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The cost-effectiveness of prehospital v. in-hospital thrombolysis for ST-segment elevation myocardial infarction in South Africa

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Background. In high-income countries, preventive, long-term and definitive care has seen mortality from cardiovascular disease (CVD) partially decline, while trends in mortality from CVD in low- to middle-income countries continue to increase at rates exceeding global averages. The burden of severe CVD-related events, especially ST-segment myocardial infarction (STEMI), has risen disproportionately with socioeconomic pressures limiting preventive or definitive supports, particularly in rural or remote areas. Access to percutaneous coronary intervention (PCI) for STEMI in South Africa (SA) remains limited, inevitably expanding the therapeutic window to include pharmacoinvasive approaches with in-hospital thrombolysis (IHT) emerging as a widespread default STEMI intervention. In addition, prehospital thrombolysis (PHT) could further bridge resource gaps and improve clinical outcomes due to time-sensitive benefits. Although not widely perceived as cost prohibitive, cost concerns may, however, act as a significant barrier to adoption.
Objective. To compare the costs and health outcomes of PHT and IHT for the management of STEMI in SA using a decision-analytic cost-effectiveness model.
Methods. A cost-effectiveness analysis was conducted using a decision tree to compare PHT and IHT for the treatment of STEMI from a provider perspective. Cost estimates for analysis were obtained from publicly accessible data, including data from government, reports on labour earnings, and industrial equipment pricing tiers, for the fiscal years 2024 and 2025. Deterministic and probabilistic sensitivity analyses were conducted to assess parameter uncertainty. The model estimated the incremental cost-effectiveness ratio (ICER) of implementing PHT relative to IHT by measuring outcomes using disability-adjusted life-years (DALYs).
Results. Over a 1-year period, PHT dominated IHT as a treatment strategy, demonstrating cost savings per DALY averted and life-year saved (LYS). Using PHT as an intervention resulted in cost savings of ZAR216 316 per DALY averted and ZAR159 450 per LYS in contrast to IHT. Savings in terms of cost and health outcomes were estimated at ZAR23.78 million, with incremental reduced deaths (n=20) and fewer life-years lost (n=149).
Conclusion. Given the substantial burden of STEMI-related morbidity and mortality in SA and the resource limitations faced by the public health sector, it is imperative to identify and implement cost-effective strategies to improve patient outcomes. In resource-constrained settings where timely access to PCI is limited, PHT represents a pragmatic and cost-effective strategy.

Keywords: cost-effectiveness, prehospital thrombolysis, in-hospital thrombolysis, ST-segment elevation myocardial infarction, South Africa, acute myocardial infarction, emergency cardiovascular care, health economics

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The burden of cardiovascular disease (CVD) continues to increase in sub-Saharan Africa, with ST-segment elevation myocardial infarction (STEMI) representing a particular life-threatening and time-sensitive manifestation.[1] Reports from Western Cape Province in South Africa (SA) confirm that the incidence of STEMI and high-risk non-STEMI cases is between 14.7 and 15.6 per 100 000, resulting in an overall 30-day all-cause mortality of 6.1% for patients presenting with acute coronary syndrome.[2]

Premature mortality, in addition to the long-term disabilities associated with CVD, has significant societal and economic implications in terms of reduced economic productivity.[3] Indirect costs resulting from premature morbidity and mortality, primarily due to lost productivity, constitute a significant proportion of the total economic burden of CVD. Estimates indicate that direct healthcare costs account for approximately 42% of the total costs of CVD, with the remaining majority attributed to indirect costs such as productivity losses due to disability and death.[4]

Reflecting broader trends observed across sub-Saharan Africa, the economic burden of CVD in SA has increased markedly since 1991, when it was estimated to account for approximately 3% of the total SA gross domestic product (GDP) (equivalent to between ZAR4.1 and ZAR5.0 billion at the time).[5] As a consequence of rising prevalence of major risk factors such as hypertension and hypercholesterolaemia the economic burden of CVD had increased by 2017 to approximately 10% of the SA GDP, equivalent to ZAR476 billion.[6] Although precise annual cost data for CVD in SA after 2017 are limited, available evidence suggests that expenditures are rising in line with global trends.[7,8] This increase is further exacerbated by rapid urbanisation and chronic underinvestment in preventive measures,[9] indicating that costs could potentially double or triple in the coming years.

Poor social health indicators and widening economic disparities underscore a growing necessity for improved healthcare strategies specific to STEMI management in SA. Primary percutaneous intervention (p-PCI) remains the preferred reperfusion strategy in the treatment of STEMI, with the option of thrombolysis if p-PCI is not achievable within the recommended timeframe of 120 minutes.[10] Endorsements for thrombolysis with fibrin-specific drugs as an alternative are also strong, however, emphasising reperfusion as a matter of principle over the choice of reperfusion strategy.[11] Much like p-PCI, time from onset of pain to thrombolysis in the treatment of STEMI is a crucial factor in minimising complications and improving patient outcomes.[12]

Door-to-needle time, which highlights healthcare system performance, is defined as the duration from hospital arrival to thrombolysis administration and is recommended as under 30 minutes.[13] Another critical metric in STEMI management, pain-to-needle time, represents the onset of chest pain to thrombolysis focusing on the total ischaemic period, and is recommended to be less than 3 hours. Although both measures are strongly supported through evidence in practice, minimisation of pain-to-needle time shows as much as 50% efficacy in mortality reduction.[14] In low-resource settings, prehospital thrombolysis (PHT) has shown to reduce pain-to-needle time significantly compared with in-hospital thrombolysis (IHT), resulting in quicker reperfusion and the potential for improved outcomes.[15] In addition, PHT enhances reperfusion for STEMI by significantly reducing time to treatment, which is crucial for improving outcomes, particularly where timely p-PCI is not achievable.[16]

