation, the risk of serious complications—such as myocardial infarction—remains high. [75] Randomised controlled trials have shown encouraging results for newer treatment strategies, such as Dual Antiplatelet Therapy (DAPT). This approach involves the combined use of aspirin and clopidogrel to prevent platelet aggregation and maintain blood flow. DAPT has demonstrated promising outcomes in reducing the incidence of major adverse limb events (MALE), amputations, and mortality. [75] Another promising intervention is Dual Pathway Inhibition (DPI), where patients receive both aspirin and a low dose of rivaroxaban—a blood thinner. DPI has been associated with a significant reduction in CLTI-related complications and comorbidities. [75]

An international comparison of CLTI treatment practices has revealed wide variations in clinical approaches. Notably, more than half of the countries examined do not follow an "endovascular-first" strategy. Moreover, several unmet needs in CLTI care have been identified, including the absence of a reliable and reproducible measure of tissue perfusion, limited access to effective wound care products, poor adherence to medical therapy, and a need for greater use of artificial intelligence in preoperative risk assessment and care optimisation. There is, however, a strong consensus among physicians internationally on the importance of shared decision-making, ensuring that CLTI patients are informed about all available treatment options. Moreover, the value of early intervention in preventing the onset of CLTI has been recognised in the literature, particularly in at-risk populations. Reducing LDL cholesterol levels was also found to play a role in preventing disease progression. [76]

Together, these findings suggest multiple areas for potential innovation—from pharmacological advances to improved diagnostics and patient engagement—highlighting opportunities to reduce the clinical and economic burden of CLTI.

Looking ahead, early intervention and improved disease management—particularly in younger populations—offer strong potential to prevent progression to CLTI and avoid serious complications such as amputation. Promising advances in wound care, diagnostics, and pharmacological therapies are already demonstrating potential to enhance outcomes and reduce pressure on health systems. However, many of these innovations require further evaluation to fully understand their long-term value and cost-effectiveness. While this study does not offer specific recommendations, it underscores the importance of continued research and evidence generation in future studies. Future studies should aim for instance to quantify the societal impact of innovative interventions, preventive strategies, and alternative treatment approaches— building on methodological frameworks already established in the literature. [77–80]

Importantly, the analytical framework used here is adaptable to other disease areas. For instance, implantable radiation sensors developed for prostate cancer treatment provide a compelling example of how device-level innovation can improve care pathways while offering efficiencies for the broader health system. Applying a similar socioeconomic lens to such case studies could generate valuable insights into the wider impact of medical innovation.

Finally, it is essential to view healthcare not simply as a cost, but as a long-term investment. When decision-makers are presented with evidence that upfront spending on effective technologies can prevent complications and reduce downstream costs, this can help unlock greater access, support medtech innovation, and ensure that meaningful solutions reach the patients who need them most.

6. Conclusion

This report aims to demonstrate how economic modelling can be used as a strategic tool for identifying high-burden disease areas and informing evidence-based planning across the medtech sector. Using CLTI as a case study, the analysis provides robust estimates of the socioeconomic burden associated with the disease, including both direct medical costs and indirect productivity losses. The findings reinforce CLTI's status as a clinically severe and economically costly condition, driven by high rates of amputation, revascularisation, hospitalisation, and long-term disability.

While these insights are useful for healthcare systems and policymakers, their main value in this report is what they offer to Irish Medtech companies. In today's competitive global market, companies need to do more than just manufacture devices, they need to understand which diseases are increasing in prevalence, where health systems are struggling, and where new technologies could make a real difference to patient outcomes and quality of life. Modelling the health and economic consequences of a disease helps with this. It gives companies a practical way to identify unmet needs, build stronger business cases, and guide R&D towards disease areas and markets of future demand.

