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A Markov cost-effectiveness modeling framework for evaluating wound dressings: A concept for practical implementation of economic evaluations in an informed dressing selection process

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Running head: **Markov cost-effectiveness modeling framework**

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Highlights

- Cost-effectiveness evaluations for wound dressings are rarely used for purchase decision-making
- We developed a new Markov cost-effectiveness model merging clinical and industry data to compare polymeric membrane dressings with passive foam dressings
- Cost analysis conducted using this modeling revealed that polymeric membrane dressings could cost half as much as passive foams over 26 weeks
- The modeling identified the less frequent changes of the inflammation-modulating polymeric membrane dressings as a key factor explaining this major cost difference
- Healthcare facilities should conduct more thorough cost-effectiveness evaluations for informed purchasing decisions, as oversimplistic approaches may lead to wrong assessments of the long-term costs

Abstract

Aims: Exemplify the potential of using health economy modeling and simulations to support and optimize wound dressing purchasing decisions. **Materials and methods:** We developed a Markov cost-effectiveness modeling framework fusing clinical and industry sources of healing and cost outcomes for evaluating dressings, focusing on polymeric membrane dressings compared to passive foam dressings without active inflammation modulation components. We calculated the wound care costs for patients with and without diabetes, as well as for infected and non-infected wounds, to illustrate the effectiveness of this model in supporting decision-making. **Results:** The model results demonstrated that polymeric membrane dressings reduce the cumulative treatment costs compared to passive foam dressings, due to fewer dressing changes and lower associated labor costs, regardless of the initial product price differences. **Conclusion:** Cost-effectiveness calculations should be performed in healthcare facilities to support purchasing decisions based on true cost analyses. Making purchasing decisions focusing on the dressing price alone may provide wrong estimates of the real cost differences.

List of abbreviations:

ICER	incremental cost effectiveness ratio
OECD	Organization for economic cooperation and development
PMD	polymeric membrane dressing
PsvFD	passive foam dressing

1. Introduction

In health economics, cost-effectiveness analyses are essential for evaluating the costs and outcomes of alternative medical interventions. In wound care, these analyses often focus on dressing costs, the frequency of changes, and the associated hospital staff time, potentially including the time for wound closure and the use of auxiliary treatments or medications. Additionally, wound care in a clinical setting includes healthcare costs associated with hospital stays, such as the application of dressings by clinicians, the treatment of potential wound infections and surgical interventions, which frequently surpass the cumulative cost of the dressings themselves. The rate of wound healing also influences the overall costs, as smaller wounds require less frequent dressing changes and less labor-intensive care.[1] Often, the easiest route for healthcare decision-makers is to prioritize dressing choices based solely on product price. However, this approach overlooks critical factors, such as the clinical labor time required for wound dressing applications, which heavily impacts the total cost of care. For example, the time required for cleansing and debriding wounds can vary based on the type of dressing. Products that enable undisturbed healing, such as those with longer wear times, can significantly reduce the overall costs by minimizing the frequency of dressing changes and the associated labor time. This highlights the need for more advanced decision-making tools that incorporate clinical outcomes and labor costs to support purchasing decisions. This conceptual work presents a Markov cost-effectiveness modeling framework designed to evaluate wound dressings, specifically comparing polymeric membrane dressings (PMDs) with passive foam dressings (PsvFDs). The PMDs are multifunctional dressings that include a wound cleanser, moisturizer, superabsorbents and a semi-permeable membrane, which together contribute to improved healing outcomes by modulating inflammation and reducing the frequency of dressing changes. In contrast, PsvFDs function passively by absorbing wound exudate without actively supporting wound healing. While PMDs have shown clinical advantages, their cost-effectiveness in comparison to PsvFDs has not been rigorously evaluated.[2,3]

The purpose of this study was to provide a comprehensive cost-effectiveness analysis comparing PMDs with PsvFDs, focusing on their long-term cost implications in wound care. Through a Markov modeling framework, clinical and industry data were used to simulate the costs of wound care for different patient populations treated with either PMDs or PsvFDs.[1,4–10] This approach exemplifies the potential of using health economic simulations to support purchasing decisions based on true cost analyses, rather than simply selecting the lowest-cost supplier, which may lead to higher long-term costs. Although computational models have been extensively used in other medical fields, such as vaccines and cardiology, their application in wound care has been limited. Few cost-effectiveness models have focused on wound dressings alone, and none have addressed non-silver-releasing foam dressings like PsvFDs. Furthermore, the available studies tend to be theoretical, lacking sufficient connection to clinical practice, which limits their real-world applicability.[1,4–10] This study aims to fill this gap by demonstrating the practicality of applying Markov modeling to real-world data and its potential use in hospital purchasing processes. The objective of this study was therefore to highlight the benefits of Markov modeling as a tool for hospitals to make informed, cost-effective decisions between different dressing types. This work specifically illustrates how the cumulative cost difference between PMDs and PsvFDs cannot be projected based solely on product price, as the frequency of dressing changes and labor costs play a crucial role in the overall cost of wound care. The findings will serve as an example of how cost-effectiveness analyses can be integrated into healthcare facilities to optimize purchasing decisions and reduce long-term costs.

2. Methods

We first developed a generic model implemented using Python code to compare the cost-effectiveness outcomes among potential alternatives of different foam dressing products. Next, to exemplify the utility and practicality of this in-silico model, we employed it to compare the cost implications between choices of applying PMDs versus PsvFDs in virtual sub-populations considered at high, medium, and low risk for wound and patient deterioration. The main model assumptions and their justifications are detailed in **Table 1**. In order to validate and obtain error margin estimates for the model regarding reported real-world (ground-truth) financial data, we reconstructed two real-world clinical cases. These methodological steps are described as follows.

2.1. Design of the in-silico model

We used a 3-state, dynamic probabilistic Markov model[a] (**Figure 1**) to evaluate the weekly accumulation of costs (in US dollars) attributed to treating patients with chronic wounds at various sizes and conditions based on the medical background and the type of the applied dressing, which was assumed here to be either a PMD or a PsvFD (**Table 2**). The current Markov modeling framework only considered the direct hospital costs incurring during inpatient care, i.e., no organizational overhead costs, rehabilitation or other post-discharge costs or loss of capacity (of the patient or their family members) to work were accounted for. As an illustrative example, we used the modeling to evaluate the cost-effectiveness of selection of a PMD versus a PsvFD throughout a 26-week-long care pathway, within the same care setting (assuming inpatient care throughout), either for a certain population or for an individual, as further detailed below.

The model was formulated using recursive functions programmed in a dedicated Python code (Python Software Foundation, www.python.org). The model generates virtual patients belonging to a population of a pre-defined size (100,000 virtual patients selected here throughout) and with pre-determined age range and gender characteristics and with a chronic wound simulated in each such virtual patient. The initial simulated wound in each patient is considered to advance towards healing such that its size (in terms of surface area per each time point) reduces over time at a rate depending on a pre-defined set of probabilities, including the weekly likelihood of that wound to become infected and the probability of the infection to regress later on, if it had occurred (**Table 3**). Each simulation step is equivalent to a week of wound care treatment. It was assumed that the type of the applied dressing, either PMD or PsvFD, does not change during the course of treatment (to clarify, the dressing type is not replaced with another type, though obviously dressing changes do occur). Each dressing type (PMD or PsvFD) had its own set of parameters characterizing the unit cost of the product, and specifically for the PsvFD, that unit

[a] A probabilistic Markov model serves as both a graphical and mathematical depiction of the potential outcomes within a series of interrelated choices within a given process, such as wound care in this context. This model offers a structured representation that evaluates possible events (states) and defines decision points, assessing the quantitative probabilistic likelihood of transitions occurring between these states in the real-world. These transitions represent the movement or change from one state to another, reflecting outcomes such as improvement or deterioration of the treated wound, as well as potential patient mortality. The graphical representation commonly employed for such modeling is termed a ‘decision tree.’ This decision tree visually organizes the potential pathways and probabilities associated with the different choices and their outcomes (**Figure 1**).

cost included the costs of the associated cleansing and adhesive materials needed for using the dressing in practice, such as saline solution/spray and tapes, respectively (**Table 2**). We further considered the cost of the nursing time required for changing the dressing and the number of dressings to be used per each treatment week (**Table 2**). The PMD and PsvFD types were then studied under equal cost conditions of labor and hospitalization, and likewise, identical likelihood of occurrence of wound infections in the (simulated) institute and patient population characteristics, and the same postulated weekly rate of reduction in wound size (**Table 3**), to facilitate consistent PMD to PsvFD comparisons. The values for the above dressing parameters (**Table 2**) and for the parameters associated with the probabilistic progression of the wounds in the chosen population (i.e., subject to or involving chance variation based on the probabilities detailed in **Table 3**) were all adopted from published literature and industry data (from multiple companies) available in the public domain, as detailed in **Tables 2** and **3** and the references cited therein.