Aims to improve outcomes and reduce costs for healthcare providers are often associated with challenges of linking cost values to specific processes or effects.[17] Pharmaceutical disbursements, including both the direct and indirect costs of thrombolytic drugs, have been posed as a significant barrier to the implementation of PHT in SA.[18] If the implementation costs of interventions are, however, not fully conceptualised, a disconnect between evidence-based practice and public health decisions results.[19] The current study thus sought to analyse the cost-effectiveness of PHT v. IHT in SA. The results may guide policy and implementation decision-making.

Methods

An Excel-based (Microsoft, USA) decision-tree model was developed to compare the cost of treatment and health outcomes of PHT with the 'standardised' practice of IHT for the management of patients with STEMI, from the provider perspective. The analysis and reporting of findings adhered to the Consolidated Health Economic Evaluation Reporting Standards (CHEERS).[20]

Comparators

Although shortening the time to reperfusion results in improved outcomes,[16] widespread adoption and systematic uptake of PHT is frequently restricted by cost considerations. The current study thus compared the cost and health outcomes of PHT and IHT, as interventions for STEMI. The selected comparators were based on evidence suggesting that, at present, all-inclusive PCI remains an unrealistic aspiration within the SA healthcare context.[21,22]

Perspective

A provider perspective was used to capture all direct medical costs incurred by the healthcare system. Although broad perspectives offer a wider scope of costs and benefits, a narrow perspective was more justified in this case as this perspective aligns with pragmatic and practical decision-making for policies or among policymakers who require targeted information, especially in contexts such as SA, where healthcare is provided in the public sector.[23,24]

The pluralist SA healthcare system, with independently governed provincial structures, creates unique challenges for providers, including barriers to service delivery and policy inconsistencies. These complexities lead to data gaps and resource allocation issues at provider level.[25,26] Using the provider perspective thus allowed the study to address directly the practical constraints and realities faced in delivering care within this diverse and multifaceted system.

Time horizon

The decision-tree model used a lifetime horizon to account for costs and outcomes over the remaining lifespan of the average patient with acute myocardial infarction (AMI), or heart attack. Based on literature and registry data, the average age of AMI in SA is generally reported to be in the mid to late 50s,[27-29] and the average lifespan in SA is 65 years.[30] We thus used a generous 16-year time horizon accounting for costs and outcomes for patients modelled from 55 to 70 years old.

Discount rate

A constant discounting rate was applied in the current analysis to account for the principle that future costs and health benefits are valued less than immediate ones.[31] Discounting both costs and health outcomes reflects the time value of financial resources and the opportunity cost of capital. By adjusting future costs and benefits to their present value, this approach supports accurate and consistent economic decision-making.[32] A constant discounting rate also simulates the reduced opportunity for growth associated with future use of wealth and helps account for uncertainty in future expenditures and health effects, thereby ensuring that monetary decisions accurately reflect the value of future costs and outcomes.[33]

Although the SA National Department of Health recommends a 5% discount rate,[34] we present results using a 3% rate to align with established economic precedents and facilitate comparability with international literature.[31] Demonstrating that local cost analysis is aligned with global best practices, increased credibility and utility of findings provides a valuable reference point for informed policy decisions, especially in contexts where local data are limited or evidence gaps exist.[35]

Selection of outcomes

Given that CVD often results in substantial long-term disability and many patients survive with chronic health impairments,[36] measuring the burden of CVD using disability-adjusted life-years (DALYs) provides a more comprehensive perspective than simply considering life-years saved (LYS). As a leading contributor to functional disability, patients who survive CVD are often predisposed to neurological deficits, such as stroke, heart failure and even secondary organ dysfunction.[37,38]

In relation to the significant disease burden in low- to middle-income countries (LMICs),[39,40] the current study compared the effects of PHT with those of IHT in terms of both mortality and morbidity, using gains in DALYs as the primary outcome measure. This measure includes influences on functional limitations, which are intended to capture a more nuanced assessment of health outcomes compared with metrics that may overlook disability burden.

Measurement and valuation of outcomes

Transition probabilities and possible clinical events within the decision-tree model were derived from the economic model established by the Goal-oriented cognitive REhAbiliTation (GREAT) clinical randomised controlled trial.[41] Furthermore, the model parameters were selected to reflect the SA healthcare setting, taking

into account local epidemiology, resource availability and system constraints to enhance the relevance and applicability of the analysis. Treatment effectiveness was based on the proportion of patients surviving with no adverse effects, reinfarction, risk of long-term consequences, disability and death. DALY weights measuring severity of conditions were sourced through the Global Burden of Disease Study conducted in 2019 by the Institute for Health Metrics and Evaluation (IHME).[42]

Measurement and valuation of resources and costs

A bottom-up microcosting approach was used to capture both fixed and variable costs of both interventions (i.e. PHT and IHT). An itemised list was created by following an ingredient method approach to achieve a level of detail sufficient for accurate cost estimates. Information on values was collected from publicly accessible budget or expense reports, medical insurer information, clinical databases and relevant government websites. All model variables and their sources are outlined in Table 1.

