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Bayesian Analysis:

A Practical Approach to Interpret Clinical Trials and Create Clinical Practice Guidelines

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Abstract

Bayesian analysis is firmly grounded in the science of probability and has been increasingly supplementing or replacing traditional approaches based on *P* values. In this review, we present gradually more complex examples, along with programming code and data sets, to show how Bayesian analysis takes evidence from randomized clinical trials to update what is already known about specific treatments in cardiovascular medicine. In the example of revascularization choices for diabetic patients who have multivessel coronary artery disease, we combine the results of the FREEDOM trial (Future Revascularization Evaluation in Patients with Diabetes Mellitus: Optimal Management of Multivessel Disease) with prior probability distributions to show how strongly we should believe in the new Class I recommendation ("should be done") for a preference of bypass surgery over percutaneous coronary intervention. In the debate about the duration of dual antiplatelet therapy after drug-eluting stent implantation, we avoid a common pitfall in traditional meta-analysis and create a network of randomized clinical trials to compare outcomes after specific treatment durations. Although we find no credible increase in mortality, we affirm the tradeoff between increased bleeding and reduced myocardial infarctions with prolonged dual antiplatelet therapy, findings that support the new Class IIb recommendation ("may be considered") to extend dual antiplatelet therapy after drug-eluting stent implantation. In the decision between culprit artery-only and multivessel percutaneous coronary intervention in patients with ST-segment elevation myocardial infarction, we use hierarchical meta-analysis to analyze evidence from observational studies and randomized clinical trials and find that the probability of all-cause mortality at longest follow-up is similar after both strategies, a finding that challenges the older ban against noninfarct-artery intervention during primary percutaneous coronary intervention. These examples illustrate how Bayesian analysis integrates new trial information with existing knowledge to reduce uncertainty and change attitudes about treatments in cardiovascular medicine.

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None.

Keywords

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"The past is prologue."

—William Shakespeare, in *The Tempest*

Two prominent schools of thought exist in statistics: the Bayesian and the classical (also known as the frequentist). The Bayesian approach, which is based on a noncontroversial formula that explains how existing evidence should be updated in light of new data,[1] keeps statistics in the realm of the self-contained mathematical subject of probability in which every unambiguous question has a unique answer—even if it is hard to find.[2] The classical approach, which relies on a frequency definition of probability based on long-run properties of repeated events, is grounded in the concept of the *P* value and may sometimes entail several reasonable approaches that yield different answers based on the question at hand.[1,3–5]

Meaning of the *P* Value

The concept of the *P* value dates to the 1920s and 1930s, when statisticians recognized that the bell-shaped curve can represent the distribution of a test statistic for all possible outcomes of an experiment, given that the null hypothesis H_0 is true. Sir Ronald Fisher reasoned that a small *P* value corresponding to the tail under the frequency-distribution curve meant that either an exceptionally rare outcome of an experiment had occurred, or the H_0 was not true.[6]

To many practitioners and some statisticians, a *P* value of 0.05 means that there is a 95% chance that the null hypothesis H_0 is false. This is understandable but wrong because the *P* value is calculated on the assumption that the H_0 is true.[4] The upshot is that the *P* value is NOT the probability that H_0 is true, and $1-P$ is NOT the probability that the alternative hypothesis H_A is true.[1,7] Instead, the *P* value is the proportion of times an observed event, or a more extreme event, will occur in a series of repetitions, given that the null hypothesis is true. In practice, the *P* value defines an error limit that prevents a statistician from wrongly rejecting a true H_0 only ≈5% of the time in the long run in, say, his or her career.[1]

Re-Emergence of Bayesian Analysis

Bayes' rule predated the use of *P* values by ≈150 years, but frequentist approaches have predominated statistical analysis for most of the past century. During the past 30 years, several scientific disciplines like engineering,[2] astrophysics,[8] and genetics[9] have supplemented or replaced frequentist statistics with Bayesian approaches.