At each simulated week, the probabilities for the wound to halt or advance positively towards closure are considered, and a pathway of progression is decided, which may change the wound condition. The simulation of the care of a specific virtual patient may also terminate according to a death probability which depends on the age, gender and medical background of the individual, as well as their wound size and probability of wound infection. For the medical background, we currently chose to focus on the presence or absence of diabetes as the only contributing factor, given its recognized dominance as an underlying condition that may affect wound healing. The wound size may decrease at each simulation step, and when the size of the simulated wound becomes smaller than 1 cm^2, the wound is considered to be near-closed, which is an end-point of the simulation for the individual. This iterative (repeatedly applied) calculation process continues for each simulated patient until this successful clinical outcome is achieved, or until the 26 weeks of the time horizon in the modeling have elapsed, or until the virtual patient 'dies'.

2.2. Protocol of simulations and outcome measures

Sub-population studies: First, the modeling (**Figure 1**) was used for Monte Carlo simulations (generating repeated random sampling) to compare the cost of care of the simulated wounds by means of PMD or PsvFD among three sub-populations, all comprising of virtual patients older than 64 years (**Figure 2**).[b] These selected sub-populations were: (i) diabetic males with an infected wound (being at the highest risk of wound and patient deterioration); (ii) diabetic females with a non-infected wound (being at a medium risk); and (iii) non-diabetic males with a non-infected wound (being at the relatively lowest risk). These different virtual sub-populations were generated to explore potential effects of diversity in patient (and patient group) characteristics. Each such sub-population comprised 100,000 virtual patients with an initial chronic wound of size 50 cm^2. The cumulative cost of treatment for each patient belonging to one of the above sub-populations was calculated by summing the expenses for the total number of the dressing products used, the nursing labor time and the cost of hospitalization (proportionally to the simulated total nursing labor time). The simulated overall death rate within each sub-population was also recorded, and these data were then further used to calculate the Incremental Cost Effectiveness Ratio (ICER), which is generally defined as the incremental change in costs divided by an incremental change in a related health outcome. In the current modeling, we constrained the Markov simulations to run up to 26 'treatment weeks' (as a 'stop condition'), so a wound healing period cannot be used to represent the 'increase in effectiveness' variable, however, we did conduct an indirect ICER analysis using the calculated death rates in the studied sub-populations. Lastly, the runtime for each sub-population analysis ranged between 13–16 seconds using a 64-bit Windows 10-based workstation with an Intel Core i5-5200U CPU 2.20 GHz and 8 GB of RAM.

Sensitivity analyses: Second, sensitivity analyses were conducted for the above simulated sub-populations, in which the same unit price was assumed for both the PMD and the PsvFD, for the purpose of isolating the indirect costs of the wound care pathway, namely, the costs of the number of dressing changes and time for a change of dressing in terms of nursing labor, from the direct material costs. These sensitivity analyses were repeated for the low-end and high-end unit costs listed in **Table 2**.

[b] We used a Markov model to simulate the progression of chronic wounds over time, with each state representing different clinical conditions. Transitions between states were based on predefined probabilities. To account for variability and uncertainty in outcomes and costs, we applied Monte Carlo simulations within this framework to facilitate evaluation of the range of possible outcomes and assessment of the cost-effectiveness of the studied dressings under the simulated clinical scenarios.

Model validation against real-world cases: Third, the model was used differently, to reconstruct two published real-world case studies, described by Stenius and colleagues[11] and by Stenius et al.[12], in order to investigate the cost-effectiveness aspect as reflected in these individual clinical case stories as they were reported, and also, importantly, to estimate error margins of the current modeling with respect to reported real-world ground truth financial data. That is, each of the two reconstructed clinical cases was run in the above modeling framework (**Figure 1**) to hypothetically study the cost implications of use of a different dressing type than that which was applied in reality, as means for further exploration of the applicability of the current Markov modeling and its verification and validation. For completeness, the first case study was of a previously healthy 38 years old woman who contracted tonsillitis that led to myocarditis, which then deteriorated to a congestive heart failure and several acute myocardial infarctions. During her stay at the surgical clinic, she developed a large category-4 sacral pressure ulcer/injury (**Figure 3**; Case #1). At the start of treatment, her wound had a size of 63 cm^2 (**Figure 3**; Case #1, left panel). After 10 weeks of using PMDs, at a reported total cost of €1700 (inflation-adjusted cost: €2226, currently $2358), the wound completely healed (**Figure 3**; Case #1, right panel). Of note, six months after the closure of her pressure ulcer/injury, this patient underwent a flap surgery for cosmetic purposes to fill a large crater that formed after the wound closure (which is the surgical incision scar shown in **Figure 3**; Case #1, right panel).[11] As this surgical cosmetic procedure was not directly related to the cost of treating the wound, it was not considered in the current cost-effectiveness analyses. The second case was of a 45 years old woman who was a heavy smoker and a vegetarian, and also a wheelchair user due to multiple sclerosis. She developed a large, category-4 pressure ulcer on her right ischial tuberosity measuring 53.5 cm^2 (**Figure 3**; Case #2, left panel). After 7 weeks of treatment using PMDs, her wound size decreased to 17.6 cm^2 (**Figure 3**; Case #2, right panel), however, for this case, the total cost of the treatment was not reported. We simulated two corresponding hypothetical individual 'virtual patient' scenarios according to which, both of the above cases were treated by PsvFDs. We then used the first case where the total cost of the treatment de facto, i.e., using PMDs, was reported, for direct validation purposes against the model-predicted cost of this treatment course for the respective individual case. This simulation then facilitated the analyses of the second case where the actual incurring costs were unknown, but the treatment information and outcomes have been documented as detailed above. The first case study reconstruction in the modeling was programed to stop when the wound size was smaller than 1 cm^2 (which was considered as acceptable closure), while the second case study stopped when the wound size was smaller than 17.6 cm^2, which aligned with the documented case, as reported.

3. Results

3.1. Monte Carlo analyses for sub-populations

The current simulations successfully reproduced the well-established nonlinear closure process of real-world open wounds, which typically follows an exponential course with the rate of change of wound area progressively decreasing as the residual wound area approaches total closure, as demonstrated in **Figure 4** which plots the wound size over time for each sub-population treated with PMDs. Moreover, the simulations also adequately represented the impeding effects of either diabetes or wound infections on the closure rate (**Figure 4**). Of note, the wound closure rate for the simulated sub-population of diabetic males was overall similar to that of the diabetic females albeit mildly slower in the first few (2-3) weeks for the males, until the simulated infection was 'mitigated' (**Figure 4**). The realism of these simulated data rendered the current modeling suitable for the further reported Monte Carlo analyses of treatment cost.