Although Ireland's medtech sector is already successful on the world stage, it may face long-term risks if it continues to depend on its recognised competencies in manufacturing. To stay ahead, the sector needs to build more strategic capabilities, such as clinical landscape mapping, health economics, market access planning, and early-stage value assessment. This is especially important for SMEs, which make up the majority of the sector but often don't have access to these types of tools and resources. A key point to highlight is that not adopting new treatment options—developed through technological innovation—because of their initial cost can lead to higher overall healthcare costs in the long run. If costly yet effective innovations are not made available to patients, this may result in more severe health outcomes and increased spending on hospital care, complications, or long-term support. Investing in these solutions early can help reduce the future burden on the healthcare system and improve outcomes for patients.

The modelling approach presented in this report offers a way forward. It shows how Irish Medtech companies can use data to spot emerging opportunities in healthcare, and to engage more effectively with payers, regulators, and investors. This framework can be applied to other disease areas too, helping companies with early-stage marketing, strategic planning, and portfolio decisions. Ultimately, it supports companies in moving earlier in the innovation process and becoming partners in health system improvement.
Over time, investing in these skills and tools will be essential for Ireland to maintain its position as a global leader in medtech. It will help the sector shift into higher-value areas, make better R&D investment decisions, and ensure that technologies developed in Ireland are truly meeting the needs of healthcare systems around the world.

The findings of this study contribute directly to Ireland's broader Moving Upstream agenda by providing evidence of how preventive, medtech-enabled interventions can reduce system costs while improving health outcomes. Together, the two reports establish both the strategic rationale and the economic foundation for Ireland's leadership in upstream medtech innovation.

7. Appendix

Appendix I: Socioeconomic data

Employment rates

Age Group	Male (%)	Female (%)
Total	64.4	54.5
15+	80.6	73.1
20-24	72.0	67.7
25-29	84.3	77.8
30-34	89.4	79.0
35-39	90.7	79.7
40-44	90.9	82.2
45-49	90.7	84.0
50-54	89.6	83.4
55-59	85.8	78.6
60-64	67.4	59.2
65-69	22.9	16.0
70-74	17.7	11.2
75+	3.6	1.3

Note: The employment rates has been adjusted based on evidence of the literature for the percentage of PAD patients in employment (see Methods section)

Gross wage

Age Group	Male (€)	Female (€)
Total	25.3	20.84
under 25	13.25	13.02
25 -29	20.38	19.25
30-34	24.01	21.61
35-39	26.26	22.4
40-44	27.59	22.59
45-49	28.57	22.49
50-54	29.22	22.16
55-59	29.9	21.99
60-64	29.33	21.69
65+	21.46	19.49

Time spent in unpaid work per week

Age Group	Male	Female
From 15 to 20 years	6.07	9.45
From 20 to 24 years	7.23	11.55
From 25 to 44 years	14.7	27.42
From 45 to 64 years	16.68	26.02
65 years or over	22.17	29.52

Appendix 2: Calculation steps for absenteeism and presenteeism and activity restriction

Absenteeism

In a first step, we apply absenteeism rates to the defined patient population, the country's employment rate and working hours. Hence, we estimate the work time loss of paid work in hours due to complication events in diabetes patients across the entire economy as written below:

$$Abs_{agc} = PA * WH_{ag} * ER_{ag} * RTW * A_c \quad (1)$$

where Abs_{agc} is the avoided age and gender specific hours of paid work lost due to absenteeism throughout the model.

Absenteeism

In a second step, we apply presenteeism to the defined patient population and the remaining working time. Hence, we estimate the productivity loss while at work in hours due to complication events in diabetes patients across the entire economy. The formula is given below:

$$Pres_{agc} = (PA * WH_{ag} * ER_{ag} * RTW - Abs_{agc}) * P_c \quad (2)$$

where $Pres_{agc}$ is the avoided age and gender specific hours of paid work lost due to presenteeism throughout the model.

Activity restriction

The following formula provides the active time loss for unpaid work activities:

$$ActRes_{ag} = \Theta_{ag} * AR$$

where $_{ag}$ is the avoided age and gender specific hours of unpaid work lost due to activity restrictions throughout the model, Θ_{ag} is the age (a) and gender (g)-specific number of activity hours AR is the rate of activity restriction.

