Probabilities of treatment effects in complete or culprit-only revascularization for NSTEMI: A Bayesian re-analysis of the SLIM trial

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ABSTRACT

Background The completeness of revascularization in patients presenting with non–ST-elevation myocardial infarction (NSTEMI) and multivessel disease (MVD) remains understudied. The SLIM trial previously demonstrated a significant reduction in a composite endpoint of all-cause death, nonfatal myocardial infarction (MI), repeat revascularization, and stroke with complete revascularization under a frequentist framework. This post hoc Bayesian re-analysis offers a probabilistic interpretation beyond conventional significance testing.

Methods The primary composite endpoint was analyzed as in the original trial, while secondary endpoints of the composite were evaluated individually. Analyses under multiple priors assessed robustness. The minimal clinically important difference (MCID) was defined as 5% absolute risk difference (ARD) for the composite endpoint and 1% for individual endpoints. The primary model used a weakly informative prior on the log relative risk (RR) scale within a normal-normal Bayesian framework.

Results Total 478 patients were randomized (complete: $n = 240$; culprit-only: $n = 238$). The posterior median RR for the composite endpoint was 0.41 (95% credible interval [CrI] 0.22–0.76), corresponding to an ARD of –7.9% (95% CrI –10.4% to –3.2%). The probability of any benefit was 99.8%, and the probability of meeting the MCID was 91.2%. For repeat revascularization, the ARD was −8.3% (95% CrI −10.0% to −4.5%), with a $> 99.9\%$ probability of clinically relevant benefit. For nonfatal MI, the ARD was −2.8% (95% CrI −4.2% to 0.9%), with a 94.8% probability of benefit. Results were consistent across all priors.

Conclusion Complete revascularization provides a high probability of clinically meaningful benefit in NSTEMI patients with MVD, primarily through reductions in nonfatal MI and repeat revascularization. (Am Heart J 2026;296:107369.)

Keywords: Non-ST-elevation myocardial infarction; Revascularization; Culprit; Randomized controlled trial; Bayesian

Although patients with myocardial infarction (MI), whether ST-elevation MI (STEMI), or non-STEMI (NSTEMI), present with one culprit lesion, multivessel coronary artery disease (CAD) is present in more than 50% of such patients[1] The South Limburg Myocardial Infarction (SLIM) trial tested the hypothesis whether complete revascularization by percutaneous coronary intervention (PCI) was superior to culprit-only revascularization in NSTEMI patients.[2,3] The SLIM-trial found a statistically significant effect in favor of complete revascularization regarding the composite clinical endpoint, consisting of 360-day all-cause death, nonfatal MI, any revascularization, and stroke (risk difference −8.5%, 95% confidence interval [CI:] −13.9% to −3.9%, $P = .003$)[3]

The original trial was analyzed under the frequentist paradigm, and statistical significance was based on the *P*-value and an assumed significance level (alpha; generally <0.05). Nevertheless, the *P*-value represents the probability of the observed or more extreme data, under the assumption that the null hypothesis is true, in an infi-

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nite number of future hypothetical trials under similar circumstances. It therefore does not represent the probability of the current data, nor can it estimate the probability of a hypothesis or treatment effect, which may be of greater interest to the treating physician.[4,5] Furthermore, the SLIM-trial was powered for the primary composite endpoint, but not for the separate secondary endpoints[2] The absence of a statistically significant difference between groups regarding these endpoints does not necessarily rule-out the presence of a clinically relevant difference.

In the current study, we present a post hoc Bayesian re-analysis of the SLIM-trial to enable a probabilistic interpretation of results under varying assumptions of both the composite endpoint and the separate secondary outcomes, with a specific focus on the posterior probability of clinically relevant treatment effects.

Methods

Study design

The SLIM-trial was an investigator-initiated, multinational, randomized controlled trial (RCT) conducted in nine hospitals across Europe. The trial protocol was approved by the medical ethical committee of the Zuyderland Medical Centre (17-T-142), and was preregistered in ClinicalTrials.gov (NCT03562572). Oral informed consent in the presence of an independent third person was obtained from all participants with subsequent written informed consent directly after the index procedure.

This Bayesian re-analysis adheres to the Reporting of Bayes used in Clinical Studies (ROBUST) criteria[6]

Patient inclusion

Adult patients (up to 85 years old) presenting with NSTEMI and multivessel disease (defined as at least one nonculprit lesion with $a \geq 50\%$ stenosis in $a \geq 2.0$mm vessel) were included after successful treatment of the culprit lesion. Patients with left main disease, chronic total occlusions, complicated primary culprit lesion treatment, indication for surgical revascularization, previous surgery, severe valvular disease, or uncertainty regarding the culprit lesion, were excluded.