The Monte Carlo analyses revealed that for all the tested sub-populations, there was considerable financial advantage to using PMDs over PsvFDs (**Table 4**). For diabetic males with an infected wound (considered as the highest risk group), the mean calculated costs of wound care per patient was \$1902 while using PMDs, as opposed to \$3853 while using PsvFDs (**Figure 5**). For diabetic females with a non-infected wound, that mean cost was \$1845 for using PMDs, compared to \$3733 for PsvFDs (**Figure 5**). For non-diabetic males with a non-infected wound, the mean was \$1191 for PMDs compared with \$2411 for PsvFDs (**Figure 5**). Overall, these results reflect a treatment cost that is approximately 50% lower for PMDs than for PsvFDs during a 26-week course of wound care. Interestingly, for both types of the studied dressings, the simulated presence of infection increased the inter-patient variability in incurring costs, which reflects that the biological variability in wound healing increases with the complexity of the pathophysiology of the underlying conditions, resulting in more variable treatment costs. The differences in death rates associated with use of the PMDs versus PsvFDs were negligible across the sub-populations, but slightly in favor for the course of treatment by means of PMDs (**Table 3**). Related to these results (**Table 4**), the ICER analysis indicated that if the willingness to pay is $7500 for a 1%-lower death rate in a population of 100,000 diabetic wound care patients, then using PMDs will theoretically lower the death rates by 0.1% to 0.2% in this population (**Figure 5**), i.e., 1 to 2 fewer deaths per 1,000 patients.

3.2. Sensitivity analyses to isolate the indirect from the direct wound care costs

In agreement with the above results, and even when the unit dressing cost (including any auxiliaries for cleansing and adhesion for use with the PsvFD) were the same for the PMD and PsvFD, that is, when effectively the PsvFD was less expensive in unit price from the PMD, the Monte Carlo analyses indicated that there was a considerable financial advantage in using PMDs over PsvFDs (**Table 5**). Specifically, when considering the low-end unit price as being the same price for the PMD and PsvFD (**Table 2**), the mean calculated costs of wound care per patient were 1.89, 1.87 and 1.89 times greater for the PsvFD than for the PMD, for the diabetic males with an infected wound, diabetic females with a non-infected wound and non-diabetic males with a non-infected wound, respectively (**Table 5**).

When considering the high-end unit price (**Table 2**) as being the same for the PMD and PsvFD (e.g., in a local wound care market that is overall expensive, or, similarly, while representing the effect of current inflation rates concerning material costs), the simulation findings were similar. Specifically, for such high-end prices, the mean calculated cost of wound care per patient was 1.86 times greater for the PsvFD than for the PMD, for all the studied sub-populations (**Table 5**). Considered together, these results demonstrate that the cumulative indirect cost of wound care is 46% to 48% lower for the PMDs compared to the PsvFDs during a 26-week course of treatment. Importantly, the above results clearly associate these cost savings while using the PMDs with the lower *indirect* (i.e., the nursing labor-related) wound care expenditure.

3.3. Real-world case study reconstructions used for validation and error margin estimates

For the first reconstructed case (**Figure 3**; Case #1) where the de facto treatment cost using PMDs was reported ($2358 following inflation adjustment and €/$ conversion),[11] the simulated cost of treatment using the same PMD dressings was conservatively approximated as the mean predicted cost for wound closure in a patient at the highest risk, i.e., $1902 (**Table 4**). This assumption of a high-risk patient has been made considering the complex medical conditions described in the respective case report, which included the severe cardiac complications of the treated woman that most likely negatively impacted her tissue perfusion quality. Thereby, her tissue repair capacity was assumed to be compromised at least as severely as how diabetes would have affected it, and likewise, the suspected infection given the size and extensive undermining of her wound[c] (**Figure 3**; Case #1). Under the above assumption, the current modeling underestimated the cost of closure of the wound in Case #1 by means of PMDs by 19%, which is reasonably close to reality, and therefore, provides validation for the model and can further be considered an error margin estimate for other simulations. Importantly, this error margin is substantially lower than the predicted cost savings of 46-48% as indicated above. In other words, even if the maximal extent of the predictive modeling error calculated from the above case reconstruction is to be considered, then use of PMDs for treatment should still save 27-29% of the total wound care costs.

While the above calculation is a highly conservative estimate of the modeling error, an alternative assumption is that the model consistently underestimates the cost of care by 18%, not just for PMDs but regardless of the type of the dressing used, in which case the use of PMDs resulted in saving of $(1-0.18)×3906 - $2358= $845 which would be added to the cost of care if a PsvFD was hypothetically chosen (i.e., so that the projected treatment cost would have totaled as $2358 + $845= $3206 for a theoretical treatment of this patient using PsvFDs). For this error estimate of a consistent underestimation of the wound care cost by the modeling, the selection of PMDs therefore saved $845/$2358= 36% of the actual incurring cost of wound care for this patient (**Figure 3**; Case #1). That is, considering both calculation paths for the error margin estimates as

[c] One of the most common causes of wound undermining is infection.

detailed above, the range of savings resulting from preferring a PMD over a PsvFD for treating this case is at least 28% to 36%, with a midrange least saving of one-third of the total cost. This result is also consistent with the findings from the sub-population studies reported above (**Figure 5** and **Table 4**).

The simulated cost of treating the second reconstructed case[12] was $351 for use of PMDs and $710 for using PsvFDs (**Figure 3**; Case #2). Though the ground truth cost had not been reported for this case (**Figure 3**; Case #2), the financial consequences of choosing PsvFDs over PMDs (assuming a consistent model underestimation error as explained above) can therefore be evaluated as paying twice the cost of wound care for the entire course of treatment for Case #2. To summarize all the above analyses, conservatively, and taking the two real-world case studies (**Figure 3**) into consideration, the savings associated with use of PMDs are third to half the cost of using PsvFDs.

Lastly, it should be noted that while patient ages in these illustrative cases differ from those assumed in the modeling work, the patient cases were included to provide an additional, real-world perspective. By integrating these case descriptions with the model-based analyses, a holistic view of the cost-effectiveness of wound care interventions is provided, which demonstrates the (inherent) gap between theoretical modeling and actual patient experiences.

4. Discussion

Chronic wounds continue to be a major threat to global healthcare systems, and in particular, they impose an ever-growing expenditure on treatment and management[13]. The burden of diabetes rises sharply,[14] an increasing number of people spend their lives in wheelchairs and beds, and the incidences of diabetic foot ulcers, venous leg ulcers and pressure ulcers/injuries all climb correspondingly, and so are the costs of wound care[15] . The COVID-19 pandemic further caused high loads on hospital resources and led to shortage of nurses, which overall, increased the occurrence of hospital-acquired pressure ulcers/injuries including device-related pressure ulcers/injuries[16]. Furthermore, the COVID-19 circumstances often led to late diagnosis or sometimes neglect of venous leg ulcers and diabetic foot ulcer cases in the community, due to more difficult access to health services[17,18]. Altogether, these factors fuel the rising expenditure on wound care, and as every dollar spent on treating wounds is not invested elsewhere, there is a pressing need to employ more sophisticated, methodological cost-effectiveness evaluations in wound care and management, as opposed to making purchase decisions that are simply driven by a low unit price.

The most basic medical device used in wound care is dressings, however, a dressing is not a stand-alone intervention, as the application and removal of dressings, preparation of the wound-bed for dressings and routine evaluations of the status of the wound and peri-wound requires the time, experience and associated costs of experienced healthcare professionals, which is typically an expenditure that substantially exceeds the dressing (materials) cost. In addition, a dressing which does not induce the optimal conditions for wound healing would imply that the healing period (if the wound eventually closes) lengthens, which in turn means that a greater number of products is to be used, and importantly, a longer time of healthcare professionals needs to be dedicated to the (longer) treatment period. This is where the cost-effectiveness component of wound care plays a major role: As the most expensive item in the cost of care is typically the nursing time (with COVID-19 escalating this), and since the nursing time almost equals the cumulative cost of all the other hospital healthcare components (i.e., the cost of a hospital bed per hour; **Table 3**), any dressing product should be evaluated in the context of the overall cost of care associated with its use. Importantly, a more expensive dressing product can outperform a cheaper product from a cost-effectiveness perspective, merely by efficiently absorbing and retaining exudate and modulating the inflammation in a wound, which forms a more supportive environment for wound healing[19] . This, in turn, keeps the healing time around the necessary minimum, and requires fewer dressing units to be applied on the wound throughout the course of treatment, which ultimately means less change events, and hence, shorter nursing labor time (which is, again, the most expensive component in the cost of the wound care bundle).