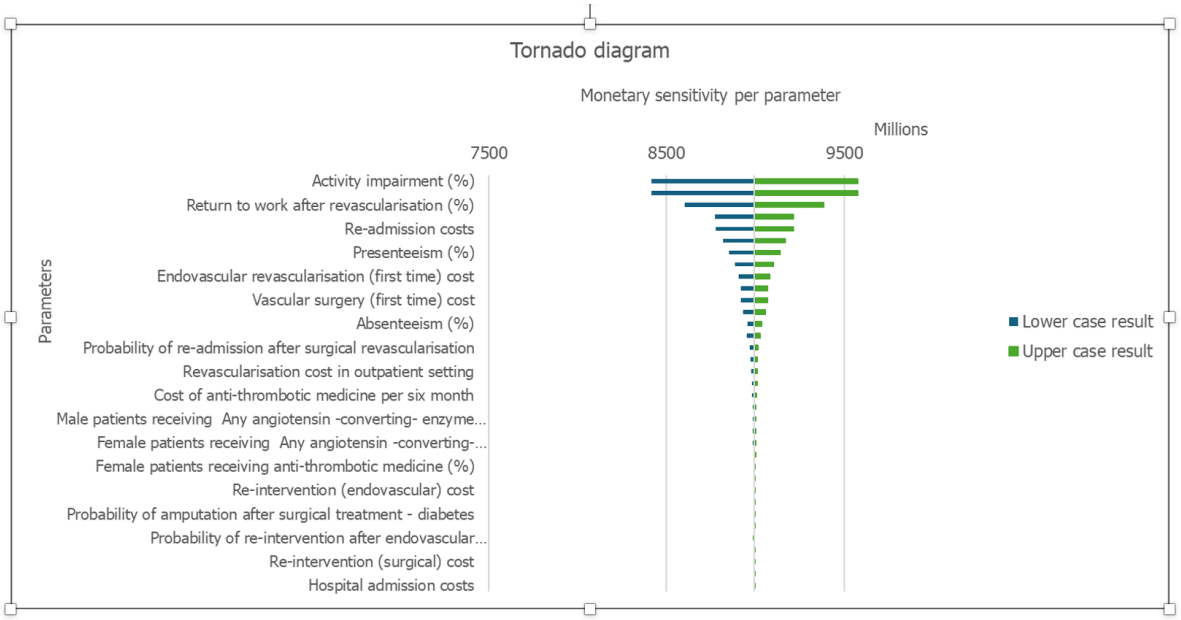
The formula's parameter and subscript description can be found in the following table.

Parameter	Description
PA	Number of patients
WH	Average number of working hours per cycle
ER	Employment rate
RTWr	Return to work rate
A	Absenteesim rate
P	Presenteeism rate

Subscript	Description
a	Age
g	Gender

Appendix 3: Discounted results

Total direct costs (excluding drug costs)	4,082,726,207.92 €
Total drug costs	143,948,875.50 €
Total paid productivity losses	786,796,889.75 €
Total unpaid productivity losses	2,336,930,179.89 €
Total costs	7,350,402 ,153.05 €



This tornado diagram illustrates the monetary sensitivity of various parameters in the model, displaying how changes in each parameter impact the overall cost estimates for CLTI management. The horizontal bars represent the monetary range (in millions) resulting from a 20% increase or decrease in each parameter. Parameters are sorted by their impact, with the most influential at the top. 'Activity impairment (%)' and 'Return to work after revascularisation (%)' have the largest monetary effect, indicating that variations in these factors lead to the most substantial changes in overall costs. The green bars show the upper-bound results, while the blue bars show the lower-bound results. This visualization helps identify which parameters contribute the most to cost variability, emphasizing key areas to prioritize for accuracy in future data collection and modelling.

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