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# Cost-effectiveness of incentives for physical activity in coronary heart disease in Germany: pre-trial health economic model of a complex intervention following the new MRC framework

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## ABSTRACT

**Objectives** The German Incentives for Physical Activity in Cardiac Patients trial is a three-arm, randomised controlled trial for secondary prevention of coronary heart disease (CHD). Guidance for developing complex interventions recommends pre-trial health economic modelling. The aim of this study is to model the long-term cost-effectiveness of the incentive-based physical activity interventions in a population with CHD.

**Methods** A decision-analytical Markov model was developed from a health services provider perspective, following a cohort aged 65 years with a previous myocardial infarction for 25 years. Monetary and social incentives were compared relative to no incentive. Intervention effects associated with physical activity were used to determine the costs, quality-adjusted life-years (QALYs) gained, incremental cost-effectiveness and cost–utility ratios. The probability of cost-effectiveness was calculated through sensitivity analyses.

**Results** The incremental QALYs gained from the monetary and social incentives, relative to control, were respectively estimated at 0.01 (95% CI 0.00 to 0.01) and 0.04 (95% CI 0.02 to 0.05). Implementation of the monetary and social incentive interventions increased the costs by €874 (95% CI €744 to €1047) and €909 (95% CI €537 to €1625). Incremental cost–utility ratios were €25 912 (95% CI €15 056 to €50 210) and €118 958 (95% CI €82 930 to €196 121) per QALY gained for the social and monetary incentive intervention, respectively. With a willingness-to-pay threshold set at €43 000/QALY, equivalent to the per-capita gross domestic product in Germany, the probability that the social and monetary incentive intervention would be seen as cost-effective was 95% and 0%, respectively.

**Conclusions** Exercise-based secondary prevention using inventive schemes may offer a cost-effective strategy to reduce the burden of CHD.

### WHAT IS ALREADY KNOWN ON THIS TOPIC
⇒ Incentives can serve as external stimuli, modifying physical activity behaviours, but their long-term cost-effectiveness among adults with coronary heart disease remains unexplored to date.

### WHAT THIS STUDY ADDS
⇒ Incentive schemes for physical activity in the secondary prevention of coronary heart disease may lead to cost-effectiveness but not to cost savings.

### HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY
⇒ Pre-trial modelling is a comprehensive health economic tool to inform complex interventions.
⇒ Investment in incentivised physical activity interventions may provide good value for money.

## INTRODUCTION

Cardiovascular diseases (CVDs) continue to be the leading cause of disease burden in the world.[1] Coronary heart disease (CHD) is the predominant type of CVD which affected 197 million people in 2019.[1] In Germany, although mortality rates have declined, high prevalence persists.[2] With over €46 billion, CVDs cause the highest costs to the German healthcare system compared with all other disease groups.[3]

Secondary prevention of CHD can improve life quality, reduce cardiovascular events and mortality.[4] However, inadequate implementation and low participation persist.[5] Physical activity (PA) is crucial in secondary prevention,[6 7] but implementing exercise recommendations remains problematic.[8] Both financial and non-financial incentives have been proposed to act as external stimuli and can foster engagement in PA programmes. Their design can influence intervention effectiveness, costs and cost-effectiveness. Reviews show partly mixed results but suggest positive

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trends for incentivised reinforcement strategies, especially in short-term interventions[9–12]

Incentivised reinforcement interventions for behaviour change are typically complex.[13] The UK Medical Research Council (MRC) updated its research framework for developing and evaluating complex interventions in 2021. Economic considerations should be a core component of all phases of intervention research.[14] Currently, we are developing a complex intervention intended to improve PA by monetary or social incentives, following the MRC framework. The INPHY trial, Incentives for Physical Activity in Cardiac Patients, is planned as a randomised controlled trial in participants with CHD in Düsseldorf, Germany.