4.1. Interpretation of the findings

To illustrate and quantify the above concepts and demonstrate the usefulness of the current Markov modeling, we selected to study the cost-effectiveness of PMDs compared to passive foam dressings. The choice to compare these dressing types was driven by the unique composition and properties of PMDs which, as opposed to PsvFDs, were shown to modulate the inflammatory status of wounds, resulting in an overall lower incidence of excess exudation rates[2,3,20–23] such that, according to the sources cited in **Table 2**, they require approximately 50% less frequent changes which should lead to substantially lower wound care costs. Indeed, our current modeling work revealed that the cost of treating wounds with PMDs is as low as ~50% of the total cost of treating them with PsvFDs (**Figure 5; Table 4**), which considerably exceeds any potential price differences between the PMD and PsvFD products that were considered in the simulations, or those existing in any particular market (**Table 2**). This important result is mainly due to the less frequent changes of PMDs throughout the course of treatment, where, for example, it was almost twice more expensive to treat simulated sub-populations of diabetic females and non-diabetic males with non-infected wounds by means of PsvFDs compared to treating them with PMDs (**Figure 5; Table 4**). This is albeit that the PMD unit price may be similar to the price of PsvFDs if auxiliary cleanser materials (saline solution/spray, gauze) and adhesion (tape) aids are not accounted for (**Table 2** and the references cited therein).

Furthermore, the current simulation results assuming the same unit price for the PMDs and PsvFDs (which implies that the PsvFD dressing cost is in fact lower, as it requires purchasing of auxiliaries such as cleansing and adhesive materials), demonstrated, as could be expected, that the cost of materials in the total cost of wound care is low to negligible with respect to the indirect costs (i.e., the cost of the nursing time). This concept has been discussed in the literature previously.[24,25] However, the current study utilizes Markov-based modeling to provide a more detailed quantification of how practitioner time contributes to the overall cost of wound care in comparison to the cost of the wound care products themselves. Moreover, this study demonstrates, for the first time, that there is interaction between the selected wound care product type and the nursing time, as some products – requiring a longer nursing time to be invested in the product and practice, inflate the nursing time and labor costs and therefore, the total expenditure despite that such products appear to be less expensive from a (simplistic) unit price perspective. Hence, for immediately translating the current findings to best practice, the relevant question to be asked by hospital administrators when attempting to project the total cost of wound care in their institute if a change in a dressing type is to be made is – how would the shift to the new dressing product type affect the *nursing time* associated with using the candidate product. Of note, quality-adjusted life year (QALY) comparisons were beyond the scope of this study, as our focus was on hospital cost savings through reduced dressing changes and associated labor costs. These may not always directly translate into favorable QALY or cost per averted death metrics, but can nevertheless considerably improve the financial performance of relevant healthcare facilities.

4.2. Model limitations

As with all modeling studies, there are inherent limitations to consider which relate to the assumptions that were made (**Table 1**). First, only two dressing types were analyzed and the model assumed consistent application of each dressing type throughout the treatment period, which may not reflect real-world scenarios where different products are used concurrently or over time. Second, the model accounted for higher survival rates in females (**Table 3**) but not for gender-specific clinical data for wound healing outcomes. Additionally, only diabetes was considered as a contributing background condition, though future work could incorporate other conditions such as obesity, cardiovascular diseases, and chemotherapy. To validate our model and place it in a real-life context, we reconstructed two real-world case studies and compared the projected costs of using PMDs versus PsvFDs. While our model revealed substantial cost savings with PMDs, the complexities of real-world wound care and variability in clinical practices mean that these findings should be interpreted with caution. Despite its limitations, our model highlights the importance of considering the overall cost of care, including nursing labor time and the frequency of dressing changes, in evaluating the cost-effectiveness of wound care interventions.

4.3. Modeling considerations in view of practicality and the future implementation potential

We refrained from utilizing weighting techniques to overrepresent or underrepresent specific age sub-groups from among those aged 64+. In the United States, Europe, the UK and Australia, a significant proportion of hospitalized individuals are typically aged 65 and above, and this is primarily attributable to the elevated prevalence of various diseases like cardiovascular problems, cancers, respiratory illnesses, and neurological disorders necessitating acute hospital care. However, when specifically examining wound care patients, presumptions regarding age demographics pose challenges. For instance, pressure ulcers/injuries can stem from brain trauma, central nervous system damage or prolonged surgeries across all age groups. Notably, research in this domain has indicated that "the influence of age might be obscured by other demographic and clinical factors".[42] Similarly, diabetic foot ulcers (DFUs) can arise from minor foot injuries at any age, typically above 50. Intriguingly, younger and middle-aged adults with DFUs often present with more severe wounds and a higher likelihood of infections, leading to hospitalization compared to older adults in similar circumstances.[43,44] Given these complexities, we opted against age-based weighting adjustments, recognizing the potential for such measures to arbitrarily skew the representation of certain patient characteristics.

The complete set of data required as inputs for the current modeling (in **Tables 2** and **3**) was not coherently available from a single country, and even if a given country would have such a hypothetical perfect set of input data, the purpose of the current work was not to develop a model that is specific for an individual country. We did restrict the data sources to include only information from developed (Organization for Economic Co-operation and Development, OECD member) countries. In this context, both the United States and the United Kingdom (from which the majority of input data were adopted) have well-established healthcare systems, and although there are some differences in healthcare delivery and reimbursement mechanisms, as well as in clinical guidelines, there is no reason to assume that findings based solely on US data would not apply in the UK and vice versa. A potential, future research goal could be to tailor the modeling to a specific country, and further to a certain healthcare system and even facility; the current work contains the entire specification for this purpose, but such future work will require additional implementation research to adjust the model parameters to the specifics of the healthcare system and setting of interest.

Lastly, hospitalization costs are always multifaceted and are extremely difficult to quantify in a single measure. In this context, the ‘cost of hospital bed per hour’ used in **Table 3** does not necessarily captures the complexities of resource allocation and the differences between inpatient and outpatient facilities. In the current healthcare landscape, where outpatient care is increasingly prevalent, relying solely on cost-per-bed may not fully represent the cost efficiency of a wound care treatment. Moreover, calculating marginal cost, which is the additional cost incurred by treating one more patient, is also challenging due to the mixture of fixed and variable costs that is inherent in hospitals. Fixed costs, such as facility maintenance and administrative expenses, remain constant regardless of patient volume, while variable costs, like medical supplies and staff salaries, fluctuate with patient numbers. This blend of costs makes it difficult to pinpoint the true incremental cost of providing care over time. With this in mind, the simplifications made in the current modeling, including in the aspect of 'cost of hospital bed per hour', were made for practicality and simplicity whereas a more academic/theoretical analysis approach would have perhaps considered additional dimensions of complexity as noted above.

