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Prehospital aspirin for acute coronary syndrome in India: modelling the health loss from a national protocol gap

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Research Article

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Abstract

India records about 1.65 million ischaemic heart disease deaths each year, yet its Standard Treatment Workflow for unstable angina and non-ST-elevation myocardial infarction begins at the primary health centre and is silent on aspirin before a patient reaches a facility, on chewing, and on formulation. Comparable international guidelines recommend 150–325 mg of non-enteric-coated aspirin, chewed, at first medical contact. We modelled what that gap costs. The counterfactual is not aspirin versus no aspirin: Indian registry data show that 97–98% of patients who reach a facility do receive antiplatelet therapy. The incremental value of a prehospital protocol therefore arises from three channels - patients who die before reaching care and so receive nothing at all, substitution of plain chewed aspirin for enteric-coated formulations, and earlier platelet inhibition among those who do arrive - net of fatal bleeding. At 55% achieved coverage the model estimates 23,867 net deaths averted annually (95% uncertainty interval 11,452 – 40,498) and 216,406 quality-adjusted life years gained (102,359–386,362), at US$ 363 per quality-adjusted life year (117–949). Benefit exceeded harm in 99.98% of 10,000 simulations. Had India adopted the protocol after ISIS-2 with realistic diffusion, 506,868 deaths (251,798–822,888) would have been averted between 1988 and 2024. Given United States inputs the model returns 8028 deaths averted against a published estimate of 13,016, indicating that it is conservative. Revising the Standard Treatment Workflow to specify prehospital, chewed, non-enteric-coated aspirin is among the least expensive interventions available to India's health system.

Introduction

People of South Asian ancestry - about 1.8 billion, roughly a quarter of humanity - carry a disproportionate burden of atherosclerotic cardiovascular disease.(1, 2) In the UK Biobank cohort, 8124 South Asian participants had an adjusted hazard ratio of 2.03 (95% confidence interval, CI: 1.86–2.22) for incident atherosclerotic cardiovascular disease compared with 449,349 European participants, while the pooled cohort equations predicted almost identical 10-year risk for the two groups.(1) In INTERHEART, South Asian adults had a first myocardial infarction at a median age of 53.0 years against 58.8 years for participants from western Europe or east Asia.(3)

India carries the largest share of this burden, and its cardiovascular mortality has risen while that of comparable high-income countries has fallen.(20) Ischaemic heart disease mortality rose from about 97 per 100,000 population in 2000 to about 111 per 100,000 in 2020, which corresponds to roughly 1.65 million deaths in 2024.(4) In the CREATE registry of 20,937 patients with acute coronary syndromes across 89 centres, the median interval from symptom onset to hospital arrival was 360 minutes (interquartile range: 123–1317).(5) Emergency medical services remain unevenly distributed, and most people do not know which number to call.(6) Aspirin is also substantially underused for secondary prevention across low- and middle-income countries, India among them.(23)

Against that background, one of the least expensive and best-evidenced interventions in acute cardiology is absent from India's national protocol. This paper quantifies what that absence costs in

terms of loss of lives and quality of life years.

A simple intervention, and an unusually uniform consensus

ISIS-2 randomised 17,187 patients with suspected acute myocardial infarction and found that one month of aspirin reduced five-week vascular mortality from 11.8% to 9.4% - a relative reduction of about 20%, or one death avoided for roughly every 42 patients treated.(7) Bleeds requiring transfusion occurred in 0.4% of both arms. Non-fatal reinfarction fell from 2.0% to 1.0% and non-fatal stroke from 0.6% to 0.3%.(7)

Formulation matters as much as timing. In a randomised, single-blind, triple-crossover study of 40 patients with type 2 diabetes, enteric-coated aspirin produced pharmacodynamic non-responsiveness in 52.8% of participants compared with 15.8% for immediate-release aspirin, with 63–70% lower peak plasma concentrations.(8) A secondary analysis of the ADAPTABLE randomised trial found enteric-coated aspirin associated with more major adverse cardiovascular events than uncoated aspirin.(9)