Pre-trial health economic modelling, one form of health economic analysis, is a recommended approach to study intervention components and underlying mechanisms by which they influence outcomes.[15] Modelling a complex intervention prior to a full-scale clinical trial can provide valuable insights to refine the intervention design, to determine suitable evaluation measures and to project long-term outcomes.[16] While health economic modelling has been conducted in the context of CVDs, critical gaps persist. Economic analyses primarily focus on simulating risk factors for primary prevention, and often aim to estimate population costs for policy purpose.[17 18] Medical decision models along clinical trials are less common, with a focus on treatment and management rather than prevention interventions,[19 20] often based on post-trial analyses. Germany lacks such analyses, as most CVD models are developed in the USA and UK. Thus, this study aims to estimate the cost-effectiveness of the complex INPHY trial for PA in the secondary prevention of CHD by performing pre-trial health economic modelling.

## METHODS

This study followed the methodological framework proposed by the Consolidated Health Economic Evaluation Reporting Standards[21] (online supplemental appendix 1).

### Population, setting and comparators

The INPHY trial will be conducted as a prospective, three-arm, randomised-controlled trial in participants with CHD in Düsseldorf, Germany (online supplemental appendix 2). The intervention aims at improving PA in terms of daily walking steps. A financial and social incentive arm will be compared with a control group without incentives. The intervention will span 24 weeks, followed by a 24-week follow-up. Choosing an adaptive goal design, the base level step count will be the origin of each personalised trajectory of step goals. Yet, regardless of the base level step count, the daily step goal in the last week will be 8500 steps for each participant.[22] Incentives will be provided on a weekly basis if the weekly PA goal is accomplished. Every participant in the financial incentive arm will receive €17.50 for reaching the weekly PA

goal, corresponding to €420 in total. Participants in the social incentive arm will designate two persons from their social environment (eg, friends and family members) to provide social support. During the intervention period, these persons will be notified via text message at the end of each week if the participant has reached the weekly PA goal, fostering positive gratification.

### Patient and public involvement

Discrete-choice experiments were conducted to elicit patient preferences regarding incentive design and the intervention. Citizens and patients were involved in the development of the instrument. The project was presented to the Citizen Advisory Board (CAB) of the institute and discussed with the CAB members. For the planned pilot study of the INPHY trial, a study CAB will be established.

### Model structure

A de novo economic decision analytical model was developed by applying a Markovian approach.[23] The Markov model comprised four mutually exclusive health states: 'history of first myocardial infarction (MI)', 'reinfarction', 'post-reinfarction' and 'death'. For the base-case analysis, a cohort of 100 individuals aged 65 years with a male to female distribution of 1:1 entered the model with a 'history of MI'. Participants moved across health states at the end of each discrete time interval, also known as a Markov cycle.[24] A cycle length of 1 year was applied to reflect the nature of this chronic disease. The cohort was simulated until the age of 90 was reached. A health services provider (health system) perspective was taken.

### Transition probabilities and intervention effect

Transition probabilities describe the likelihood of moving from one state to another, thereby governing the direction and speed of transitions. They were derived from epidemiological estimates.[25] The probability of dying was obtained from the national life table of Germany.[26] To account for the increased disease-specific probability of dying for individuals with CHD, standardised mortality ratios in terms of relative risks were applied to cycle-specific general population mortality rates for the 'history of MI', 'reinfarction' and 'post-reinfarction' states.[27 28]

Participants in exercise-based programmes such as the INPHY trial may exhibit different transitions between health states. To address this, we adjusted transition probabilities to consider intervention effects. However, data on the dose–response relationship between walking steps (the primary pedometer-derived metric in INPHY) and clinical outcomes, especially in individuals with CHD in Germany and globally, are limited.[8 29 30] Therefore, we transformed walking steps into metabolic equivalents (MET),[31] a more standardised measure in PA studies. The PA per week was categorised into 'least active' (<24 MET×hour/week), 'intermediate' (24–56 MET×hour/week) and 'most active'