Cost estimates for clinically qualified and relevant healthcare professionals, including emergency care practitioners, medical doctors and nurses, were based on annual salary scales obtained through the SA Department of Public Service and Administration.[43] Procedural equipment and drug costs were sourced from government tenders published by the Western Cape Department of Health.[44] To assess cost reasonableness and improve the accuracy of data, all prices were compared with and benchmarked against historical data from industry supply logistics records and medical equipment manufacturers.

Currency, price date and conversion

Economic inflation adjustments were made using a basket of goods approach, standardising costs by accounting for inflation through the consumer price index (CPI), allowing for comparisons over time, and facilitating currency conversion. Global market sources were used for costs of equipment, such as electrocardiogram (ECG) machines, identifying these in USD and adjusting to local cost at 2024 ZAR values using the CPI formula.

Rationale and description of model

A decision-tree model (Fig. 1) was constructed to compare short-term clinical outcomes, as well as costs associated with PHT and IHT, in patients presenting with STEMI. In contrast to Markov models, which remain effective in multiduration analysis with chronic conditions or dynamic health states over extended periods,

Table 1. Model parameter range and probability distribution

Parameter	Base case*	Range*	Probability distribution	Source
Costs*				
IHT annual costs (per patient event)†	1 087 244.77	924 158.05 - 1 250 331.49	Gamma	Medicine price registry database 2021[45]
PHT annual costs (per patient event)‡	630 066.30	609 612.99 - 650 519.614	Gamma	Mediclinic private tariff schedule 2024[46]
IHT treatment	21 850.48	11 113.24 - 32 587.72	Gamma	
PHT treatment	21 258.84	11 297.96 - 31 219.72	Gamma	
Cost of treating complications				
Stroke treatment	19 072.07	899.85 - 27 789.43	Gamma	Viljoen 2016[47]
CABG treatment	24 212.08	8 730 - 39 931.60	Gamma	Netcare private patients' tariffs 2023[48]
PCI treatment	39 813.85	29 757.00 - 65 000.00	Gamma	Stassen *et al.* 2017[49]
Long-term disability costs				
Cost death (average annual salary)	287 784	244 616.40 - 330 951.60	Gamma	Business Tech report 2022[50]
Costs stroke, mild	55	46.75 - 63.25	Gamma	
Costs stroke, moderate	95	80.75 - 109.25	Gamma	
Costs stroke, moderate + cognition problems	590	501.50 - 678.50	Gamma	Grimmer *et al.* 2020[51]
Costs stroke, severe	1 230	1 045.50 - 1 414.50	Gamma	Grimmer *et al.* 2020
Costs stroke, severe + cognition	2 400	2 040.00 - 36 516.00	Gamma	Grimmer *et al.* 2020
Costs stroke disability care	41 057	34 898.05 - 47 215.01	Gamma	Matizirofa *et al.*[52]
Government disability grants (R1 500 per person/ per month converted to yearly rate)	18 000	15 300.00 - 20 700.00	Gamma	disabilityinfosa.co.za[53]
Costs management chronic IHD	1554	1 320.90 - 1 787.10	Gamma	Kohli-Lynch *et al.*[54]
DALY weights				
Stroke, mild	0.019	0.01 - 0.032	Beta	GBD study 2019[42]
Stroke, moderate	0.07	0.046 - 0.099	Beta	GBD study 2019
Stroke, moderate + cognition problems	0.316	0.206 - 0.437	Beta	GBD study 2019
Stroke, severe	0.552	0.377 - 0.707	Beta	GBD study 2019
Stroke, severe + cognition	0.588	0.411 - 0.744	Beta	GBD study 2019
Acute myocardial infarction, 3 - 28 days	0.074	0.049 - 0.105	Beta	GBD study 2019
Chronic IHD chronic	0.08	0.02 - 0.24	Beta	GBD study 2019

IHT = in-hospital thrombolysis; IHD = ischaemic heart disease; CABG = coronary artery bypass graft; PCI = percutaneous coronary intervention.
*All costs in South African rand (ZAR).
†Inclusive of clinical support staff, facility surcharge fees and occupational charges, relevant equipment including devices and consumables.
‡Inclusive of clinical support staff, ambulance transport costs (metropolitan and long distance), relevant equipment including devices and consumables.