In clinical reasoning, Bayes' rule is crucial for explaining how the probability of disease depends on both pretest probability and a test result (Appendix A in the Data Supplement).[3] Bayesian analysis is now appearing in clinical trials, and in a major shift, the American College of Cardiology and American Heart Association have recently proposed using Bayesian analysis to create clinical practice guidelines.[10] In an early exercise, Bayesian

methods supported the usefulness of percutaneous coronary intervention (PCI) for left main coronary artery disease (Appendix B in the Data Supplement).[11]

Bayesian Methods for Clinical Trial Analysis

If we suppose that θ is a theoretical parameter denoted by the log odds ratio (OR), $\log_e$ OR, which summarizes the mortality difference between a new therapy and control, prior knowledge about θ from existing randomized clinical trials (RCTs) is denoted by $p(\theta)$. The prior probability $p(\theta)$ may take the form of a bell-shaped curve to show that some values of θ are more probable than others. When we observe some new trial evidence y, which is commonly presented in the form of an OR but for mathematical consistency analyzed as $\log_e$ (OR) and presumed to be conditional on θ, we represent the relation by $p(y|\theta)$ and call it the likelihood.[1–3,12,13]

In Bayesian analysis, θ is a random variable, but in frequentist statistics, the parameter θ is a fixed but unknown value.[1,12] In both statistical approaches, y depends on θ, but in a Bayesian framework, the likelihood $p(y|\theta)$ describes the conditional probability of y for each possible value of θ. The likelihood may assume any mathematical function, but continuous data are commonly represented with a normal distribution (N):

$$\log_e(\mathrm{OR}) \sim \mathrm{N}[\theta, V], \quad (1)$$

where θ represents the underlying hypothesis about the treatment effect and V is its variance (Appendix B in the Data Supplement).[1–3,12,13]

To see how a new trial updates our understanding of θ, we need to move from the probability of the new data y given the underlying hypothesis θ to the probability of the underlying hypothesis θ given the new data y,[13] and this is achieved by using Bayes' theorem[2,3]:

$$\begin{aligned} p(\theta|y) &= \frac{p(y|\theta)\cdot p(\theta)}{p(y)}, \quad (2)\\ &= \frac{p(y|\theta)\cdot p(\theta)}{\sum p(y|\theta)\cdot p(\theta)},\\ &= \frac{p(y|\theta)\cdot p(\theta)}{\int p(y|\theta)\cdot p(\theta)\cdot d\theta}. \end{aligned}$$

The posterior $P(\theta|y)$ on the left-hand side of the equation increases when there is a strong pre-existing belief in the hypothesis θ or strong new evidence y. The denominator, given by various forms of $P(y)$, plays a normalizing role so that $P(\theta|y)$ integrates to 1. The importance of normalization emerges in a familiar example from clinical reasoning when the number of true positives is divided by the sum of true and false positives to calculate $P(\theta|y)$, which is the probability of disease θ given a test result y (Appendix A in the Data Supplement).

Bayesian analysis often entails complex computations. Until recently, user-friendly software had been scarce, but the availability of high-speed laptop computers and Markov chain

Monte Carlo modeling has made the approach more accessible. For the practitioner considering Bayesian analysis, minimal requirements include a dim knowledge of basic calculus,[13] the ability to think in logarithms, and the allure of writing code for statistical programs like [R],[14] an open-source program that links applications running Bayesian inference Using Gibbs Sampling (BUGS). As a benefit, [R] is free of charge, capable of generating stunning graphics, and ready to install (Appendix B in the Data Supplement).

The present review starts with a simple example that uses normal probability distributions to illustrate how Bayesian analysis combines information from various sources. This is followed by gradually more complex examples that use hierarchical, network, and cross-design analyses to tackle issues that may not be amenable to traditional statistics. The aim of the review is (1) to identify parallels between Bayesian and traditional approaches and (2) to describe statistical tools firmly grounded in probability that help to discover what works in cardiovascular medicine.

Methods

To perform traditional meta-analyses, we use the open-source statistical program [R] 3.0.3[14] and library package meta 3.8–0.[15] To generate conjugate-normal models, we combine normal probability distributions from older trial data (prior) and new trial results (likelihood) to generate the posterior (Appendix C in the Data Supplement).[3] To perform more complex computations, we use a version of BUGS called OpenBUGS[13,16] that allows Markov chain Monte Carlo modeling to specify the posterior distribution (Appendixes D and E in the Data Supplement). In the Data Supplement, we show how BRugs[16] connects [R] with OpenBUGS to draw samples from any posterior distribution. When we use Markov chain Monte Carlo modeling, we base the posterior inference on 10 000 draws of the Gibbs chain.[3,13]

Results

What Form of Revascularization Is Preferred for Diabetic Patients With Multivessel Coronary Artery Disease?