**Table 1** Markov model parameters and physical activity effects on outcomes

| Input | Data | Source |
|---|---|---|
| **Markov model parameters** | | |
| Standardised mortality ratio (SMR) in the 'history of first MI' state | 2.00 (1.99–2.01) | Smolina et al, 2012[27]; NICE, 2020[28] |
| SMR in the 'reinfarction' state | 4.50 (4.43–4.57) | Smolina et al, 2012[27]; NICE, 2020[28] |
| SMR of death in the 'post-reinfarction' state | 3.00 (2.95–3.05) | Smolina et al, 2012[27]; NICE, 2020[28] |
| Annual probability of a reinfarction | 0.04 | Stone et al, 2014[25] |
| Annual probability of dying | life-tables | DESTATIS, 2020[26] |
| **Physical activity effects on outcomes** | | |
| Relative risk (RR) of a new MI in an intermediately active group comparing with a least active group | 1.02 (0.86–1.22) | Stewart et al, 2017[32] |
| RR of a new MI in an active group comparing with a least active group | 0.90 (0.74–1.08) | Stewart et al, 2017[32] |
| RR of death in an intermediately active group comparing with a least active group | 0.75 (0.65–0.87) | Stewart et al, 2017[32] |
| RR of death in an active group comparing with a least active group | 0.70 (0.60–0.82) | Stewart et al, 2017[32] |
| The threshold between a least active and intermediately active group, MET.h/week | 24 | Stewart et al, 2017[32] |

MET, metabolic equivalents; MI, myocardial infarction.

($>58$ MET×hour/week). The categorisation was based on the STABILITY trial,[32] analysing mild, moderate and vigorous PA and subsequent MI and mortality in a large cohort of participants (n=15 486) with stable CHD. A baseline step level of 3000 steps per day was assumed in the model. Based on different PA categories ('least active', 'intermediate' and 'most active'), we applied exercise-related intervention effects using adjusted relative risks for morbidity and mortality (table 1). In our base-case analysis, intervention effects were only applied during the intervention year, assuming potential benefits would lapse afterwards. Figure 1 outlines the probability equations for various transitions.

## Costs and health effects

Annual cost estimates were applied to both health states and interventions. Direct medical costs from the primary and secondary care level were considered from German cost data[33–36] (online supplemental appendix 3). The costs of the monetary and social incentive intervention per year (excluding direct incentive costs) were estimated at €549.46 and €510.7 per person, respectively. The costs were developed on an activity-based costing basis (online supplemental appendix 4).

Health outcomes can be measured in utilities ranging from 0 (equivalent to death) to 1 (perfect health). They were applied annually to the different Markov
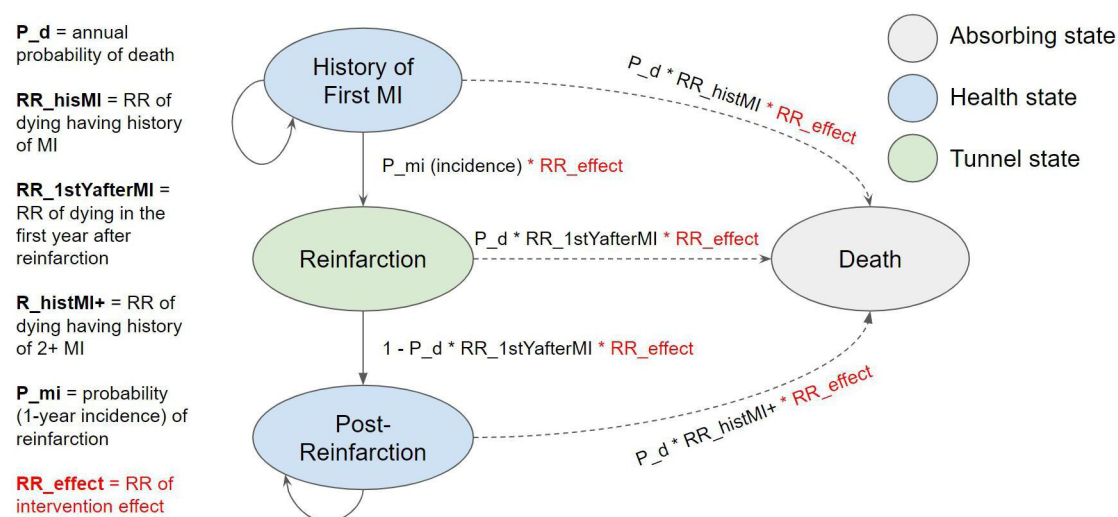