4.4. Concluding remarks

Any healthcare organization that wishes to remain sustainable and financially viable must employ contemporary cost-effectiveness modeling for informed decision-making, i.e., not just base their routine purchase decisions on buying the cheapest products in the market to cut down expenses, but also consider the impact on the overall clinical outcomes and financial metrics.[8,9] Surprisingly, there are just a few published articles on cost-effectiveness modeling of wound dressing usage[4–7], with some of the models being on the academic side and not allowing easy translation to a health organization environment due to overcomplexity of the model and the databases used. Cost-effectiveness modeling in wound care has been criticized for poor reporting of the methods utilized[45,46] and related to that, there is overall lack of awareness to state-of-the-art health economics research and data among wound care clinicians.[47] Our current model exemplifies and simplifies the use of cost-effectiveness modeling for wound dressing selection, while still allowing to adjust the simulations to specific sub-populations of patients who require ongoing wound care. The modeling process (**Figures 1**,**2**) is relatively simple to realize in software for organizations wishing to implement this work in practice. From the perspective of wound dressing manufacturers, the current approach and modeling framework can be extended to study additional dressing options and performances or patient conditions. For example, such modeling can be used at the product design phase, or when setting a target price for a new dressing product prior to launching, or for adjusting prices to specialized care centers which treat specific patient populations, or for evaluating costs of new products designed to achieve certain pre-set clinical dressing performance goals. From a customer's perspective, a healthcare organization can use a modeling framework similar to the one reported here to make decisions that more holistically consider the care pathways for wounds in the relevant facility and for the treated patient populations, from diagnosis to closure, and the associated cost of care. This is as opposed to the simplistic and potentially misleading approach sometimes taken by healthcare administrators, of choosing the least expensive dressing supplier through a bid and tender process, but too often ultimately paying substantially more for the overall cost of wound care over time. Given that national health registers analyses have proven that the prevalence of chronic wounds significantly increased in 2020 (which was associated with the breakout of the COVID-19 pandemic)[48] and there is no certainty that wound rates would return to the pre-pandemic levels, practical implementation of economic evaluations of dressing selection in health organizations is now more relevant and timelier than ever.

Figures captions

Figure 1 The Markov model repeatedly processes specific patient, wound and dressing parameters to calculate the estimated cost of a 26-week treatment period. In each week, the wound may progress to a certain extent towards healing, or the patient may die, depending on pre-set probabilities for these events (as specified in **Table 3**).

Figure 2 Structure of the input parameters and results of the Monte Carlo simulations within the Markov model.

Figure 3 Wounds of the two case studies described in the text, at their initial (left column) and final (right column) conditions. PMDs= Polymeric membrane dressings.

Figure 4 Progress of closure of the simulated wounds over the 26-week time course of treatment for each of the three studied sub-populations of people older than 64 years while treated with a polymeric membrane dressing.

Figure 5 Boxplot of the costs of wound care per patient belonging to each of three studied sub-populations of people older than 64 years. Values are the mean costs in US$. Incremental cost effectiveness ratio (ICER) analysis depicted in the top right frame further indicated that if the willingness to pay is $7500 for a 1%-lower death rate in a population of 100,000 diabetic wound care patients, then changing from passive foam dressings (PsvFDs) to polymeric membrane dressings (PMDs) will theoretically lower the death rates by 0.1% to 0.2% in this population, i.e., 1 to 2 fewer deaths per 1,000 patients (**Table 4**).

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Tables

Table 1: The main assumptions and their justifications to achieve estimated costs and outcomes of wound care using different dressing types simulated by means of a Markov model. PMD= Polymeric membrane dressing; PsvFD= Passive foam dressing.

Assumption	Description	Rationale or Justification	Source
Data from OECD countries	The data is derived from the USA and the UK	These countries have well-established healthcare systems	Various OECD health data reports as detailed in Table 2 and 3
Fixed probabilities for wound progression and healing	Probabilities for wound progression, infection and healing assumed to be constant	Literature provides average probabilities that can be used in models to predict general trends in wound healing	Published clinical studies and industry reports as detailed in Table 2 and 3
Exclusion of post-discharge costs	The model considers only direct hospital costs during inpatient care	Focusing on inpatient costs allows for a clearer analysis of immediate wound care costs and reduces complexity	Simplicity for modeling
Use of average costs for materials and labor	Costs are averaged across different sources and adjusted for inflation	Using averaged costs provides representative values for modeling purposes and helps generalize findings	US Bureau of Labor Statistics and industry reports as detailed in Table 2 and 3
Costs of dressings	Prices for PMDs and PsvFDs are fixed for the duration of the model	Simplifies the model and reflects the common practice of fixed pricing contracts in healthcare procurement	Simplicity for modeling
Only two dressing types studied (PMD and PsvFD)	The model compares only polymeric membrane dressings with passive foam dressings	These are representative types with distinct differences, making the comparison illustrative	Selection based on product characteristics as detailed in Table 2
Consistent use of dressing type throughout treatment	The same type of dressing is assumed to be used throughout the treatment period	Simplifies the model and may reflect common clinical practice for consistency in treatment	Simplicity for modeling and potential clinical practice
Exclusion of organizational overheads	Overhead costs such as administration and facility maintenance not included	These costs may be less variable and are not directly tied to specific wound care interventions	Simplicity for modeling and focus on direct costs
Uniform patient characteristics	Virtual patients are generated with uniform age, gender, and wound characteristics	Ensures consistency in simulations and focuses on the effect of dressings rather than patient variability	Simplicity for modeling
Weekly infection and healing probabilities	Weekly probabilities of infection and healing are used	Reflects the continuous nature of wound healing and infection risk, and aligns with clinical monitoring intervals	Simplicity for modeling
Fixed nursing labor costs	Hourly costs of nursing labor are fixed	Provides a stable basis for cost calculations and may also reflect common contractual wage agreements in healthcare	Simplicity for modeling; KPMG nursing labor cost study, Bureau of Labor Statistics as detailed in Table 3
Diabetes as the only background condition	Only diabetes is considered as an underlying condition affecting wound healing	Diabetes is a well-documented major factor influencing wound healing, providing a clear case for analysis	Clinical literature on diabetes and wound healing as detailed in Table 3

Table 2: Parameters used in the Markov model for the wound care analyses simulating application of the two dressing types. PMD= Polymeric membrane dressing; PsvFD= Passive foam dressing.

Parameter		PMD Value	PMD Source	PsvFD Value	PsvFD Source
Cost (inflation adjusted*) [US$ per item]		$4.1 (adjusted for inflation up to 2023)	PolyMem® brochure**[26]	$7.9*** (adjusted for inflation up to 2023)	PolyMem brochure[26]
Change time [minutes per dressing]		12	PolyMem® brochure**[26]	15	PolyMem brochure[26]
Change Frequency [# of dressings per week]	**Non-infected**	1.6	Ogden (2007)[27]	2.5	Davies et al. (2019)[28]
	Infected	2.4****	Literature & company data[29–33]	3.7	Davies et al. (2019)[28]

*Costs were adjusted for inflation up to 2023 based on the USA Consumer Price Index using the inflation calculator of the U.S. Bureau of Labor Statistics (https://www.bls.gov/data/inflation_calculator.htm).

**PolyMem® is a widely registered trademark of Ferris Mfg. Corp. (Fort Worth, TX, USA).

***The unit cost for PsvFDs is considered to include the costs of any associated cleansing and adhesive materials needed for using this dressing type in clinical practice, such as saline solution/spray, gauze and tapes. Often, in a particular market, the cost of a PsvFD dressing per se is lower than the cost of the PMD dressing, but when considering that use of PsvFDs in practice requires auxiliary materials for cleansing and adhesion, the total unit cost of a PsvFD may exceed that of the PMD, as the above data indicate.

****The data indicate only a single dressing change per week but in order to conduct a more conservative calculation the same proportion as for the use of PsvFDs was considered.

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Table 3. General parameters used in the Markov model.