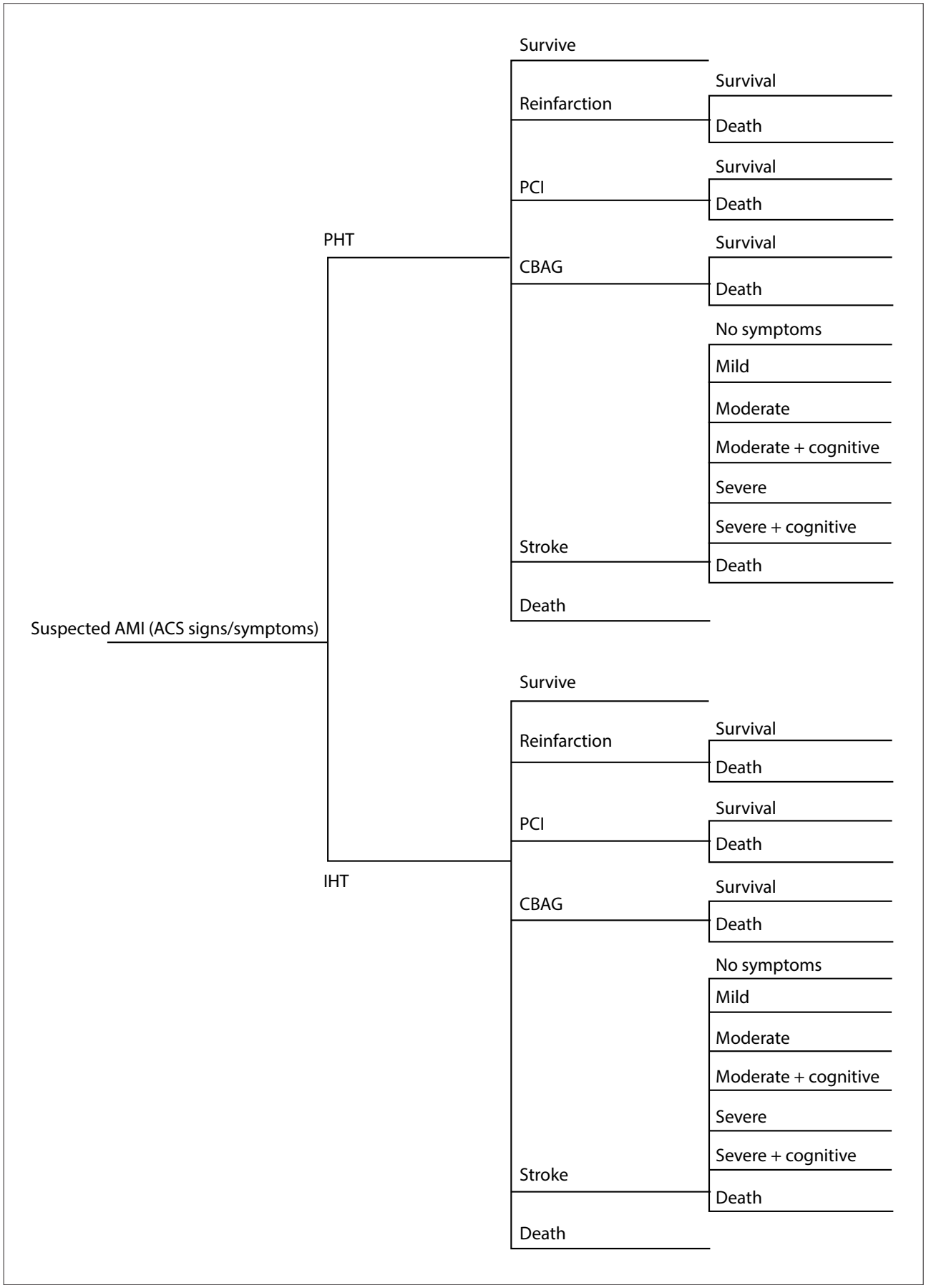


Fig. 1. Decision-tree model. (ACS = acute coronary syndrome; IHD = ischaemic heart disease; CABG=coronary artery bypass graft; PCI= percutaneous coronary intervention.)

decision trees are particularly well suited for modelling point-in-time interventions.[55] Decision trees are well supported in healthcare economics for guiding clinical or policy decisions in low-resource settings relevant to the context of the study,[56] allowing for a clear, unidirectional representation of possible outcomes and associated costs and effects.

The decision-tree model simulated a cohort of patients who, after receiving either IHT or PHT, might experience one of several mutually exclusive clinical events within the first year: survival without complications, reinfarction, stroke, need for revascularisation procedures, or death. Transition probabilities for each outcome were derived from published clinical studies and meta-analyses.[57-59] Each terminal node in the tree represents a distinct health state, to which costs and utilities were assigned for the cost-effectiveness analysis. Bleeding risks were not included as a specific chance node in the model, as incidence of major bleeding and intracranial haemorrhage is low and does not differ significantly between PHT and IHT for STEMI when guideline-recommended protocols are followed.[60] Furthermore, bleeding complications are managed separately as part of clinical decision-making processes and consequentially are not a primary driver of cost or clinical outcomes, with exclusion unlikely to affect overall cost-effectiveness results.

Analytics and assumptions

Based on the underlying pathophysiology and analytical assumptions regarding probable outcomes, STEMI is associated with predictable complications, including embolic events that may lead to stroke, reinfarction and death. Subsequent interventions such as PCI or coronary artery bypass graft (CABG) are determined by timely reperfusion and the extent of myocardial damage due to infarction. We assume that all patients who experience adverse effects from either PHT or IHT interventions will experience additional disability.

Survival was modelled without accounting for disabilities, based on methodological considerations and to simplify the comparative analysis and focus on the primary outcomes of the interventions. Although a lifetime horizon was used to model outcomes, emphasis was also placed on immediate mortality risks, recognising that certain acute complications might not have been captured fully within the modelled timeframe. Importantly, evidence strongly suggests that thrombolysis reduces mortality even in the presence of complications,[61] underscoring the significance of early intervention.

Effect of uncertainty

Parameter uncertainty was explored through both deterministic and probabilistic sensitivity analyses, providing a comprehensive understanding of how variable changes influence cost-effectiveness outcomes.[62] A deterministic (one-way) sensitivity analysis was performed to assess the effect of uncertainty in key model parameters on the incremental cost-effectiveness ratio (ICER) and across plausible ranges reflected in the literature. Specifically, we varied the proportion of patients experiencing reinfarction in terms of both PHT and IHT, as this clinical outcome directly influences subsequent healthcare costs and patient morbidity. Additionally, treatment costs for PHT and IHT were individually adjusted within plausible ranges to evaluate their influence on total costs. The analysis included variation in DALYs associated with IHD, reflecting the health burden captured by each intervention. A tornado diagram was used to illustrate the parameters that had the greatest influence on the ICER (Fig. 2).