Guidance on this point is unusually consistent across health systems (Table 1). The 2025 ACC/AHA/ACEP/NAEMSP/SCAI guideline recommends 162–325 mg of non-enteric-coated aspirin, chewed, at first medical contact, as a class I, level A recommendation.(10) The 2023 European Society of Cardiology guidelines recommend a 150–300 mg oral loading dose.(11) The United Kingdom's National Institute for Health and Care Excellence recommends 300 mg as soon as possible.(12) The 2024 American Heart Association and American Red Cross first aid guidelines advise a lay rescuer to have an adult with non-traumatic chest pain chew 162–324 mg of aspirin while awaiting emergency services.(13) The National Health Service, St John Ambulance and the British Red Cross all instruct the public to chew 300 mg while waiting for an ambulance.(14)

Table 1
Aspirin recommendations for suspected acute coronary syndrome, selected guidelines and national bodies

Guideline or body	Dose	Formulation	Chewed	When
2025 ACC/AHA/ACEP/NAEMSP/SCAI (10)	162–325 mg	Non-enteric-coated	Yes	At first medical contact (class I, level A)
2023 European Society of Cardiology (11)	150–300 mg oral	Not specified	-	At first contact or diagnosis
NICE, United Kingdom (12)	300 mg	Not specified	-	As soon as possible
2024 AHA / American Red Cross first aid (13)	162–324 mg	Not specified	Yes	While awaiting emergency services
NHS, St John Ambulance, British Red Cross (14)	300 mg	Not specified	Yes	While waiting for the ambulance
ICMR Standard Treatment Workflow, India (15)	325 mg loading	Not specified	Not specified	At PHC/CHC level, i.e. after arrival

ACC: American College of Cardiology; AHA: American Heart Association; ACEP: American College of Emergency Physicians; NAEMSP: National Association of EMS Physicians; SCAI: Society for Cardiovascular Angiography and Interventions; NICE: National Institute for Health and Care Excellence; NHS: National Health Service; ICMR: Indian Council of Medical Research; PHC: primary health centre; CHC: community health centre.

India's protocol gap

The Indian Council of Medical Research Standard Treatment Workflow for unstable angina and non-ST-elevation myocardial infarction, issued in October 2019, organises management by facility tier.(15) The workflows are part of a national programme to standardise care across India's tiered health system, which makes them an efficient point of leverage: a change made once propagates to every tier.(21) Its first management column is headed "PHC/CHC level" and begins: "ECG, Troponin. Start - Aspirin, Clopidogrel, Heparin/LMWH, High dose atorvastatin, Metoprolol". The accompanying drug panel specifies an aspirin loading dose of 325 mg followed by 75 mg once daily.

Three things are therefore true of the workflow. It contains no step that occurs before the patient reaches a facility. It does not instruct that the tablet be chewed. And it does not specify formulation, in a market where enteric-coated 75 mg tablets predominate. The dose is right; the route into the patient, and the moment, are missing.

The consequences are not confined to India. Indian-trained physicians practise across the world, and clinicians elsewhere reasonably look to Indian guidance when treating patients of South Asian origin. A

national workflow that omits prehospital aspirin is read, wrongly, as evidence that the step is optional for this population.

Why the counterfactual is not aspirin versus no aspirin

Estimates of the burden of India's non-adoption have until now rested on an assumption that does not survive contact with Indian registry data. In CREATE, 98.2% of patients with ST-elevation myocardial infarction and 97.4% of those with non-ST-elevation myocardial infarction or unstable angina received antiplatelet drugs in hospital.(5) For a patient who reaches a facility alive, aspirin is already close to universal. The alternative to a prehospital protocol is therefore not "no aspirin"; for most survivors of the journey it is "aspirin somewhat later".

Treating the counterfactual as aspirin versus nothing, and then scaling a United States model output by the ratio of Indian to American ischaemic heart disease mortality, conflates two different quantities and cannot be reconciled with a 98% in-hospital treatment rate. We therefore rebuilt the analysis from first principles around three distinct channels through which a prehospital protocol adds value (Fig. 1).