Parameter	Value	Additional comments or explanations	Source
Hourly cost* of labor of a wound care clinician [US$]	$87** (adjusted for inflation up to 2023)	The cost of nurse hour (costs were converted from pound to dollar with rate of 1.383).	Scanlon et al. (2005)[10] KPMG (2017)[34] Bureau of Labor Statistics (2021)[35]
Hospitalization cost* [US$]	$110.5 (adjusted for inflation up to 2023)	Cost of hospital bed per hour in the United States, excluding the wound care clinician labor cost	Statista (2018)[36]
Annual death rates [Array data]	Arrays	Arrays of probabilities of annual deaths in the United Kingdom by age and gender, i.e., the annual death rates are function of both age and gender	World Health Organization Mortality statistics (2005)[37]
Added death risk associated with diabetes [%]	12	Applies to patients who are older than 70 years. The added death risk is multiplicative.	Tachkov et al. (2020)[38]
Incidence of diabetes [%]	10.5	The incidence of diabetes in the United States	National Diabetes Statistics Report (2020)[14]
Weekly rate of reduction in wound size [%]	21.9	This is the reference value for a non-infected wound in a non-diabetic patient; infection and diabetes decrease this rate each by 50%.	Winblad (2011)[39] Cardinal et al. (2008)[40]
Critical wound size for a greater death risk [cm^2]	40	The critical wound size above which a patient is assumed to have a greater risk of death if their wound becomes infected	Kantor et al. (1998)[41]

Weekly infection risk [%]	2.3	The weekly probability of the wound to become infected	Scanlon et al. (2005)[10]
Added risk of death for a large and infected wound* [%]**	50	The added risk of death for patients with a large (>40cm^2) and infected wound	Vitale et al. (2024)[49]
Probability of an infection to regress [%]	30	The weekly probability of an existing infection to regress	Assumption
Critical wound size for the simulation to stop [cm^2]	1	The critical wound size which is considered to be near-closure, following which the simulation stops	Assumption

*Costs were adjusted for inflation up to 2023 based on the USA Consumer Price Index using the inflation calculator of the U.S. Bureau of Labor Statistics (https://www.bls.gov/data/inflation_calculator.htm).

** The reported domain of hourly costs is $75 to $89; the chosen value ($87) is in the high range, to reflect that many healthcare professionals who routinely treat wounds are certified and experienced wound care clinicians such as Wound Ostomy and Continence (WOCN) registered nurses.

*** This translates to a hazard ratio (comparing mortality rates between diabetic and non-diabetic patients with wounds) which is 1.5.[49] This assumption reflects that severe wound infections considerably impact patient mortality, however, there is also 30% probability for an infection to regress with treatment (in the following table item), reflecting that while infections increase the death risk, effective treatment can regress it and accordingly, the eventual impact on mortality can be mitigated.

Table 4. Calculated costs of wound care, time to closure and death rates for each of the studied sub-populations. All costs are presented in 2023 US$. PMD= Polymeric membrane dressing; PsvFD= Passive foam dressing.

	Calculated mean costs of wound care per patient [US$]		Calculated mean time to closure [Weeks]*		Calculated death rates by sub-population [%]	
Sub-population (all older than 64 years)	**PMD**	**PsvFD**	**PMD**	**PsvFD**	**PMD**	**PsvFD**
Diabetic males with an infected wound	1902	3853	26	26	5.3	5.4
Diabetic females with a non-infected wound	1845	3733	26	26	4.1	4.3
Non-diabetic males with a non-infected wound**	1191	2411	16.7	16.7	3.0	3.0

*The mean time to closure was calculated using the number of cycles that each patient in each population needed to heal, excluded the dead patients and with a stop condition of 26 cycles. Accordingly, where a 26-week time to closure is specified, the simulations had reached the stop condition and therefore, the PMD and PsvFD treatments were similar in their impact on the healing duration, with cost differences driven by other factors such as the frequency of dressing changes and labor costs.

The variation in the cost data detailed in this Table were depicted in **Figure 5, as quartiles in the boxplot which are more indicative of the central tendency and the spread of the central portion of the data than the standard deviations or the 95% confidence intervals (which are proportional to the standard deviation values). Of note, a difference exceeding 5% between the mean and median values was detected here in the cost data for the sub-population of non-diabetic males with a non-infected wound, which might indicate non-normality of the cost data distribution and that has motivated the boxplot presentation in **Figure 5**.

Table 5. Calculated costs of wound care for low-end and high-end, equal dressing costs (listed in Table 1, first row) per patient for each of the studied sub-populations, for the purpose of sensitivity analyses to isolate the indirect (labor) from the direct (materials) cost of care. All costs are presented in 2023 US$. PMD= Polymeric membrane dressing; PsvFD= Passive foam dressing.

	Calculated mean costs* of wound care per patient for *low-end* dressing cost [US$]		**Calculated mean costs* of wound care per patient for *high-end* dressing cost [US$]**	
Sub-population (all older than 64 years)	**PMD**	**PsvFD**	**PMD**	**PsvFD**
Diabetic males with an infected wound	1902	3595	2069	3853
Diabetic females with a non-infected wound	1845	3448	2007	3733
Non-diabetic males with a non-infected wound	1191	2254	1298	2411

*Variability measures for the PMDs and PsvFDs are provided in **Figure 5** (boxplots). Coefficient of variations pooled for the high-end and low-end PsvFDs considered in these sensitivity analyses were 2.2%, 0.8% and 9% for the sub-populations of diabetic males with an infected wound, diabetic females with a non-infected wound and non-diabetic males with a non-infected wound, respectively.

Yaniv T, Beeckman D, Gefen A. A Markov cost-effectiveness modeling framework for evaluating wound dressings: A concept for practical implementation of economic evaluations in an informed dressing selection process. J Tissue Viability. 2024 Nov;33(4):938-948. doi: 10.1016/j.jtv.2024.10.001.

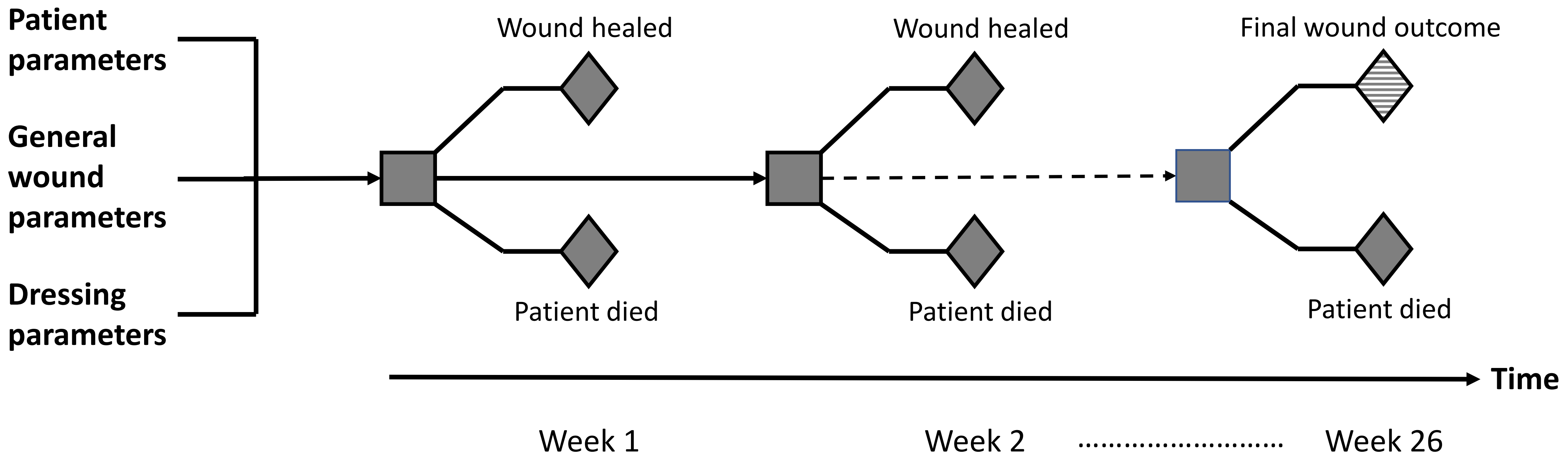


Figure 1

Yaniv T, Beeckman D, Gefen A. A Markov cost-effectiveness modeling framework for evaluating wound dressings: A concept for practical implementation of economic evaluations in an informed dressing selection process. J Tissue Viability. 2024 Nov;33(4):938-948. doi: 10.1016/j.jtv.2024.10.001.