A probability sensitivity analysis model quantified uncertainty by replacing fixed input parameters with appropriate probability distributions, which accounted for variability in cost and clinical outcomes. A Monte Carlo simulation of 10 000 iterations was run.[63] Results were summarised using a cost-effectiveness plane (Fig. 3). All analyses were undertaken with the support of a health economist, who guided specification of assumptions, costing and analytic procedures.

Results

In cost-effectiveness analysis, an intervention is considered 'dominant' if it is both more effective and less costly than the alternative.[64] Our results indicated that PHT was more effective and less costly than IHT (Table 2). The base case ICER, which compared relative interventional values,[65] confirmed the dominance of PHT over IHT. Furthermore, sensitivity analysis demonstrated that the cost-effectiveness results were highly sensitive to the rates of reinfarction and stroke. This suggests that interventions that reduce reinfarction and stroke rates would not only improve clinical outcomes but also enhance overall cost-effectiveness substantially.

The ICER derived from our primary analysis (Table 2) signified lower cost and fewer DALYS, representing a dominant scenario. Outcomes indicated that PHT was associated with fewer deaths (n=20), fewer life-years lost (n=149) and more DALYs averted (n=110), and PHT was less costly than IHT, saving approximately ZAR23.78 million.

To quantify uncertainty and support potential policy decisions, confidence intervals were applied across multiple metrics, including DALYS, LYS and discounted cost. Although the requirements for specific thresholds remain complex, a negative ICER may help simplify decision-making processes for policymakers based on the value proposition.[66] The confidence intervals remaining entirely negative confirmed that PHT is consistently less costly than IHT. In this case, the use of PHT, in contrast to IHT, leads to health improvements while also reducing overall healthcare costs, which is desirable from both an economic and public health perspective. Mean discounted cost differences between PHT and IHT confirmed that PHT was consistently less costly than IHT, reinforcing findings that PHT remains the dominant choice of strategy.

The sensitivity analysis identified the proportion of patients experiencing reinfarction in the IHT group as the most influential factor affecting the ICER, resulting in both clinical and economic consequences (Fig. 2). As reinfarction incidents are infrequent but associated with significantly increased mortality, higher rates of complications and increased healthcare utilisation,[67] incremental cost-effectiveness is driven by differences between reperfusion strategies. Observations in this regard emphasise that the cost-effectiveness advantage of PHT over IHT may be contingent on the reinfarction rate associated with IHT. Reducing time to IHT to improve outcomes would, however, significantly alter cost-effectiveness.

Crucially, the proportion of reinfarction incidents is not a fixed value and varies depending on patient characteristics and time sensitivity. It is thus important to contextualise findings and to emphasise strategies that minimise reinfarction risk for clinical and economic outcomes. The range for PHT costs in the sensitivity analysis demonstrated that, although changes in the cost of PHT influence the ICER, effects are not as significant as the effect of varying infarction rates. The effects of PHT treatment costs were shown to be similar to IHT, although analysis showed that changes in the cost of PHT led to incremental changes in the ICER, concluding that changes in costs associated with PHT make it more cost-effective than IHT.

The analysis further showed that reducing treatment costs associated with IHT leads to an increase in ICER value, indicating an improvement in the overall cost-effectiveness of IHT relative to PHT. In contrast, increasing IHT treatment costs causes the ICER to

decrease further, reflecting a worsening cost-effectiveness profile for IHT compared with PHT, as the cost gap widens. These results suggest that while lowering IHT costs could make it a more economically attractive strategy, raising costs exacerbates its disadvantages relative to PHT. Subsequently, if drug prices or hospital charges increase, economic arguments for the adoption of PHT over IHT become more compelling as these would not only be clinically more effective but also a fiscally responsible strategy for STEMI management.

Analysis also indicated that although variations in IHT treatment costs do affect the ICER, this effect is relatively modest when compared with the influence of clinical outcome parameters. In the current study, the confidence intervals associated with IHT treatment costs were narrower and less influential than those for key clinical outcomes, suggesting that the cost-effectiveness of PHT in contrast to IHT in the management of STEMI in SA is driven by differences in clinical effectiveness rather than by fluctuations in treatment costs.

The analysis further demonstrated that variations in PHT treatment costs, whether decreased or increased, consistently resulted in a lower ICER. This indicates that changes in PHT costs generally enhanced cost-effectiveness compared with IHT. The moderate effect of adjustments to this parameter suggests that while treatment costs represent a significant driver of the model, these were not the most influential factor in the overall analysis.

A probabilistic sensitivity analysis on the cluster-based cost-effectiveness plane (Fig. 3) demonstrated a dispersion of 10 000 Monte Carlo simulation outcomes representing possible combinations of incremental costs and effects. The reference point positioned in the cost-effectiveness plane illustrates the base case analysis.

The majority of simulated outcomes on the cost-effectiveness plane clustered within the southeast and northeast quadrants, demonstrating that PHT is highly likely to provide greater health benefits than IHT, and often at a comparable lower cost. Only a small portion of simulations fell into the northwest quadrant, indicating that scenarios where PHT is both more costly and less effective than IHT are rare. The narrow confidence intervals around the ICER further reinforce the robustness of these findings, suggesting that in the SA context, PHT consistently outperforms IHT in terms of both effectiveness and cost.