Table 2
Modelled annual impact of prehospital aspirin adoption in India, 2024, by achieved protocol coverage

Outcome	Conservative (35% coverage)	Central (55% coverage)	Ambitious (75% coverage)
Channel A: pre-arrival deaths averted	4514 (2056–8711)	9550 (4407-18 060)	14 547 (6737-27 492)
Channel B: formulation	5165 (2113-10 619)	8116 (3321-16 687)	11 067 (4529-22 755)
Channel C: time-shift	3106 (158–7214)	6560 (341 – 14 994)	10 038 (515 – 22 747)
Fatal bleeds (subtracted)	290 (48-1652)	611 (101–3484)	930 (154–5288)
Net deaths averted per year	12 619 (6080-21 729)	23 867 (11 452 – 40 498)	35 053 (16 650 – 59 501)
QALYs gained per year	114 731 (54 730 – 206 270)	216 406 (102 359–386 362)	318 023 (148 907 – 566 637)
Non-fatal reinfarctions prevented	5271 (2394–9973)	9968 (4480-18 693)	14 643 (6553-27 529)
Non-fatal strokes prevented	1602 (681–3180)	3021 (1278–5947)	4443 (1876–8728)
Benefit-to-harm ratio	44.6 (7.1-295.8)	39.8 (6.4-264.2)	38.3 (6.1-253.3)
Cost per QALY gained (US$, PPP)	434 (139–1123)	363 (117–949)	338 (109–884)
Productivity preserved (INR Cr/year)	511 (213–1097)	963 (399–2046)	1415 (581–2994)

Values are medians with 95% uncertainty intervals from 10 000 Monte Carlo draws. Coverage is achieved protocol coverage; incremental coverage is measured against a baseline prehospital aspirin use of 16.9%. QALY: quality-adjusted life year; UI: uncertainty interval; INR: Indian rupees; Cr: crore.

Table 3
Cumulative counterfactual, 1988–2024, central scenario with logistic diffusion from 1990

Outcome	Median	95% uncertainty interval
Net deaths averted	506 868	251 798–822 888
QALYs gained	4.54 million	2.20–7.91 million
Productivity preserved (US$, PPP, discounted)	6.67 billion	2.76–13.49 billion

Channel A concerns patients who die before reaching any facility. They receive nothing under current arrangements, so for them a bystander- or dispatcher-delivered tablet is the only route to treatment and the full trial effect is in play. This is the dominant channel. Channel B concerns formulation. Because ISIS-2 was conducted with plain aspirin, its observed relative risk reduction already embeds plain-aspirin

non-response; backing out the full-responder effect and reapplying the enteric-coated non-response rate implies a relative risk reduction of 0.200 for plain aspirin against 0.151 for enteric-coated. Specifying plain, chewed aspirin therefore recovers about 5.8% of deaths among everyone who receives aspirin at all. Channel C concerns the time-shift for patients who do reach a facility and would have received aspirin regardless. We model this as small, because ISIS-2 found near-parallel absolute benefit across its 0–4, 5–12 and 13–24 hour strata, unlike thrombolysis.

Fatal bleeding is subtracted across the whole community chest-pain population that acts on the protocol, the great majority of whom are not having a myocardial infarction.

Methods

We modelled India annually from 1988 - the year ISIS-2 reported - to 2024. Ischaemic heart disease mortality rates were interpolated log-linearly between anchors of 84 per 100,000 (1990), 97 per 100,000 (2000) and 111 per 100,000 (2020) and applied to World Bank population estimates.(4, 16) Acute myocardial infarction was taken as 55% of ischaemic heart disease deaths, of which 60% occur before arrival at a facility and 45% of those effectively instantaneously. Of the remainder, 55% were treated as reachable in time given symptom recognition and tablet availability.

Coverage is expressed as achieved protocol coverage and is incremental to observed practice. The control arm of the ACS QUIK trial recorded prehospital aspirin use of 16.9%, which we used as the contemporary baseline, rising linearly from 5% in 1988.(17) Scenarios are 35%, 55% and 75% achieved coverage. Because ISIS-2 randomised patients who had survived to hospital, and deaths before arrival are enriched for primary arrhythmic mechanisms on which an antithrombotic has less purchase, aspirin efficacy in channel A was discounted to 0.80 of the trial relative risk reduction.

Quality-adjusted life years assume a mean age at infarction of 57.5 years, 20 years of remaining life expectancy multiplied by 0.65 for post-infarction excess mortality, a utility of 0.80 and a 3% discount rate, following standard recommendations for the conduct of cost-effectiveness analysis.(24) Non-fatal infarctions and strokes averted are added in ISIS-2 proportions. Productivity was valued by the human-capital method using World Bank gross domestic product per person employed in constant 2021 purchasing-power-parity dollars for each year, discounted at 3%, and then multiplied by 0.45 to approximate friction costs. Programme costs comprise the tablets consumed plus a national campaign.