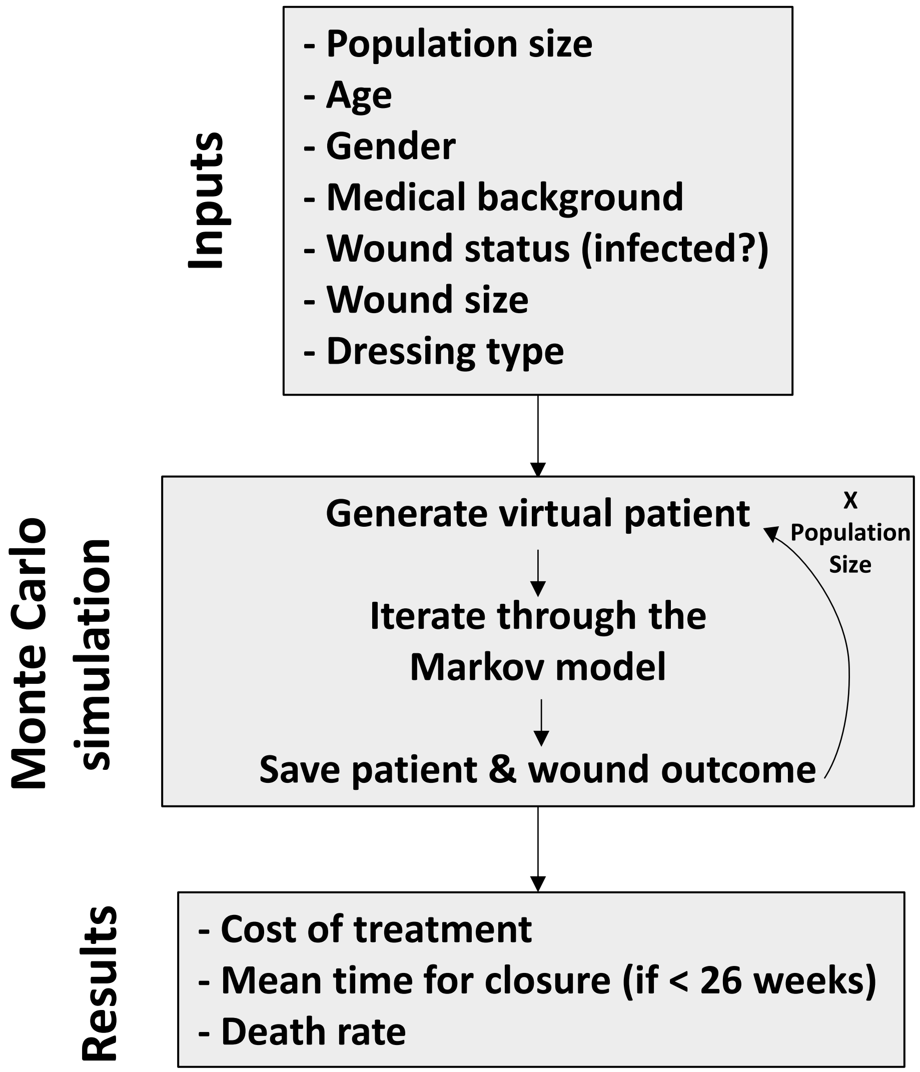


Figure 2

Yaniv T, Beeckman D, Gefen A. A Markov cost-effectiveness modeling framework for evaluating wound dressings: A concept for practical implementation of economic evaluations in an informed dressing selection process. J Tissue Viability. 2024 Nov;33(4):938-948. doi: 10.1016/j.jtv.2024.10.001.

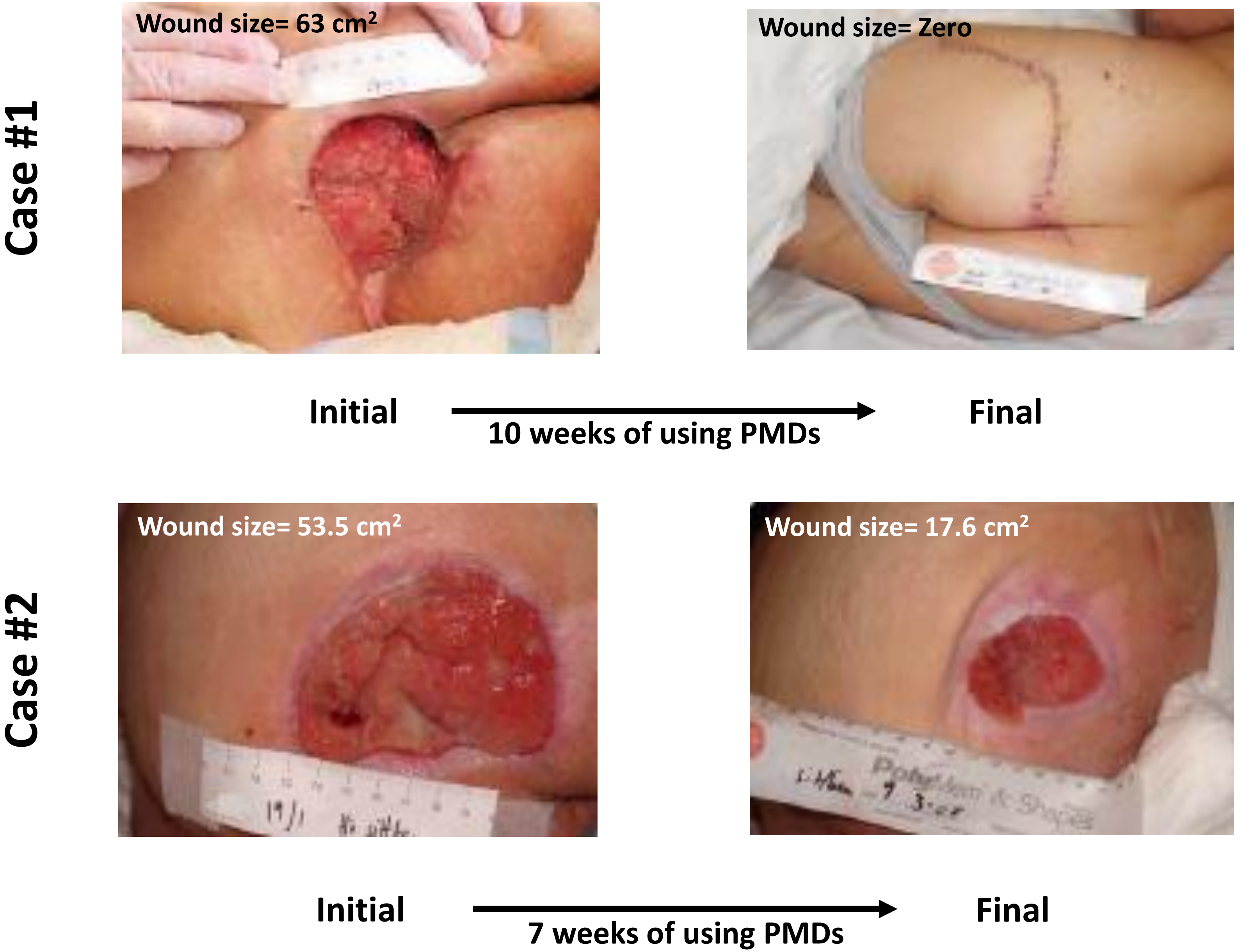


Figure 3

Yaniv T, Beeckman D, Gefen A. A Markov cost-effectiveness modeling framework for evaluating wound dressings: A concept for practical implementation of economic evaluations in an informed dressing selection process. J Tissue Viability. 2024 Nov;33(4):938-948. doi: 10.1016/j.jtv.2024.10.001.