Study interventions

The intervention group (complete revascularization) underwent complete revascularization guided by fractional flow reserve (FFR) during the index procedure, and subsequent PCI was performed when FFR ≤ 0.80. Staged PCI within the intervention group was allowed within 72 hours.

The control group underwent culprit-only revascularization. Of note, the determination of the culprit was based on the interventional cardiologist's interpretation of the coronary angiogram, electrocardiographic (ECG) examination, or findings on noninvasive imaging in both groups.

Outcomes, follow-up, and sample size calculation

The primary outcome was a composite of 360-day all-cause death, nonfatal MI, any revascularization, and stroke. Secondary outcomes comprised the separate endpoints of the primary composite. The 360-day timepoint served as the primary analysis for this study, in line with the definition of the primary outcome of the original trial.

A sample size of 226 patients per group was deemed necessary to achieve a power of 80% (two-sided alpha-level 5%) using a baseline event rate of 10.5% during interim analyses, for the primary composite outcome under the frequentist paradigm. With adjustment for expected drop-out, 478 patients were eventually included (complete $n = 240$, culprit-only $n = 238$).[2,3] The analysis of the secondary endpoints was not adjusted for multiplicity in the primary analysis,[3] though this is less of a concern when using the Bayesian approach.

Rationale for a Bayesian approach

A Bayesian approach, even in a post hoc setting, can provide valuable additional information that can be extracted from a time- and resource-intensive RCT such as the SLIM-trial. Under the conventional frequentist paradigm, analyses that result in a *P*-value above the assumed significance level (alpha) are often considered both statistically and clinically insignificant. Nevertheless, clinical care is often more nuanced, and this should be reflected in trial interpretation. Through the Bayesian paradigm, the posterior probability of various treatment effect sizes can be estimated, with a particular focus on clinical relevance. Moreover, the robustness of findings can be tested under various prior assumptions. For a more in-depth explanation of Bayesian intricacies and terminology such as *prior, likelihood*, and *posterior*, we refer to recent explanatory reviews by our group.[4,5]

Outcome measures

The original SLIM-trial analysis used a time-to-event analysis, expressed in hazard ratios (HRs). To facilitate a clinically intuitive interpretation of our findings, the current re-analysis used the 360-days absolute event rates, expressed in absolute risk differences (ARDs) with corresponding 95% credible intervals (CrIs).

Minimal clinically important differences

Bayesian inference facilitates the estimation of the probability of *any* beneficial/harmful treatment effect (ie, an absolute risk difference exceeding 0%) in addition to that of any desired magnitude of effect, including clinically relevant ones. The current study comprised a post hoc analysis. Therefore, its results should be considered

Table 1. List of prior distributions' specifications and information sizes implemented for the analysis of the primary composite endpoint

Priors*	Mean log RR, SD	95% CrI	Median RR	95% CrI	Information size of a hypothetical trial
Weakly informative	[0, 2]	−3.92 to 3.92	1.00	0.02-50.00	NA
Skeptical	[0, 0.36]	−0.70 to 0.70	1.00	0.50-2.00	A trial of 198 patients (99 per arm) with 14 events per arm
Pessimistic	[0.46, 0.87]	−1.25 to 2.17	1.58	0.29-8.76	A trial of 44 patients (22 per arm) with 3 versus 2 events.
Enthusiastic	[−0.46, 0.87]	−2.17 to 1.25	0.63	0.11-3.50	A trial of 44 patients (22 per arm) with 2 versus 3 events.
Literature-based	[−0.30, 0.14]	−0.57 to −0.03	0.74	0.57-0.97	Based on the NSTEMI-subpopulation of the FIRE-trial, with an event rate of 72/467 in the complete arm, and 98/469 in the culprit-only group, totaling a number of 936 patients[8]

*Prior elicitation was based reproducibly on Heuts et al,[4,5] in which a weakly informative prior follows a normal distribution with a mean centering around 0 and an SD of 2 on the log RR scale. The skeptical priors centers around 0 with 10% probability of the MCID, while the pessimistic (+MCID) and enthusiastic (-MCID) center around the respective MCID with 30% probability of any benefit (pessimistic) or harm (enthusiastic). Finally, the literature-based prior was based on the difference in the primary endpoint of death, MI, stroke, or revascularization (similar to the SLIM-trial) of the NSTEMI subpopulation of the FIRE-trial[8]
CrI, credible interval; *MCID*, minimal clinically important difference; *MI*, myocardial infarction; *NA*, not applicable; *NSTEMI*, non-ST-elevation MI; *RR*, relative risk; *SD*, standard deviation.

with care, since they are based on a minimal clinically important difference (MCID) that was not prespecified. In line with previous studies,[7] an MCID of −5% ARD was considered clinically relevant for the primary composite outcome, while an MCID of −1% ARD was deemed clinically relevant for the separate endpoints given their lower event rate. We also explored other treatment effect sizes as well (between −10% and +2% for the composite endpoint, and −5% to +5% for the separate secondary endpoints). As such, MCIDs were not used to determine significance, but rather to attach clinical interpretations to the derived posterior. This facilitates the estimation of the probability of any desired threshold of clinical relevance, which may differ between settings, clinicians, and readers.