Summary results from the 10 000 Monte Carlo simulations (Table 3) demonstrated a mean value of ZAR374 979.97 with the 95% confidence interval for the ICER ranging from -ZAR278 943.47 to ZAR1 028 903.42, indicating that the true ICER is likely to fall within this interval. The wide range of the confidence interval in the analysis reflects the uncertainty around the ICER estimate, influenced by variability in the data.

The ICER for LYS mean value (-ZAR226 504.59) confirmed overall cost saving for PHT and, as the entire confidence interval remained negative per LYS, reinforced that PHT consistently dominates – even when accounting for statistical uncertainty. The mean discounted cost differences between PHT and IHT were estimated at -ZAR23 862 040.58 with the 95% confidence interval, and likewise demonstrated that PHT is less expensive than IHT across a range of plausible values.

Discussion

Perceptions of healthcare have transformed over time from a being stigmatised commodity to becoming a basic necessity, and today it constitutes a human right in most contexts.[68] The concept of healthcare as a right is, however, related to access, which is distinct by implication and application, with systems of government often straining to deliver both comprehensively. As a result, cost-effectiveness has become a significant factor in decision-making, influencing and determining how human resource allocations are prioritised.[69] Cost-effectiveness analysis serves as a crucial tool in LMICs to help guide the allocation of limited resources and maximise health outcomes amid high or increasing burdens of disease.[70] The current study compared the costs of PHT and IHT, as PHT potentially expedites reperfusion times essential for improved health outcomes and costs. PHT was found to dominate in this case.

CVD is increasingly a significant health concern in SA and, as an underlying cause of STEMI, has substantial implications for DALYs, reflecting broader trends across sub-Saharan Africa.[71] Rapid urbanisation and lifestyle changes leading to increased CVD factors

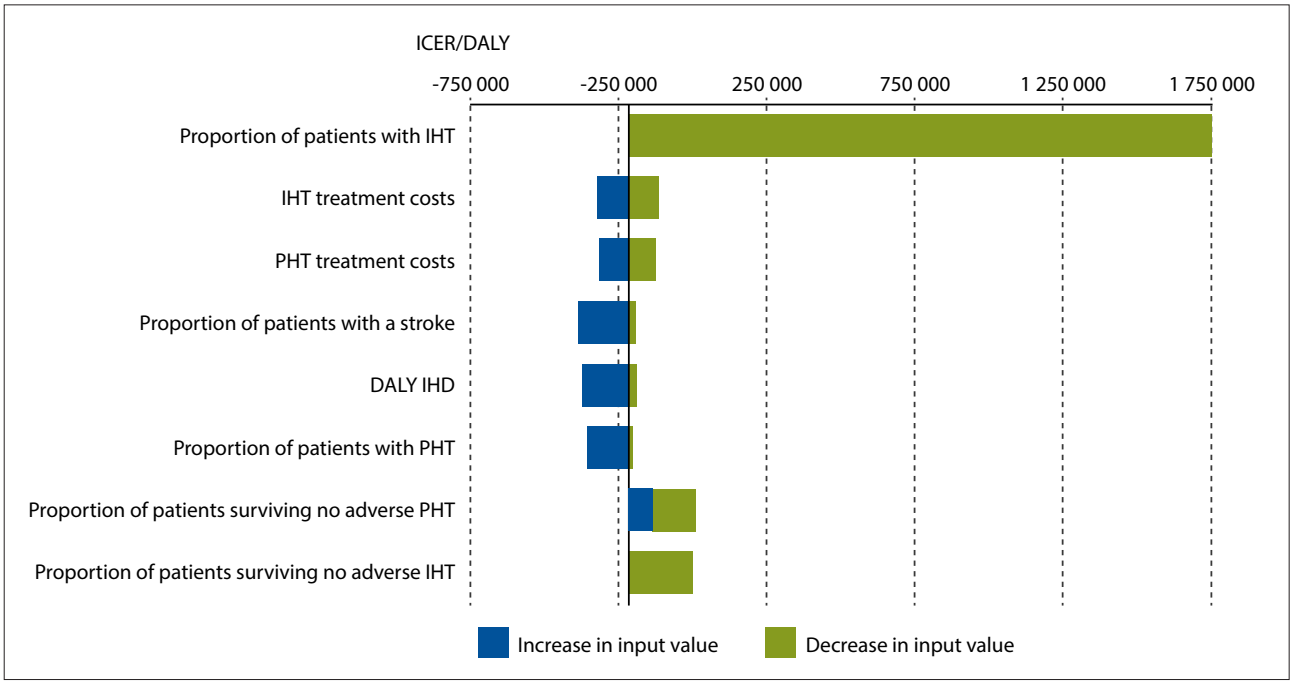


Fig. 2. Tornado diagram of one-way sensitivity analysis. (ICER = incremental cost-effectiveness ratio; DALY = disability-adjusted life year; IHT = in-hospital thrombolysis; PHT = prehospital thrombolysis; IHD = ischaemic heart disease.)

with limited health access and preventive services have resulted in a health crisis in the region. A specific focus on cost-effectiveness as a healthcare strategy, by analysing cost–benefit and related harms, has thus become a crucial aspect of policymaking.[72]

Proxy data, hypotheticals and assumptions through analytical models could simulate costs for interventions not implemented; however, the absence of real-world data poses significant statistical challenges and uncertainty.[73,74] Moreover, prioritising resources based on interventions that are not available gives rise to ethical concerns, as well as practical considerations such as feasibility and acceptability.[75] The SA healthcare system is not well positioned to deliver p-PCI access, with only 62 facilities offering the service, most of which are located centrally.[49] Given their population coverage, the costs of PHT were compared with IHT as realistic or achievable reperfusion strategies in this context.