**Figure 1** Four-state Markov model with probability equations between transitions. The intervention in terms of relative risks (RRs) is applied to depict the intervention-associated effect on health outcomes. MI, myocardial infarction.

**Table 2** Annual costs and utilities associated with each health state

| Health state | Cost of care (€) | Source | Utility (QALYs) | Source |
|---|---|---|---|---|
| History of first MI | 1873 | Lutter *et al*, 2019[33] | 0.842 | NICE, 2011[37]; NICE, 2020[28] |
| Acute reinfarction | 14 315 | Schmid, 2015[34] | 0.779 | NICE, 2011[37]; NICE, 2020[28] |
| Post-reinfarction | 2482.2 | Lutter *et al*, 2019[33]; Sehested *et al*, 2019[35] | 0.821 | NICE, 2011[37]; NICE, 2020[28] |
| Death | 2247.6 | Bonafede *et al*, 2015[36] | 0 | by definition |

MI, myocardial infarction; NICE, National Institute for Health and Care Excellence; QALY, quality-adjusted life-year.

states.[28 37] Because of a conservative modelling approach and because trial data regarding the impact of INPHY's intervention arms on health-related quality of life has not collected yet, incremental utilities associated with participating in the INPHY trial were not applied.

The model applied an annual discount rate of 3% in accordance with WHO recommendations.[38] Tables 1 and 2 summarise key parameter values.

### Equity, diversity and inclusion statement
Our author group includes three women and four men, spanning junior, mid-career and senior researchers from different disciplines (medicine, health sciences, statistics, public health and economics). Several of us have immigrant backgrounds and belong to under-represented communities. While our model featured both genders, we recognise its limitations in replicating the full diversity of the INPHY study population.

### Outcomes and analyses
Outcomes over a lifetime period were calculated and included cumulative costs and quality-adjusted life-years (QALYs) gained associated with each intervention arm. Incremental cost-effectiveness ratios (ICERs) in terms of cost per life year (LY) and incremental cost-utility ratios (ICURs) in terms of cost per QALY gained were determined.

The base-case assumed the following adherence parameters. First, participants adhered to the predetermined daily goal of walking steps on 5 out of 7 days. Second, the level of PA on non-adhering days was as much as at the mean of all last weeks. Third, the level of PA in the remaining 28 weeks of the intervention year was assumed to be different for the intervention arms based on behaviour research.[39] While the monetary incentive group returned to baseline PA after the 24-week intervention (as the financial contributions were not paid any longer), the social incentive group was assumed to achieve the mean PA of the previous intervention weeks. Fourth, no effect of PA was assumed on health outcomes in the years after the intervention year.

Probabilistic sensitivity analysis (PSA) and scenario analysis were conducted to explore how the direction and magnitude of model outputs change on variation in inputs. PSA was performed with simultaneous random variation of input parameters using a second-order Monte Carlo simulation with 100 iterations and an assigned probability distribution (online supplemental appendix 5).

The Markov model and its analyses were conducted using the software programme R and the library 'hesim 0.5.1' (health economic simulation modelling).