Prior justification

Bayesianism is often perceived as subjective due to the introduction of prior information into the analysis. Consequently, a weakly informative prior is an unbiased and reasonable starting point for any Bayesian re-analysis of an RCT. For the current study, priors are defined on the log relative risk (RR) scale, assuming a normal distribution. In line with contemporary recommendations,[4] the weakly informative prior has a mean (μ) of 0 and standard deviation (SD, σ) of 2 on the log RR scale.

To assess the robustness of findings, the (in)sensitivity of the posterior to various prior assumptions can be evaluated. For this purpose, we constructed skeptical (representing a prior belief of no difference, with a high certainty), pessimistic (representing a prior belief that the intervention is harmful, with relatively low certainty), and enthusiastic prior (representing a prior belief that the intervention is beneficial, with relatively low certainty), in line with previous recommendations[4] Table 1 presents the settings (on log RR and RR scale), rationale, and equivalent sample size of a hypothetical trial (ie, information size) of the various priors.

The aforementioned reference priors represent potential beliefs a clinician may have based on previous experiences, and these may be considered subjective as well. To formulate a prior grounded in currently available evidence from the literature, we derived a prior from the NSTEMI-subpopulation of the FIRE-trial (Table 1)[8]

The primary composite outcome will be analyzed under the aforementioned variety of priors, while the separate secondary endpoints will only be analyzed under the weakly informative prior.

Statistical analysis

The treatment effect was modelled on the log RR scale, which provides a natural parameterization for binary outcomes and aligns with the frequentist Wald estimator used in the original trial report. For each endpoint, the observed event data from the complete revascularization and culprit-only groups were used to compute the maximum likelihood estimate of log RR and its standard error via the standard Wald formula. For analyses involving zero events in one arm, a standard Haldane-Anscombe correction was applied by adding 0.5 to each cell.

A normal–normal conjugate Bayesian model was used for all analyses. For each analysis, a prior distribution on the log RR scale was combined with the normal likelihood derived from the Wald estimator, yielding a closed-form posterior distribution. Consequently, no Markov Chain Monte Carlo sampling algorithm was required. Posterior inference on log RR was based directly on the analytic posterior distribution. For interpretability, posterior draws (200,000) were generated from the posterior normal distribution and transformed to the RR and subse-

Table 2. Baseline characteristics

	Complete revascularization ($n = 240$)	Culprit-only revascularization ($n = 238$)
Demographics		
Age, mean (SD), y	65.6 (10.1)	66.2 (11.1)
Sex, no. (%)		
Male	182 (76.5)	165 (69.3)
Female	56 (23.5)	73 (30.7)
Medical history		
Hypertension, no. (%)	151 (63.4)	153 (64.3)
Hypercholesterolemia, no. (%)	124 (52.1)	143 (60.1)
Family history for cardiovascular disease, no. (%)	108 (45.6)	111 (47.0)
Diabetes Mellitus, no. (%)	65 (27.3)	41 (17.2)
Previous PCI, no. (%)	49 (20.6)	44 (18.5)
Previous myocardial infarction, no. (%)	37 (15.5)	36 (15.1)
Previous cerebrovascular accident, no. (%)	19 (8.0)	29 (12.2)
COPD, no. (%)	16 (6.7)	16 (6.7)
Previous congestive heart failure, no. (%)	4 (1.7)	2 (0.8)
eGFR <30ml/min/1.73m2, no. (%)	7 (2.9)	3 (1.3)
Prior medication use[*]		
Aspirin, no. (%)	72 (30.3)	66 (28.0)
P2Y12-inhibitor, no. (%)	28 (11.8)	29 (12.3)
OAC, no. (%)	14 (5.9)	22 (9.3)
Physical examination		
BMI, mean (SD), kg/m2	28.0 (4.7)	27.0 (4.5)
Systolic blood pressure, mean (SD), mmHg	133 (24)	136 (23)
Diastolic blood pressure, mean (SD), mmHg	74 (12)	74 (13)
Killip class[†]		
I, no. (%)	229 (96.6)	219 (92.8)
II, no. (%)	8 (3.4)	14 (5.9)
III, no. (%)	0 (-)	3 (1.3)
Additional examination		
ST-segment deviation, no. (%)[‡]	81 (34.0)	75 (31.5)
Maximum high-sensitive troponin, median [IQR], ng/L[§]	71 [28-252]	60 [26-190]
Maximum creatinin kinase, median [IQR], U/L[‖]	120 [83-207]	118 [75-201]
Other		
Current smoker, no. (%)	83 (35.0)	76 (32.2)
GRACE score, mean (SD)[¶]	108 (31)	107 (33)