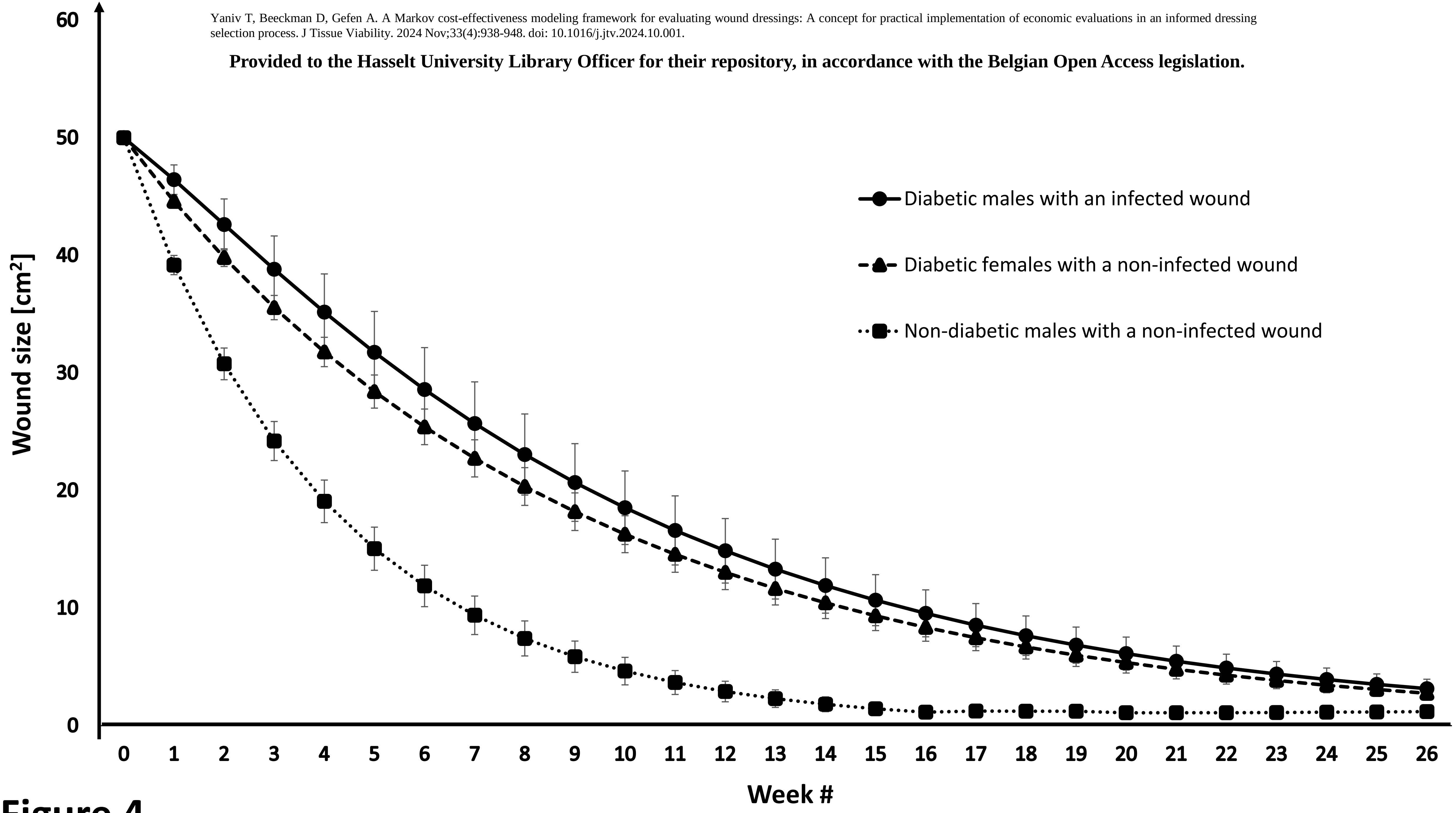
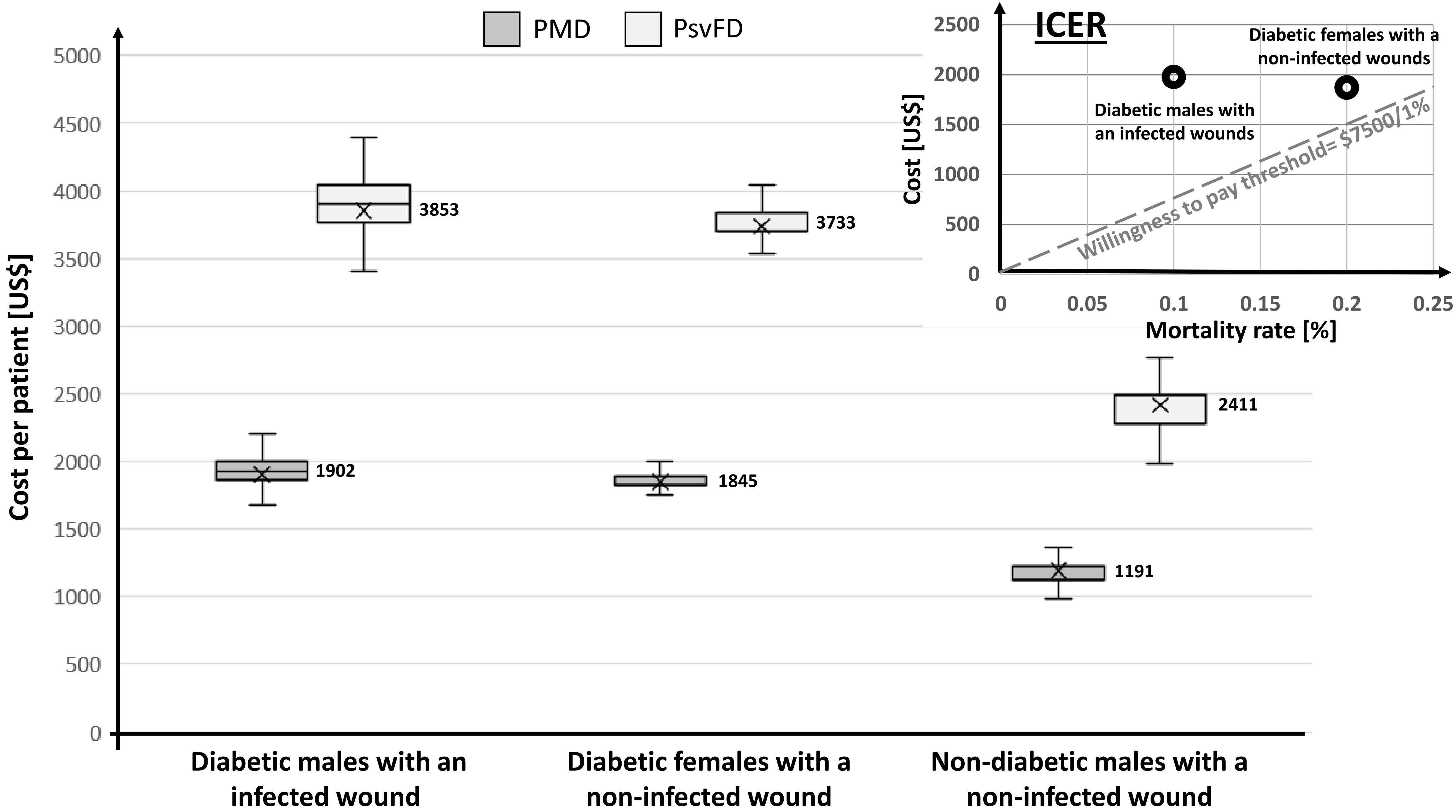


Figure 4



Yaniv T, Beeckman D, Gefen A. A Markov cost-effectiveness modeling framework for evaluating wound dressings: A concept for practical implementation of economic evaluations in an informed dressing selection process. J Tissue Viability. 2024 Nov;33(4):938-948. doi: 10.1016/j.jtv.2024.10.001.

Figure 5