For the cumulative analysis, coverage follows a logistic diffusion curve beginning in 1990 and reaching plateau around 2008, rather than switching on instantly. Uncertainty was propagated by Monte Carlo simulation with 10,000 draws over 35 parameters, using beta distributions for proportions, lognormal for relative risks and uniform where evidence was weakest. One-way sensitivity analysis was run at the 2.5th and 97.5th percentiles of each parameter. All model code and parameters are provided as supplementary material.

Findings

Of about 909,000 acute myocardial infarction deaths in India in 2024, roughly 546,000 occured before the patient reached a facility; of those, about 300,000 were not instantaneous and about 165,000 were plausibly reachable by a bystander tablet in time (Fig. 1A).

At 55% achieved coverage the model estimates 23,867 net deaths averted annually (95% uncertainty interval, UI: 11,452 – 40,498), 216,406 quality-adjusted life years gained (102,359–386,362), about 9968 non-fatal reinfarctions and 3021 non-fatal strokes prevented (Table 2, Fig. 2). In the deterministic base case, which is what Fig. 1B decomposes because medians of a simulated distribution do not sum, channel A contributes 10,063 deaths averted, channel B 8,534 and channel C 6,778, against 668 fatal bleeds, for a net of 24,707. Benefit exceeds harm by about 40:1 (6.4-264.2), and benefit exceeded harm in 99.98% of the 10,000 simulations. At 35% and 75% coverage, net deaths averted are 12,619 (6,080 – 21,729) and 35,053 (16,650 – 59,501) respectively.

The intervention costs about US$ 363 (117–949) per quality-adjusted life year gained, roughly 4% of India's gross domestic product per capita at purchasing-power parity, placing it among the most cost-effective interventions available at national scale. Friction-adjusted productivity preserved is about INR 963 crore (399-2,046) per year at central coverage.

Had India adopted the protocol from 1990 with realistic diffusion, an estimated 506,868 deaths (251,798–822,888) and 4.54 million quality-adjusted life years (2.20–7.91) would have been averted between 1988 and 2024, with about US$ 6.7 billion (2.8–13.5) in productivity preserved (Fig. 4). Because both India's ischaemic heart disease burden and its output per worker were far smaller in the early years - gross domestic product per person employed in 1990 was 27% of its 2024 value - the annual figures cannot simply be multiplied by 37 years. Estimates that do so, and that omit discounting and any adjustment for friction costs, overstate cumulative productivity loss by roughly an order of magnitude.

The result is most sensitive to the ISIS-2 relative risk itself, to the residual time-shift effect and to the proportion of ischaemic heart disease deaths attributable to acute infarction (Fig. 3).

Uncertainty and limitations

Several limitations deserve emphasis. The formulation channel rests on a single crossover study of 40 patients with type 2 diabetes taking daily aspirin, from which we extrapolate to a single loading dose in the general population.(8) That channel contributes about a third of the total benefit, and the extrapolation is the weakest link in the analysis. A trial of chewed plain versus enteric-coated aspirin in suspected acute coronary syndrome would resolve it directly, and would be inexpensive.

Applying the ISIS-2 relative risk reduction to people dying before they reach care assumes that a treatment tested in hospital survivors transports to a group enriched for arrhythmic death. We discount it to 0.80, but the true value is unknown; at 0.55 the central estimate falls by about 21%.

Our benefit-to-harm ratio of about 40:1 is more favourable than the roughly 14:1 implied by Russo and colleagues for the United States.(18) Two things explain the difference: India's chest-pain population contains a higher proportion of true infarctions, and we model coverage incremental to an existing 16.9% baseline. At the upper bound of our bleeding parameter the ratio falls to about 6:1, which remains clearly favourable. Aspirin should still be withheld in trauma, active bleeding and known allergy, and no protocol removes the risk of administration in aortic dissection.

The model scales from ischaemic heart disease mortality rather than measured infarction incidence, and India lacks a national registry that would allow direct estimation. The reachability ceiling, the instantaneous-death fraction and the community chest-pain episode rate are all assumptions informed by literature rather than Indian measurement.

As external validation, supplying the model with United States inputs returns 8,028 net deaths averted against the 13,016 estimated by Russo and colleagues for that setting.(18) The model is thus conservative relative to the only published comparator, by a factor of about 0.6.