BMI, body mas sindex (calculated as weight in kilograms divided by height in meters squared); COPD, chronic obstructive pulmonary disease; eGFR, estimated glomerular filtration rate; GRACE, Global Registry of Acute Coronary Events; PCI, percutaneous coronary intervention.

[*] Medication use at admission and discharge is shown elsewhere [3].

[†] Class I, no clinical signs of heart failure; class II, presence of rales and/or an S3 gallop; and class III, acute pulmonary oedema.

[‡] Defined as ST depression ≥1mm or ST-elevation <1mm suggestive of myocardial ischemia that did not meet criteria for ST-segment elevation myocardial infarction.

[§] The upper reference limit (99th percentile) was 14ng/L; values above this threshold were considered elevated.

[‖] Reference values: 171U/L for males and 145U/L for females; values above thresholds were considered elevated.

[¶] Score incorporates age, heart rate, systolic blood pressure, serum creatinine, Killip class, cardiac arrest at admission, ST-segment deviation, and elevated cardiac biomarkers (range, 1-372; higher values indicate greater risk of in-hospital and postdischarge mortality).

quent ARD scale. Posterior summary measures included posterior means/medians, and 95% CrIs for RR and ARD.

All analyses were performed in Python (NumPy, SciPy, Matplotlib) using custom code developed for this re-analysis, which is available through: https://github.com/samuelheuts/SLIM/tree/main.

Results

Patient and procedural characteristics

Between June 2018 and July 2024, 478 patients were included in the SLIM-trial (complete $n = 240$, culprit-only $n = 238$). Their baseline characteristics are presented in Table 2. Importantly, the mean age was 65.9 years, the majority were males (72.9%), 32.8% had ST-deviation upon ECG, the mean GRACE-score was 107, 75.6% of patients had two-vessel disease, and the median SYNTAX-score was 11.

Primary outcome analysis under a weakly informative prior

A primary outcome event occurred in 13 patients in the complete group (5.5%), and 27 patients in the culprit-only group (13.6%). Under a weakly informative prior, the posterior median difference between groups on the RR scale was 0.41 (95% CrI 0.22-0.76), translating to a −7.9% median difference on the ARD scale (95% CrI −10.4% to −3.2%). The resulting posterior probability of any beneficial treatment difference (ie, ARD

Table 3. Posterior distributions for the primary composite endpoint under a weakly informative prior (primary analysis) and various reference priors (secondary analyses)

Priors	Median RR	95% CrI	Mean ARD	95% CrI	*P*(any benefit)	*P*(MCID)
Primary analysis						
Weakly informative	0.41	0.22-0.76	−7.9%	−10.4 to −3.2%	99.8%	91.2%
Secondary analyses						
Skeptical	0.60	0.37-0.95	−5.4%	−8.4 to −0.6%	98.5%	58.8%
Pessimistic	0.47	0.26-0.84	−7.1%	−9.9% to −2.1%	99.5%	83.5%
Enthusiastic	0.42	0.24-0.76	−7.8%	−10.3 to −3.2%	99.8%	90.7%
Literature-based	0.66	0.52-0.86	−4.4%	−6.5 to −1.9%	99.9%	31.8%

ARD, absolute risk difference; *CrI*, credible interval; *MCID*, minimal clinically important difference; *P*, probability; *RR*, relative risk.

Table 4. Posterior probabilities of different effect sizes of the primary and secondary analysis of the composite endpoint

	Posterior probabilities of ARD thresholds						
Priors	<−10%	<−8%	<−6%	<−4%	<−2%	<0%	<2%
Primary analysis of the composite endpoint							
Weakly informative	6.5%	47.9%	82.9%	95.6%	99.0%	99.8%	100%
Secondary analyses of the composite endpoint							
Skeptical	0%	4.9%	36.8%	74.8%	93.0%	98.5%	99.7%
Pessimistic	2.1%	30.8%	71.0%	91.1%	97.7%	99.5%	99.9%
Enthusiastic	4.6%	44.2%	81.6%	95.6%	99.1%	99.8%	100%
Literature-based	0%	0%	7.4%	65.6%	97.0%	99.9%	100%

ARD, absolute risk difference.