### RESULTS
In the base case, the incremental QALYs gained from the monetary and social incentive, relative to control, were, respectively, estimated at 0.01 (95% CI 0.00 to 0.01) and 0.04 (95% CI 0.02 to 0.05) (table 3). In comparison to control, implementation of the monetary and social incentive interventions increased the costs by €879 (95% CI €744 to €1047) and €909 (95% CI €537 to €1625), respectively. Calculations of ICERs and ICURs, relative to control, reveal that the social incentive intervention was cost-effective with an ICER of €21 598/LY and ICUR of €25 912/QALY (95% CI €15 871 to €38 868) while the monetary incentive was cost-effective with an ICER of €99 103/LY and an ICUR of €118 958/QALY (95% CI €82 930 to €196 121).

**Table 3** Incremental quality-adjusted life-years (QALYs), incremental costs and incremental cost-effectiveness and cost-utility ratios (ICER/ICUR) for the intervention arms, relative to no intervention, with 95% CIs

| Outcome | Monetary incentive | Social incentive |
|---|---|---|
| Incremental QALY (relative to control) | 0.01 (95% CI 0.00 to 0.01) | 0.04 (95% CI 0.02 to 0.05) |
| Incremental costs (relative to control), € | €879 (95% CI €744 to €1047) | €909 (95% CI €537 to €1625) |
| ICER, €/LY | €99 103 (95% CI €68 919 to €166 042) | €21 598 (95% CI €12 611 to €42 150) |
| ICUR, €/QALY | €118 958 (95% CI €82 930 to €196 121) | €25 912 (95% CI €15 056 to €50 210) |

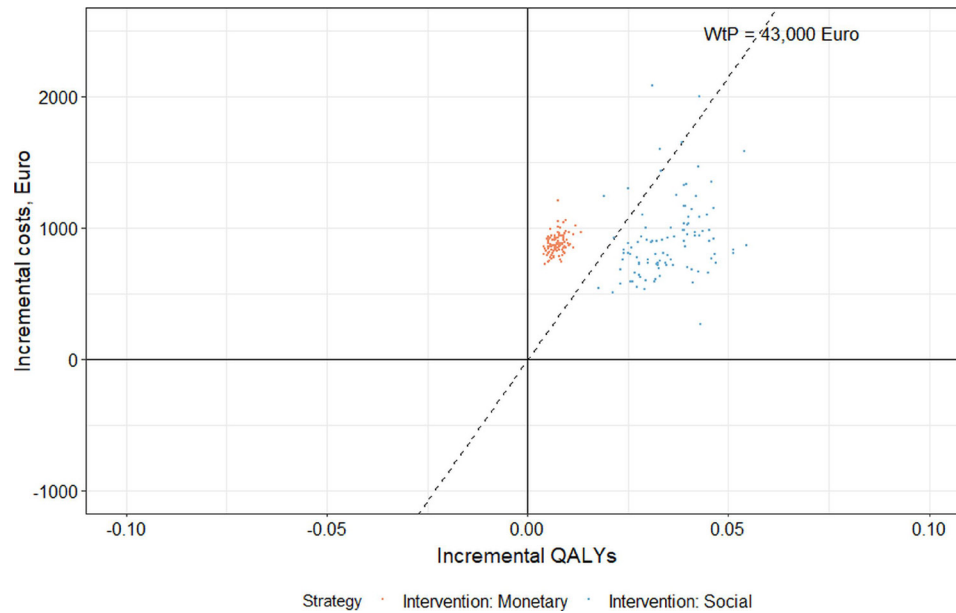ICUR, incremental cost–utility ratio.

**Figure 2** Cost-effectiveness plane. Incremental costs (ΔC) and effects (ΔE) of the intervention arms over a hypothesised maximum acceptable incremental cost-effectiveness ratio, that is, willingness-to-pay (WtP) threshold of €43 000/QALY gained (dotted line). QALY, quality-adjusted life-year.