Finally, the roughly two-fold higher baseline cardiovascular risk in South Asians would, if anything, amplify absolute benefit; we have not modelled it, which pushes in the same conservative direction.(1)

What should change

The Indian Council of Medical Research should revise the Standard Treatment Workflow to add a step that precedes the primary health centre: at first suspicion of acute coronary syndrome, 300–325 mg of plain, non-enteric-coated aspirin, chewed, in the absence of trauma, active bleeding or known allergy. The change is a single line, and the evidence for it has been stable for more than three decades.

The Ministry of Health and Family Welfare should ensure that plain 300–325 mg aspirin, not only the enteric-coated 75 mg tablet, is stocked in primary health centres, ambulances and pharmacies, and should carry a single public message: call 108 or 112, chew one plain aspirin, rest. Ambulance services, including GVK EMRI and Ziqitza, should authorise paramedics to give chewed aspirin at first suspicion, and dispatchers should be scripted to instruct callers to do so - an approach shown to raise prehospital aspirin delivery substantially.(19) India has done this kind of system redesign before: the Tamil Nadu ST-elevation myocardial infarction programme built a functioning hub-and-spoke network within a single state health system.(22) Low-cost, high-coverage interventions of this type are precisely those that Disease Control Priorities identifies as the priority for cardiovascular care in low- and middle-income settings.(25)

Because roughly 60% of infarction deaths occur before any facility is reached, dispatcher and bystander routes carry most of the available benefit. A protocol that reaches only ambulance crews will capture a minority of it.

The same reasoning applies beyond India. Countries with long prehospital intervals, high infarction burden and a predominance of enteric-coated formulations should examine whether their own protocols specify the moment, the route and the formulation, and not merely the dose.

Conclusion

India's Standard Treatment Workflow specifies the right dose of aspirin at the wrong moment, by an unspecified route, in an unspecified formulation. Correcting that could avert of the order of 24,000 deaths a year at plausible coverage, at a few hundred dollars per quality-adjusted life year, with benefit exceeding harm in virtually every simulation we ran. The estimates carry wide uncertainty and depend on assumptions we have set out openly; the direction of the conclusion does not depend on them. The intervention costs about two rupees.

Declarations

Contributors

AG conceived the study, built and validated the model, conducted the analysis, and wrote the manuscript.

Competing interests

The author declares no competing interests.

Funding

None.

Data availability

All model code, parameters, distributions and source data are provided as supplementary material, enabling full reproduction of every figure in this paper. All input data are publicly available from the cited sources.

Declaration on the use of AI-assisted technologies

During preparation of this work the author used an AI assistant to rebuild and validate the quantitative model, generate figures, and edit the manuscript. The author reviewed and edited all content and takes full responsibility for it.