<0%) was 99.8%, and the posterior probability of the specified MCID (ie, ARD <5%) was 91.2% (Table 3). Table 4 presents the posterior probabilities for a range of treatment effects, between −10% and +2%. Figure 1A presents the findings under a weakly informative prior graphically.

Primary outcome analysis under various other priors

The posterior median RR ranged from 0.42 (enthusiastic) to 0.66 (literature-based[8]), while the posterior median ARD ranged from −4.4% (literature-based[8]) to −7.8% (enthusiastic) under a variety of priors. The probability of any benefit was high across all priors (98.5%-99.9%), while the probability of the MCID ranged between 31.5% to 90.7%, depending on the prior (Table 3). Table 4 presents the posterior probability estimates of various treatment effect size thresholds under these priors. In addition, Figure 1B-E present these findings graphically.

Secondary outcome analysis

All secondary outcomes were only analyzed under a weakly informative prior. Mortality occurred infrequently at 360 days (5 versus 3 events), resulting in a median posterior ARD of 0.7% (95% CrI −0.7% to 6.2%), a posterior probability of any difference in favor of complete revascularization of 25.7%, and of a clinically relevant mortality reduction by complete revascularization of 0.2%. These differences are less precise due to the low number of events (Table 5, Figure 2A)

At 360 days, MI occurred in 5 versus 12 patients, resulting in a median posterior ARD of −2.8% (95% CrI −4.2% to 0.9%), a posterior probability of any beneficial effect of 94.8%, and of 88.4% for the MCID. These results are more robust due to an increased rate of events (Table 5, Figure 2B).

Any revascularization during follow-up was performed in 7 versus 27 patients, leading to a median posterior ARD of −8.3% (95% CrI −10.0% to −4.5%), a posterior probability of any benefit of 99.9%, and a probability of 99.9% that this reduction was more than 1% ARD (Table 5, Figure 2C).

Finally, stroke was very infrequent (1 versus 0 events). The resulting ARD, after correction for 0-events, was 0.2% (95% CrI −0.2% to 4.6%). These results were far less reliable and posterior inference is imprecise for stroke due to the extremely low event rate and required adjustment (Table 5, Figure 2D).

Table 6 presents an overview of posterior probability estimates for various treatment effect size threshold between −5% and +5% ARD for all separate secondary endpoints under a weakly informative prior.

Discussion

This Bayesian re-analysis of the SLIM-trial found a 91.2% probability of a clinically relevant difference in the primary composite endpoint of 360-day all-cause death, MI, revascularization, and stroke, in favor of an FFR-guided complete versus culprit-only revascularization strategy in patients presenting with NSTEMI and MVD.

Table 5. Posterior probabilities of different effect sizes of the separate endpoints of the composite

Priors	Median RR	95% CrI	Mean ARD	95% CrI	*P* (any benefit)	*P* (MCID)
Analyses of the separate endpoints of the composite						
Mortality	1.56	0.41-5.95	0.7%	−0.7 to 6.2%	25.7%	0.2%
Myocardial infarction	0.44	0.16-1.18	−2.8%	−4.2 to 0.9%	94.8%	88.4%
Repeat revascularization	0.27	0.12-0.60	−8.3%	−10.0 to −4.5%	99.9%	99.9%
Stroke	1.92	0.16-23.12	0.2%	−0.2 to 4.6%	30.2%	0%

ARD, absolute risk difference; *CrI*, credible interval; *MCID*, minimal clinically important difference; *P*, probability; *RR*, relative risk.

Table 6. Posterior probabilities of different effect sizes of the separate endpoints of the composite

	Posterior probabilities of ARD thresholds										
Priors	<−5%	<−4%	<−3%	<−2%	<−1%	<0%	<1%	<2%	<3%	<4%	<5%
Analyses of the separate endpoints of the composite											
Mortality	0%	0%	0%	0%	0.2%	25.7%	58.3%	77.2%	87.2%	92.6%	95.5%
Myocardial infarction	0%	7.0%	44.1%	73.8%	88.4%	94.8%	97.6%	98.9%	99.5%	99.7%	99.9%
Repeat revascularization	96.2%	98.4%	99.3%	99.7%	99.9%	99.9%	100%	100%	100%	100%	100%
Stroke	0%	0%	0%	0%	0%	30.2%	80.8%	91.1%	94.9%	96.8%	97.8%