## Sensitivity and scenario analyses

The results of the simulations of the multivariate sensitivity analysis were projected in a cost-effectiveness plane (figure 2). Dots representing the simulations in the north-east quadrant indicate that both the monetary and social incentive interventions were more costly but also more effective in terms of QALYs gained, relative to control. None of the incentive interventions dominated usual care, that is, were more effective and less costly (south-east quadrant). Likewise, none of the incentive interventions were dominated by usual care, that is, were less effective and more costly (north-west quadrant).

To ascertain whether the additional QALY benefit justifies the additional costs, the willingness-to-pay (WtP) threshold of Germany was applied as a diagonal line. Although Germany does not apply a specific willingness-to-pay threshold for the introduction of new interventions, this model followed the WHO's practice recommendations to use thresholds of one to three times (1–3×) gross domestic product (GDP) per capita.[38] Therefore, a conservative willingness-to-pay threshold of €43 000 per QALY gained was assumed, corresponding to one time (1×) the 2021 per-capita GDP in Germany. Most scenarios from the social incentive intervention fell in the area below this threshold and may be deemed cost-effective. The simulations from the monetary incentive intervention laid above the threshold, suggesting it may not be cost-effective for the German setting.

Figure 3 presents the results as a cost-effectiveness acceptability curve. The CEAC shows the relationship between the probability of the incentive interventions' cost-effectiveness and a range of hypothesised willingness-to-pay thresholds per additional QALY gained. At the threshold of €43 000 per QALY gained, the probability

that the social and monetary incentive intervention would be seen as cost-effective was 95% and 0%, respectively. A cost-effectiveness probability of 100% was reached for the social incentive intervention at a willingness-to-pay threshold of €67 400/QALY gained. For the monetary incentive intervention, the probability of cost-effectiveness was at 6% and 62% at double and triple the threshold, that is, €86 000/QALY gained and €129 000/QALY gained, respectively. A cost-effectiveness probability of 100% was reached for the monetary incentive intervention at a threshold of €208 700/QALY gained.

Table 3 displays the results for the eight different scenarios simulated, which explored the impact of variation in the base-case assumptions.

## DISCUSSION

Addressing the lack of health economic research concerning CHD secondary prevention, this is the first to model the long-term cost-effectiveness of incentivised reinforcement interventions for PA both internationally and in Germany. In line with MRC recommendations for complex interventions, economic and clinical consequences of monetary and social incentives were estimated using a decision analytical Markov model, before implementation in a clinical trial. This modelling exercise suggests that health effects are observed for both intervention arms, compared with control. The social incentive intervention was more cost-effective, than the monetary incentive intervention (table 3).

To identify whether interventions are good value-for-money, cost-effectiveness parameters are compared with cost-effectiveness thresholds specific to local healthcare systems. Unlike England, Germany does not establish specific threshold values. Thus, categorising the listed
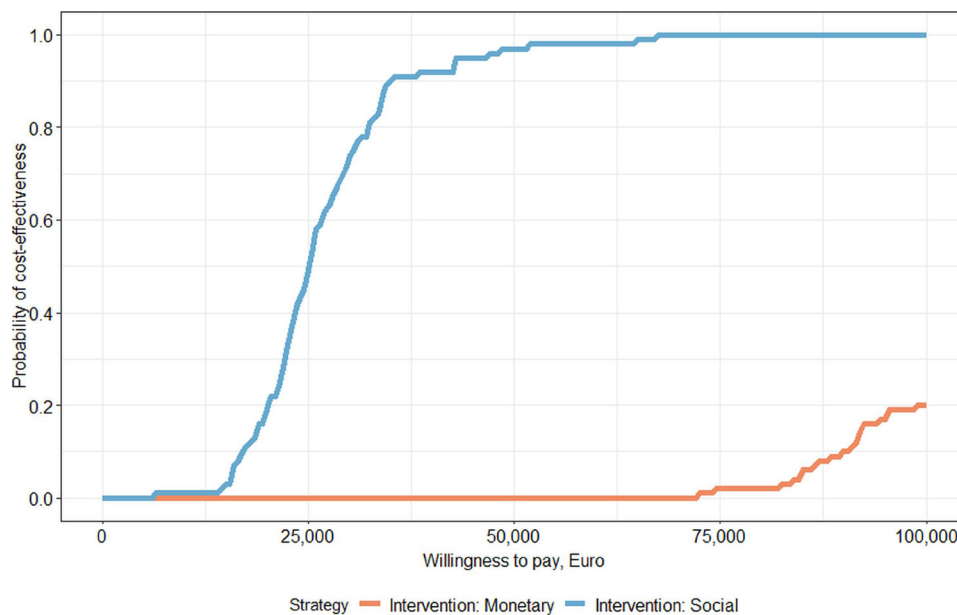
**Figure 3** Cost-effectiveness acceptability curve (CEAC). The CEAC represents the probability that each intervention arm is cost-effective (y-axis, ranging from 0 to 1) for given willingness-to-pay thresholds (x-axis).