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Figures

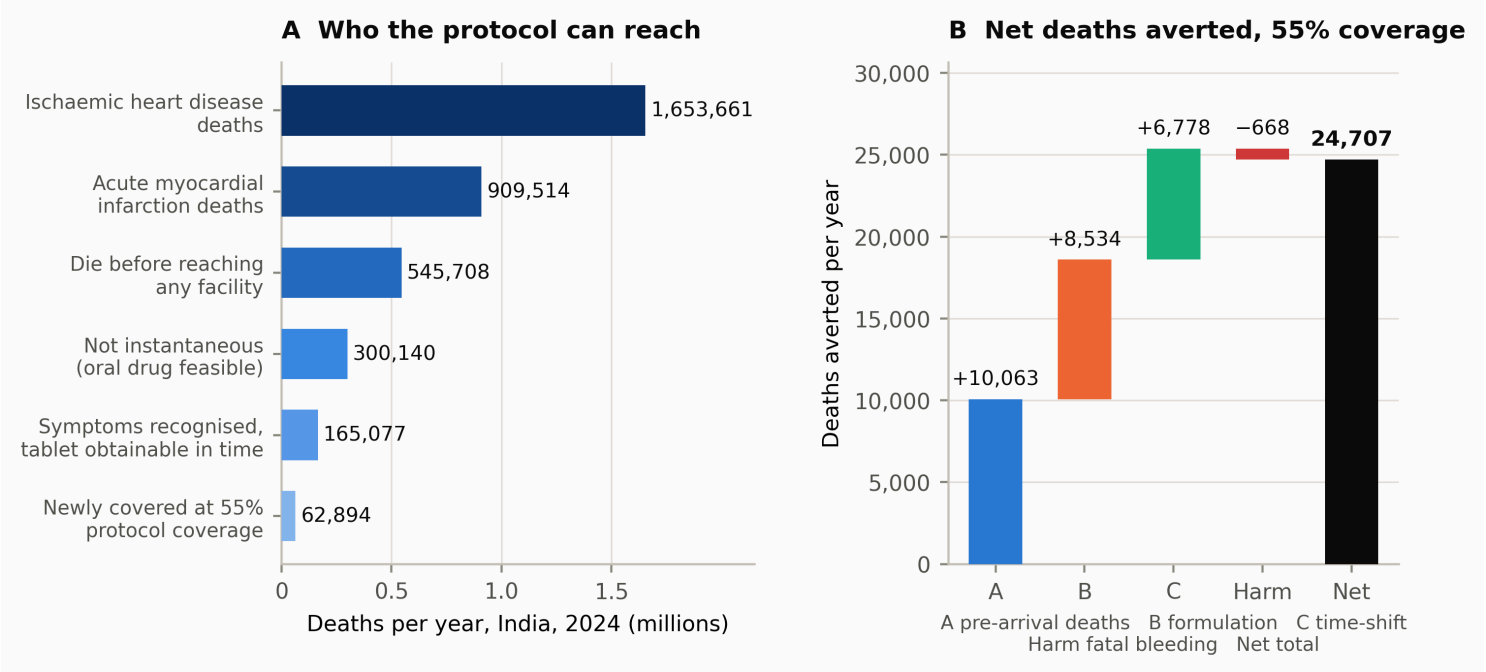


Figure 1

Where the benefit comes from. (A) The population an Indian prehospital aspirin protocol can reach, India, 2024. (B) Decomposition of net deaths averted at 55% coverage into channel A (pre-arrival deaths), channel B (formulation), channel C (time-shift) and fatal bleeding. Panel B shows the deterministic base case (24 707 net deaths averted); because the medians of a Monte Carlo distribution do not sum, the simulated medians reported in Table 2 (23 867) differ slightly and cannot be displayed as an additive waterfall.

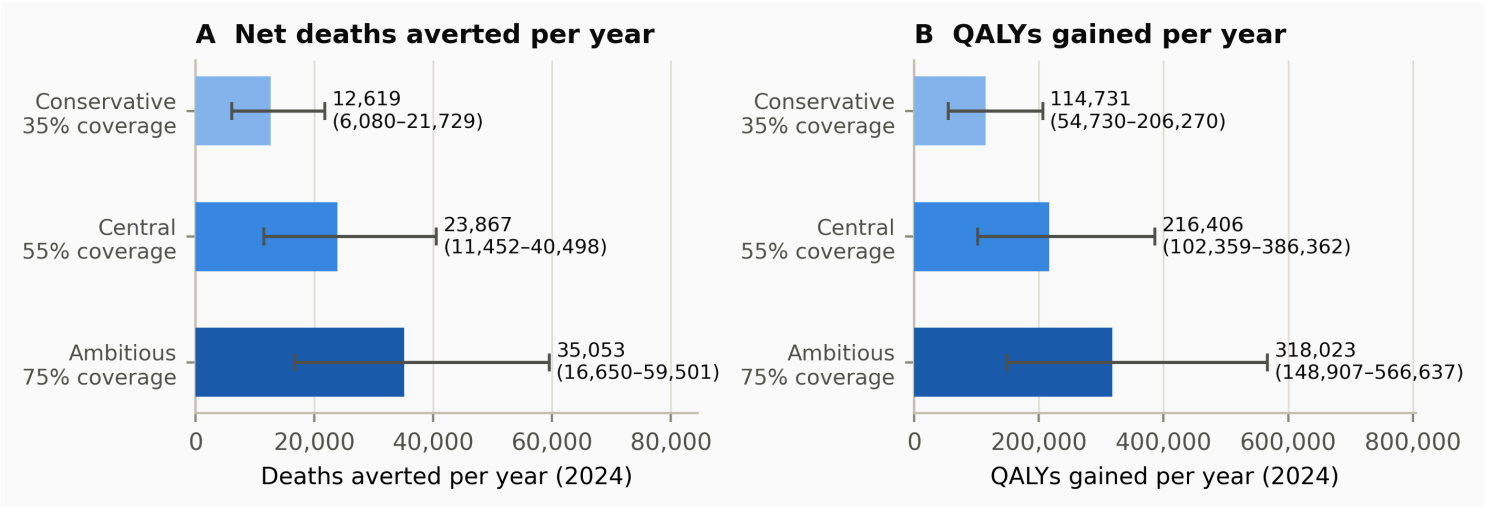


Figure 2

Modelled annual outcomes by achieved protocol coverage, India, 2024. (A) Net deaths averted. (B) Quality-adjusted life years gained. Bars show medians; whiskers show 95% uncertainty intervals from 10 000 Monte Carlo draws.