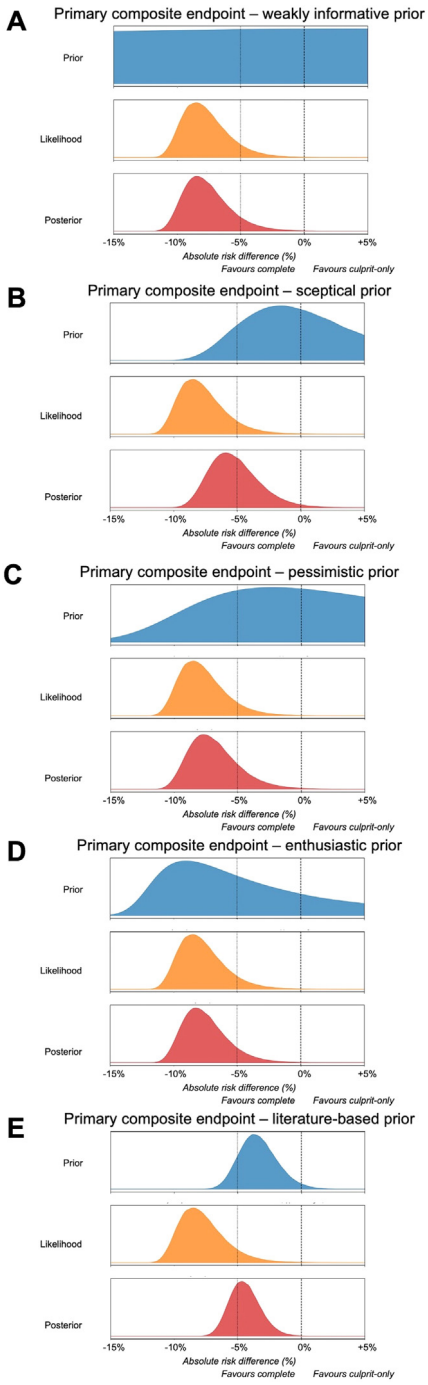
ARD, absolute risk difference.

Analyzing the secondary endpoints, it became apparent that these results were largely driven by reductions in revascularization- and MI-rates, with a 99.9% and 88.4% probability of achieving a clinically relevant difference regarding these endpoints, respectively. These results were robust when analyses under a variety of prior conceptions were performed. When information from the literature was taken into account, a 4.4% absolute risk reduction in the primary composite endpoint was considered to be the most probable effect.

Several RCTs have evaluated the effectiveness of complete over culprit-only revascularization by PCI in patients presenting with acute coronary syndromes.[8-13] Most of these trials included patients with STEMI, and only the FIRE trial—focusing on elderly patients—included a subpopulation of individuals with NSTEMI[8] Most of the trials favored the complete revascularization strategy group through a statistically significant reduction in the primary endpoint, that could consist of death and MI, with[8-10,13] or without[8,11] the inclusion of revascularization during follow-up. A subsequent recent patient-level meta-analysis including both STEMI and NSTEMI patients demonstrated a statistically significant benefit of complete revascularization for the combined endpoint of cardiovascular death and MI (HR 0.76, 95% CI: 0.67-0.87), cardiovascular death alone (HR 0.76, 95% CI: 0.62-0.93), and all-cause death (HR 0.85, 95% CI: 0.73-0.99)[14] However, this pooled analysis was dominated by STEMI patients. Indeed, the majority of NSTEMI patients were contributed by the FIRE trial[8] (and a minority by FULL-REVASC,[9] meta-analytic NSTEMI HR 0.71, 95% CI: 0.52-0.98, p-for-interaction = 0.65, implying consistency in treatment effects between STEMI and NSTEMI subgroups). However, the FIRE trial focused solely on elderly patients (mean age 80 years),[8] and FULL-REVASC only included (a small number of) high-risk NSTEMI patients,[9] leaving an important knowledge gap in the optimal treatment strategy of nonelderly, nonhigh-risk NSTEMI patients. Moreover, the higher risk population in FIRE led to a higher baseline event rate in its NSTEMI population (20.9%)[8] In turn, the ARD seen in FIRE (−5.5%) actually only translates to an RR of 0.74. As the current re-analysis was performed primarily on the (log) RR scale, the FIRE-trial's results are less positive than those of SLIM in terms of relative risk. The combination of this reduced (relative) effect size and the important amount of information (>900 patients) that the FIRE-trial contributes as a prior to the eventual posterior, jointly explain the paradoxically lower probability of a clinically relevant treatment effect under this prior (31.5%).