ICURs as cost-effective or not is challenging. Given Germany's 2021 per-capita GDP of approximately €43 000,[40] a probability of cost-effectiveness of 95% for the social incentive intervention was reached. When three times per-capita GDP was applied, a 62% probability of cost-effectiveness was reached for the monetary intervention. Comparing INPHY's cost-effectiveness results to the American Heart Association's value levels,[41] the social and monetary incentive interventions would be of 'high value' (<US$50 000/QALY) or 'intermediate value' (US$50 000–US$150 000/QALY), respectively.

Based on scenario analyses, maintaining post-intervention activity is crucial for cost-effectiveness, even in the first year. Encouraging lasting lifestyle changes extending the trial period is recommended. Considering the potential for sustained impact from reinforcement schemes on PA,[42 43] prolonging interventions could enhance cost-effectiveness, with intervention costs offset by health gains (scenarios 2–3). Participants with low baseline step counts benefit less sustainably from intervention effects (scenario 4). Conversely, in scenario 5, higher baseline step counts led to improved ICURs (€100 140/QALY and €25 334/QALY for monetary and social incentives). This highlights the significance of thorough baseline assessments in feasibility studies.

The extent of INPHY's impact on participants' adherence to its interventions and beyond remains unclear. The model makes assumptions regarding adherence variables. The monetary incentive group returns to baseline activity levels as financial contributions cease while the social incentive group maintains the average step count from previous intervention weeks, assuming the formation of exercise habits due to social integration. This assumption framework for INPHY is informed by prior

**Table 4** Results of the scenario analyses

| Scenario | ICUR (cost/QALY) | |
| --- | --- | --- |
| | **Monetary incentive** | **Social incentive** |
| Post-intervention PA during the first year: maximum of previous weeks | 34 662 | 25 912 |
| 2-year effect period with the same (continuing) effect as in year 1 | 107 543 | 25 535 |
| 5-year effect period with the same (continuing) effect as in year 1 | 84 674 | 24 539 |
| 65 years, 2000 steps | 139 050 | 26 378 |
| 65 years, 4000 steps | 100 140 | 25 334 |
| 65 years at 4 MET (moderate/brisk walking) | 65 419 | 23 528 |
| 55 years, 3000 steps | 214 894 | 39 412 |
| 75 years, 3000 steps | 83 087 | 20 812 |

ICUR, incremental cost–utility ratio; MET, metabolic equivalents; PA, physical activity; QALY, quality-adjusted life-year.

research on incentivised reinforcement schemes.[9 10 12 44 45] However, this evidence primarily comes from studies of the general and overweight or obese populations, not specifically cardiac populations. For individuals with CHD, research is currently underway to establish the effectiveness of incentives in promoting PA, but early results seem promising.[46]