Contrary to general assumptions and for results to be valid, cost value is dependent on utilising context-specific thresholds that reflect local abilities to pay for health gains.[76] Reflective of economic marginal returns and the opportunity cost of health spending, the SA 'benchmark' threshold is estimated at ZAR38 000 (USD3 015) per DALY averted.[77]

The health benefits of thrombolysis are greatest when patients are treated expeditiously following symptom onset.[78] Timely reperfusion in coronary artery occlusion – both during and after STEMI – is crucial to preventing irreversible myocardium damage and improving outcomes, thereby reducing healthcare burdens. Evidence shows that PHT reduces time to receipt of thrombolysis treatment on average by 38 minutes compared with IHT, subsequently lowering short-term mortality in STEMI.[16] Moreover, by strategically targeting 'high-yield' areas through the analysis of geographical patterns of disease occurrence, healthcare providers could further lower costs while maximising the effect of treatment. Preferential implementation in remote or rural areas may also improve outcomes for these vulnerable communities. Research indicates that a focus on high-yield areas potentially reduces time to PHT by 52 - 78 minutes and decreases adjusted 1-year mortality by up to 30% compared with IHT.[79,80] Although subject to health system development and infrastructure, strategic purchasing practice, in contrast to passive approaches, improves resource allocation and creates a better incentive for providers aiming to achieve improved health outcomes.[81] Variations in costs associated with IHT treatment highlight that clinical outcomes play a more substantial role in cost-effectiveness than direct costs of treatment.

This observation aligns with existing research that demonstrates that clinical effectiveness remains the primary driver of cost-effectiveness in STEMI interventions, not necessarily the use of interventions with the lowest upfront costs.[59,82,83] The findings in this study underscore the importance of optimising clinical outcomes, as improvements in survival and quality of life are likely to yield greater gains in cost-effectiveness than efforts focused on reducing IHT treatment costs. From a policy perspective, resource allocation in SA should prioritise strategies aimed at improving clinical outcomes, including timely reperfusion and system-wide improvements in STEMI care pathways. In this regard, investing in PHT for administration by emergency personnel and optimising referral networks could yield health and economic benefits.

We argue that the analysis of the findings, which demonstrated the dominance of PHT over IHT for STEMI, highlights critical opportunities for SA healthcare system improvement. Despite PHT being within the scope of emergency care practitioners in SA, its use by them remains extremely limited. Disconnects between policy and practice are particularly concerning, given the well-established evidence that PHT significantly reduces time to reperfusion and improves outcomes for STEMI patients, especially in settings where access to PCI is severely limited.

The primary rationale for implementing PHT as a standard practice and for transitioning responsibilities for its administration from