This also highlights the novelty and importance of the SLIM-trial, as this was the first RCT exclusively including NSTEMI patients, providing the highly anticipated evidence for complete revascularization in this important and prevalent patient population[3] In the original frequentist analysis, a statistically significant reduction in the primary composite endpoint was observed, which seemed to be solely driven by revascularization during follow-up (revascularization 3.0% vs 11.5%, $P < .001$, MI 2.1% vs 5.1%, $P = .09$). Indeed, under the frequentist paradigm, a trial's result is interpreted in a binary fashion ("negative" or "positive"), dismissing potentially important findings in the analysis of secondary endpoints that the trial was originally not powered for. This is of particular importance, as repeat revascularization during follow-up is often regarded as a "softer" endpoint,[15] that may be prone to "subtraction anxiety" in unblinded trials—a circumstance in which the patient (and treat-

Figure 1. Prior, likelihood, and posterior distributions of the primary composite endpoint under various priors.



ing physician) may know that an intervention is experimentally subtracted, leading to a perceived increase in symptomatology and decision to initiate treatment (ie repeat revascularization)[16] However, based on the more nuanced current Bayesian interpretation of the SLIM-trial, it is highly likely that complete revascularization also leads to *any* reduction in nonfatal MI (94.8% probability), and the probability of a clinically relevant reduction even exceeded 88%. This potential (clinically relevant) difference in MI, despite not being statistically significant, became not only apparent from the 390-day extended follow-up analysis in the original publication,[3] but it would also be in line with the available complete revascularization in STEMI literature[14] The dismissal of such a clinically relevant treatment effect based on a nonsignificant *P*-value from a frequentist analysis could be problematic, and potentially harmful. Moreover, patients with STEMI generally have a higher early risk of adverse events, including mortality, as compared to NSTEMI patients,[17] and it may take a considerable amount of time to accrue a sufficient number of events to establish statistical significance for these endpoints in the NSTEMI subpopulation. Importantly, most nonfatal myocardial infarctions occurred late during follow-up and were adjudicated as spontaneous rather than procedure-related, supporting their interpretation as novel events[3]

Consequently, this post hoc Bayesian analysis demonstrates that the primary endpoint of the SLIM-trial was not only reduced to a statistically significant degree, but this effect was most probably also clinically relevant (91.2% posterior probability). The reduction in the composite outcome was primarily driven by a decrease in revascularization procedures, but likely also through less occurrence of nonfatal MI in the complete revascularization group. Longer term follow-up of the SLIM-trial is warranted to evaluate the eventual effects of these differences on survival.