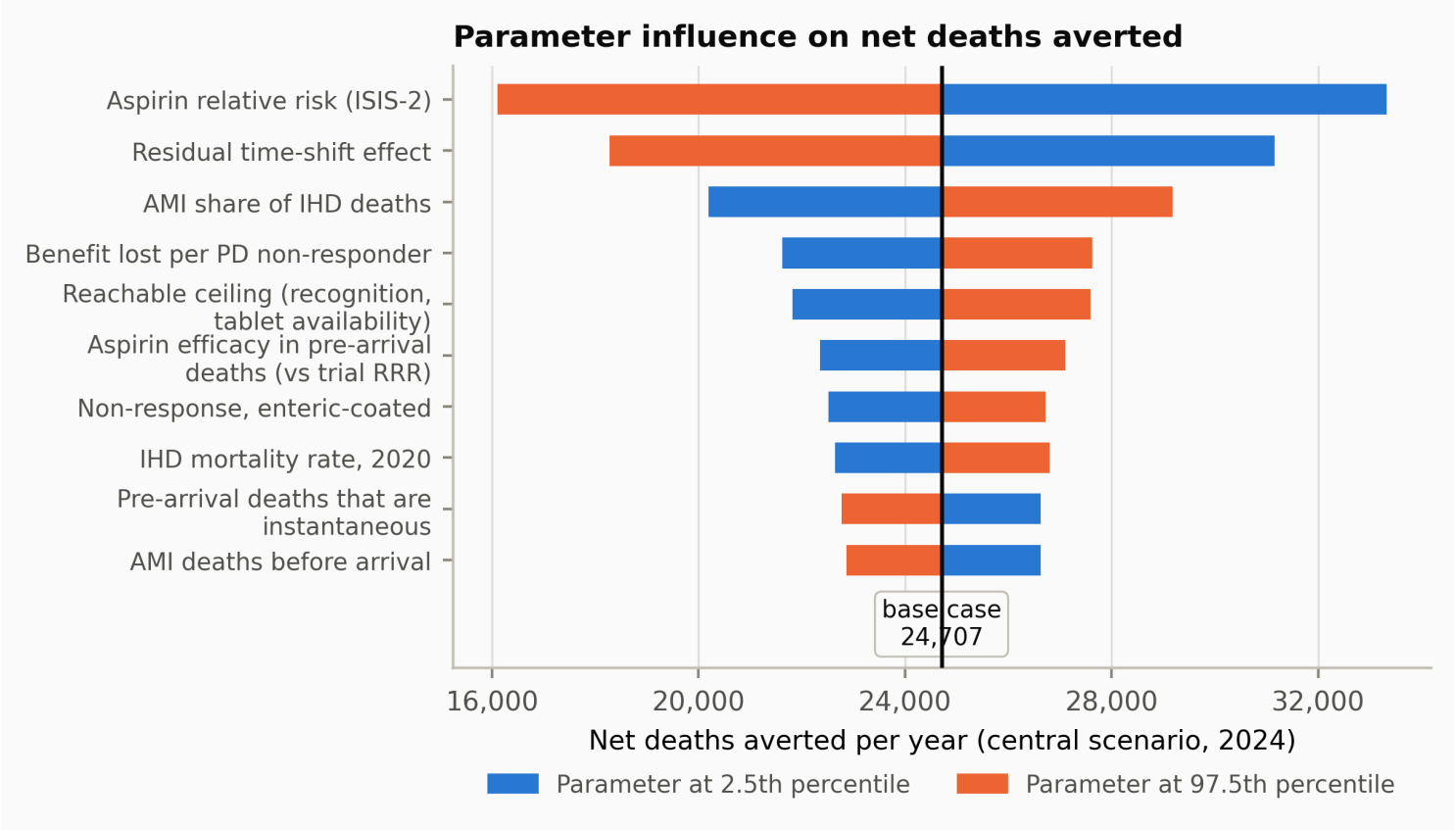


Figure 3

One-way sensitivity analysis of net deaths averted, central scenario, 2024. Each parameter is set to its 2.5th and 97.5th percentile in turn, holding all others at their central values.