Drawing direct head-to-head comparisons with previous research is limited. Few international studies have explored the cost-effectiveness of incentive-based PA programmes using modelling techniques, although not specific to the CHD population. For example, Verhoef *et al* examined the cost-effectiveness of the Give-it-a-Go programme, offering leisure centre memberships to physically inactive individuals in London.[47] Using lifetime Markov modelling, increased costs were estimated at £67.25 and QALYs at 0.0033 compared with control. The incremental cost/QALY was £20 347. While the cost-effectiveness of Give-it-a-Go was similar to INPHY's social incentive arm, differences in model assumptions existed. Although participants in Give-it-a-Go had comorbidities such as CHD, diabetes or stroke, the model assumed all participants to be healthy. Additionally, mental health gains from PA were added, which were not applied in our model. Omitting mental health gains in Give-it-a-Go significantly increased the incremental cost/QALY to nearly £1.5 million. Another example is the Australian ACHIEVE study, where participants received incentives like clothing, supermarket vouchers and cookbooks on reaching PA targets.[48] The post-trial analysis, assuming 1 year of maintained intervention effects, estimated an ICER of $A74 683/QALY (95% CI $A12 054 to $A520 362), with 24% probability of cost-effectiveness at a willingness-to-pay threshold of $A50 000/QALY. Despite differences in population, incentive design and study type, the cost-effectiveness estimates were comparable to INPHY's pre-trial model.

## Strengths and limitations

Engaging in pre-trial health economic modelling, aligned with established guidelines, is recommended to inform behavioural intervention development.[14] Despite its potential benefits, modelling is often underused, possibly due to its complexity and a preference for feasibility and efficacy studies.[49] State-transition models, such as Markov models, are valuable for simulating chronic disease progression. While they have demonstrated utility in research and policy,[50] they may not fully capture the population's diversity in CHDs. Relying on averages limits the scope of inferences since CHD physiological changes are continuous, and costs and benefits can vary accordingly.

This study uses a comprehensive four-state model of CHD development that incorporates both chronic states and an acute tunnel state of reinfarction. Simultaneously, as all models are approximations of clinical reality, this model was only able to capture one episode of recurrent infarction, although in clinical reality individuals can suffer multiple reinfarctions. These limitations could be addressed by adding additional states and incorporating time dependency into transitions, if more disaggregated, long-term data on CHD in Germany and the world was available.

The model primarily focused on CHD-related costs and QALYs, overlooking potential benefits for conditions such as hypertension, dyslipidaemia or diabetes, which could enhance cost-effectiveness. Additional quality-of-life estimates for exercise-based interventions were not added, despite strong evidence that PA improves life quality.[51] Including incremental utilities for the exercise arms, once quantified, would likely improve cost-effectiveness.

## Directions for research, practice and policy

This study has affirmed various domains within CHD prevention that would benefit from additional research, practice and policy attention. First, investigating the long-term effects of PA programmes, using randomised controlled trial designs rather than prospective observational studies. Second, evaluating the suitability of pedometers and their PA metric 'steps', which are not designed for measuring more vigorous forms of exercise (eg, swimming and cycling). Third, determining the optimal type, amount and delivery method of incentives, including the exploration of combined approaches, for PA. Fourth, undertaking longer range follow-up of incentive-based PA interventions to assess sustainability and adherence profiles of participants. Fifth, integration of pre-trial modelling studies in the design and evaluation of complex interventions for behaviour change.

## CONCLUSIONS

An urgent need prevails to address the growing burden of CHD with cost-effective lifestyle interventions. Given the lack of pre-trial health economic models on exercise-based prevention programmes, this study is the first to model the long-term cost-effectiveness of monetarily and socially incentivised PA interventions, relative to no intervention. On balance, this analysis indicates that both incentive strategies were associated with more costs but also more effectiveness than control. This study prepares the economic evaluation and development of a complex behavioural PA trial and highlights what implications can be drawn for future prevention research. Research funders and policy-makers can use this evidence while additional research is needed to fill evidence gaps on unknown effects and uncertainty.

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