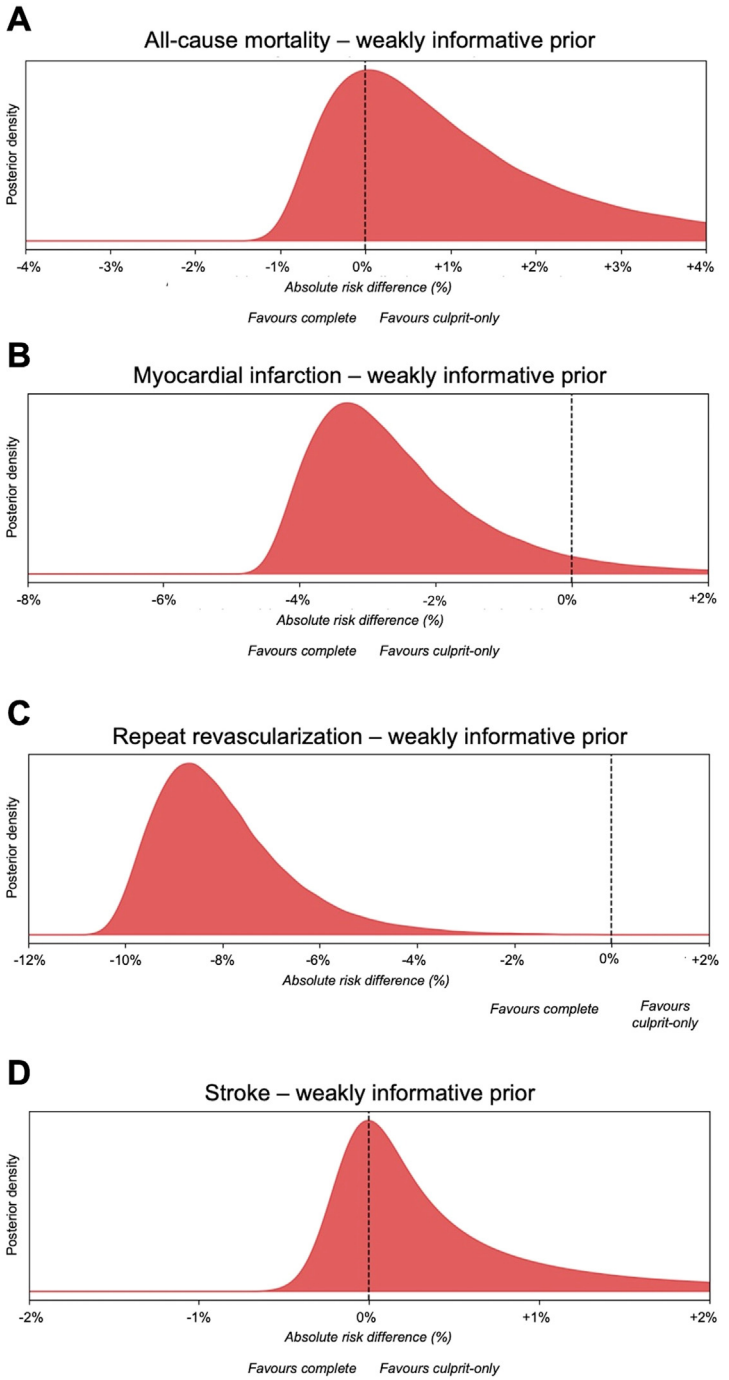
Interpretation

In the present analysis, the evidence for *any* benefit of complete revascularization (ARD <0%) is extremely strong (posterior probability 99.8% under the weakly informative prior), implying that remaining uncertainty primarily concerns the magnitude rather than the existence of benefit. By contrast, the probability that the treatment effect exceeds the predefined MCID (ARD <5% for the composite endpoint) was 91.2%, which can be interpreted as strong evidence that the expected benefit is not merely nonzero but also clinically meaningful. Importantly, the probability of exceeding the MCID varied across priors (ie, lower under the literature-based prior). This distinction is clinically useful: it supports adoption of complete revascularization as the default strategy to reduce the composite endpoint, while transparently communicating that the most plausible absolute gain may differ across settings and baseline risks.

Limitations

This post hoc Bayesian analysis has the same limitations as those reported in the frequentist analysis, such as the open-label design, lack of screening data, and the difficulty in determining the culprit lesion in NSTEMI.

Figure 2. Posterior distributions of the separate endpoints of the composite under a weakly informative prior.



Furthermore, the SYNTAX-score was relatively low, and these results may not be generalizable to patients with more complex multivessel disease that is amenable to surgical revascularization.

The SLIM-trial was not powered for its separate secondary endpoints, and a probabilistic interpretation of these outcomes was of particular interest to the current Bayesian re-analysis. Nevertheless, the Bayesian paradigm is often criticized for its perceived subjectivity, and this is most apparent in a post hoc re-analysis. Indeed, the determination of the prior and the MCID could be directed in such a manner that the resulting posterior ben-

efits complete revascularization. To counteract these potential sources of bias, we have constructed reference priors in line with previously reported (objective) recommendations,[4] while a range of posterior probabilities for plausible MCID thresholds was reported.

Finally, the literature-based prior was derived from the FIRE-trial,[8] which seems highly appropriate at first glance given FIRE's similar composite endpoint, and the large subpopulation of NSTEMI patients. However, the elderly patients in FIRE were at an increased baseline risk of adverse events, markedly affecting the difference between absolute and relative treatment effects when compared to the lower-risk population of the SLIM-trial.

Conclusion

This post hoc Bayesian re-analysis of the SLIM-trial confirmed the presence of a clinically relevant reduction in the primary composite endpoint in favor of an FFR-guided complete revascularization strategy in NSTEMI patients. This difference was driven by a reduction in revascularization during follow-up by a high degree of certainty, and most probably also through a decrease in the incidence of nonfatal MI. Consequently, the findings of the SLIM-trial are in line with previous RCTs in the STEMI population. Therefore, this re-analysis consistently supports the use of an FFR-guided complete revascularization strategy by PCI in NSTEMI patients with low-complexity MVD.

Conflict of interest

TP reports personal fees from Diagram BV not related to this work. AH reports receiving grants from Abbott during the conduct of the study; receiving grants to the institution from Medtronic, Boehringer Ingelheim, and Sanofi not related to this work; and serving as consultant for Celecor Therapeutics in relationship with the CELEBRATE trial and is a member of the data and safety monitoring board of the COMBINE INTERVENE trial.

CRediT authorship contribution statement

Samuel Heuts: Writing – original draft, Visualization, Methodology, Formal analysis, Data curation, Conceptualization. **Tobias FS Pustjens:** Writing – original draft, Visualization, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Árpad Lux:** Writing – review & editing, Visualization, Validation, Conceptualization. **Andrea Gabrio:** Writing – review & editing, Validation, Supervision, Methodology, Conceptualization. **Arnoud WJ van 't Hof:** Writing – review & editing, Supervision, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Conceptualization. **Saman Rasoul:** Writing – original draft, Supervision, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization.

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