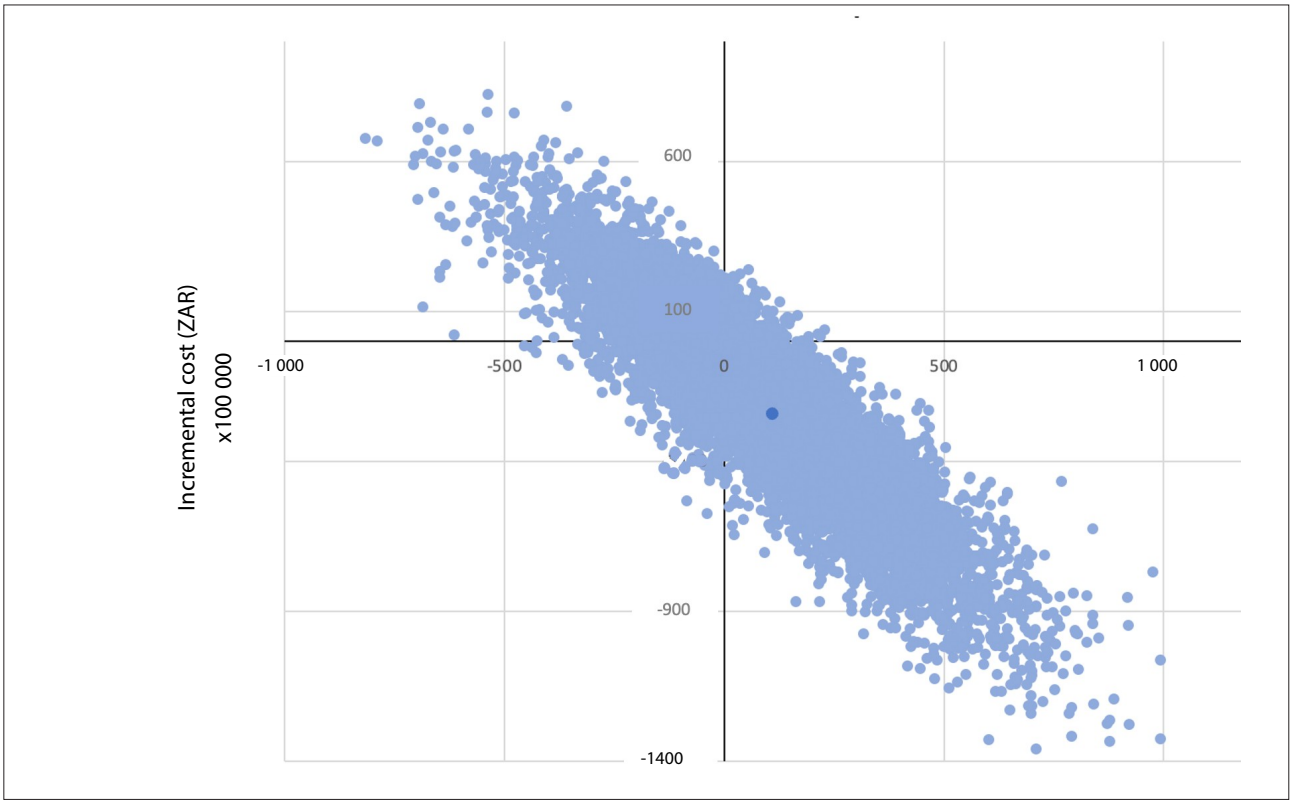


Fig. 3. Cost-effectiveness plane (ZAR per DALY averted).

Table 2. Incremental cost-effectiveness ratio

Comparator	Deaths	YLL	Costs (in ZAR)	DALYs
IHT	73	535	564 158 950.61	3 819
PHT	53	386	540 378 837.92	3 709
Incremental change	20	149	(23 780 112.69)	-110

IHT = in-hospital thrombolysis; PHT = prehospital thrombolysis; DALY = disability-adjusted life year; LYS = life years saved.

Table 3. Monte Carlo simulation summary results

ICER DALY, 95% CI		
Significance level	0.05	
Mean	374 979.97	
Standard deviation	33 364 054.25	
Sample	10 000	
Confidence value	653 923.45	
Confidence interval	(278 943.47)	1 028 903.42
ICER LYS, 95% CI		
Significance level	0.05	
Mean	(226 504.59)	
Standard deviation	9 017 557.04	
Sample	10 000	
Confidence value	176 740.87	
Confidence interval	(403 245.46)	(49 763.72)
Discounted cost, 95% CI		
Significance level	0.05	
Mean	(23 862 040.58)	
Standard deviation	30 674 081.69	
Sample	10 000	
Confidence value	601 200.95	
Confidence interval	(24 463 241.53)	(23 260 839.62)

ICER = incremental cost-effectiveness ratio; DALY = disability-adjusted life year; CI = confidence interval; LYS = life years saved.

the in-hospital setting to the prehospital environment is the well-established relationship between shorter time to thrombolytic treatment and improved clinical outcomes.[84] Furthermore, multiple studies and systematic reviews have demonstrated that, when safely administered by trained providers, PHT not only accelerates reperfusion but also maintains a safety profile comparable to IHT, with similar rates of in-hospital adverse events such as bleeding and stroke.[16] Shifting responsibilities in administration of thrombolysis for STEMI from the in-hospital setting to the prehospital environment is therefore a logical evidence-based progression, particularly in the SA context, where delays in definitive reperfusion therapy are common.[22]

Conclusion

Poorly equipped STEMI management systems lead to increases in burdens of illness and ineffective strategies, particularly in comparable instances where improved options exist.[85-87] It is essential that SA's limited resources are utilised optimally, with the contextualised interventions described in research findings implemented in real-world practice to improve health outcomes.[88]

IHT persists as a cornerstone of STEMI care in SA due to the structural and socioeconomic barriers limiting PCI access. Our findings confirm that PHT is more effective and less costly than IHT. Ostensibly, the use of PHT has the potential to substantially improve access to reperfusion in STEMI care and, when considered from both health and economic perspectives, may represent a reasonable and potentially advantageous strategy.

Based on the sensitivity of the cost-effectiveness of IHT treatment, any escalations in drug prices or hospital expenses in SA further erode the economic viability of in-hospital administration options. In contrast, PHT remains comparatively insulated from cost pressures, reinforcing its position as a cost-effective strategy, particularly in resource-constrained environments.

We argue that the use of thrombolysis in the prehospital phase represents a practical, scalable intervention to bridge gaps in timely STEMI care, optimising patient outcomes and addressing inequalities in access to advanced cardiac therapies in SA. Relevant stakeholders and policymakers are encouraged to reanalyse current STEMI management practice and to establish evidence-based interventions to include PHT, specifically to reduce treatment delays and expand reperfusion to locations with limited access to current guideline-directed therapies.

Study limitations

While this analysis provided valuable insights into the relative cost-effectiveness of IHT and PHT in the management of STEMI, several limitations should be considered when interpreting these findings. Longer time horizons favour the capture of the full consequences of clinical interventions,[89] whereas this study used a cross-sectional interpretation with the aim of addressing the research question and enabling more immediate decision-making regarding resource allocation. Real-world data show thrombolysis survivors experience complications over time, including higher rates of heart failure complications.[90] However, in this study, these additional complications were excluded from the assumptions to maintain analytical clarity, modelling immediate survival without disabilities. Although bleeding risks remain a critical post-thrombolysis consideration,[60] the exclusion of this outcome from our model reflects the need for contextualised acute STEMI management that is mortality- and morbidity focused.

This study reported on average cost-effectiveness, which might mask distributional effects across patient subgroups, healthcare settings or regions where additional approaches, such as scenario or subgroup analysis, could be useful. Reflective of inherit statistical challenges and the nature of standard confidence interval analysis, considerable uncertainty was evidenced around ICER estimates. Although sensitivity analysis was conducted to explore how changes in key parameters affected the ICER and confidence intervals informing the robustness of the findings, further research with expanded sample sizes or non-parametric data may also be useful.

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