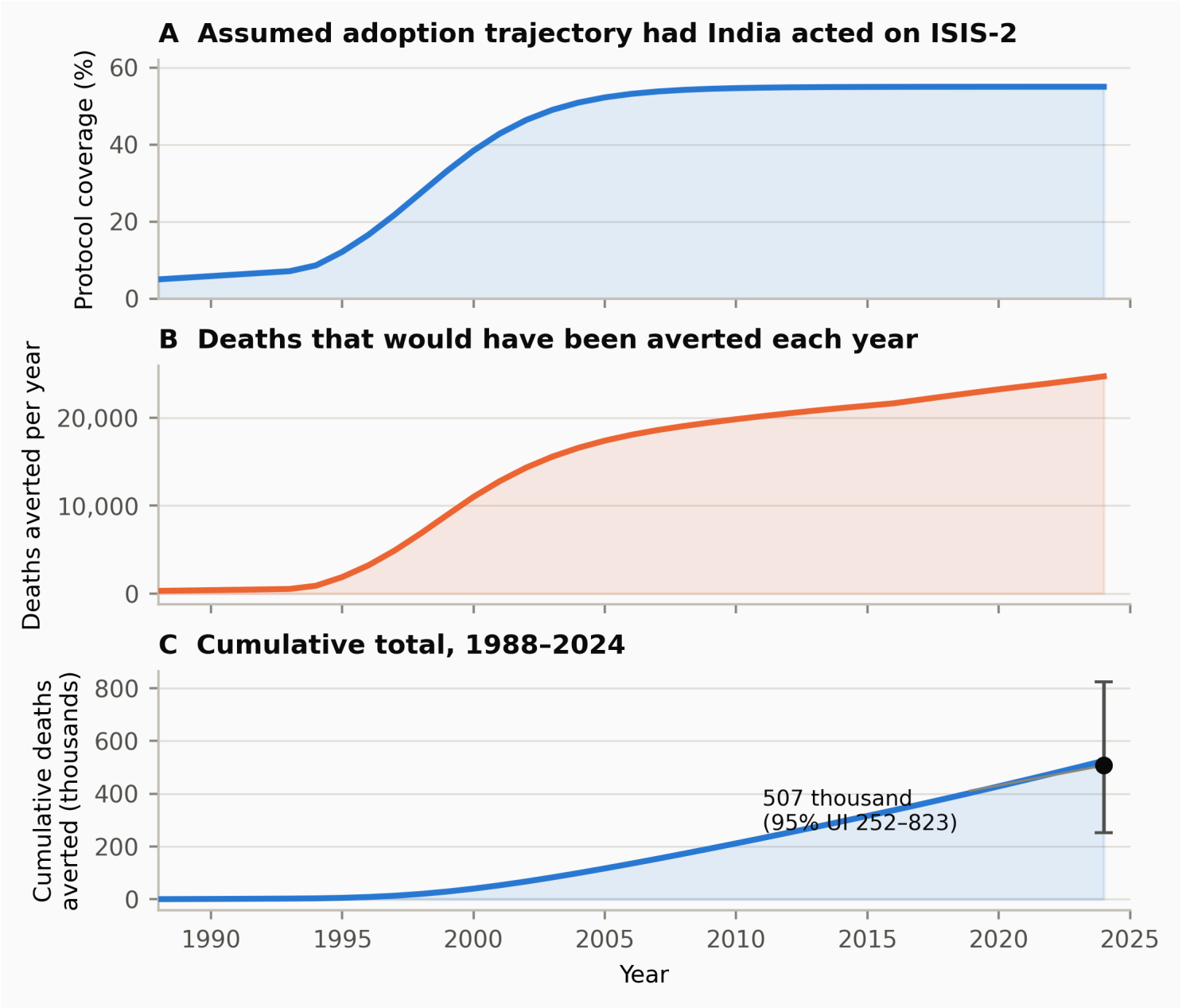


Figure 4

Counterfactual adoption, 1988-2024. (A) Assumed logistic diffusion of protocol coverage from 1990. (B) Deaths that would have been averted in each year. (C) Cumulative total, with the 95% uncertainty interval at 2024.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- AppendixS1Parameters.pdf
- PolicyBrief.pdf