Conjugate-Normal Analysis—For patients with diabetes mellitus and multivessel coronary artery disease (CAD) requiring revascularization, the 2011 guideline stated that,[17] “Coronary artery bypass graft (CABG) surgery is probably recommended in preference to PCI to improve survival in patients with multivessel CAD and diabetes mellitus, particularly if a LIMA graft can be anastomosed to the LAD artery (Class IIa; Level of Evidence B).”

In 2012, the results of the FREEDOM trial (Future Revascularization Evaluation in Patients with Diabetes Mellitus: Optimal Management of Multivessel Disease) appeared.[18] Although FREEDOM was a dedicated trial of diabetic patients with multivessel CAD, the finding of borderline lower mortality after CABG than after PCI at 5 years (relative risk, 0.63; P=0.049) was not considered definitive, because a P value of 0.044 was predefined as the cutoff for the primary end point, and the trial was not powered for mortality.[18]

A traditional meta-analysis of 8 trials including FREEDOM suggested that CABG was superior to PCI, but only 2 of 8 trials had significant *P* values favoring surgery.[19] To show how strongly the borderline results from FREEDOM changed the probability of surgical superiority, we use Bayesian analysis to establish[20,21]:

- the plausibility of a surgical advantage based on evidence from older RCTs (the prior distribution),[22–29]
- support for a surgical advantage from the FREEDOM trial itself (likelihood),[18] and a
- final opinion about the advantage of CABG over PCI (the posterior distribution).

As outlined in the Table and detailed in Appendix C in the Data Supplement, Bayesian methods combine information from different sources and generate a posterior inference that is a compromise between the prior and the data.[1] As shown in Figure 1, the posterior inference contains a maximum (mode) at 0.58 with a 95% Bayesian credible interval (BCI) that extends from 0.48 to 0.71.

Compared with traditional statistics, which uses a frequency definition of probability for the null hypothesis H_0, Bayesian analysis generates direct probability statements about the treatment hypothesis, which is arguably more interesting than the null. In this instance, the Bayesian approach identifies with 95% probability that mortality is 29% to 52% lower after CABG than it is after PCI. More precisely, the Bayesian approach identifies with 99.9%, 99.9%, and 96.8% probabilities that mortality rates are at least 10%, 20%, or 30% lower after CABG than they are after PCI. The strength of evidence for CABG can also be expressed by the Bayes factor, which uses small values close to 0.00 to simultaneously provide strong evidence against the H_0 and for the H_A (Appendix C in the Data Supplement).[3,31] In this exercise, the Bayes factor is 0.01, a value that is defined as decisive evidence favoring CABG.[3]

Skeptical and Noninformative Priors—Some critics are concerned that selecting a prior for Bayesian analysis is a subjective process, but 8 RCTs are the source of evidence for the prior in the present example (Figure 1A). If we think that this prior is too enthusiastic, we can repeat the analysis using a skeptical prior centered at a θ of 0.00 to simulate the null hypothesis and find weaker (posterior OR, 0.82; 95% BCI, 0.67–1.00) but credible support for CABG over PCI (Figure 1B).

If we start with even greater indifference about the superiority of CABG and use a noninformative prior to reflect the belief that all values of θ are equally likely (ie, equipoise), we let the likelihood of the data dominate the posterior inference. When this happens, we get a remarkable result. As shown in Figure 2, a Bayesian hierarchical meta-analysis that starts with a noninformative prior generates a posterior inference (posterior OR, 0.55; 95% BCI, 0.37–0.76) that converges with the result obtained in a traditional meta-analysis (OR, 0.54; 95% confidence interval, 0.38–0.76). Such coincidences are expected when the traditional random-effects model uses an empirical Bayesian approach to estimate between-trial variation.[32] The similarity turns out to be a convenience for practitioners who erroneously use Bayesian language to describe traditional confidence intervals.[3]

Strength of Evidence—In a normal distribution, the strength of evidence is represented by curve width. Narrower curves exclude more values for θ and thus represent stronger sources of evidence than broader curves.[1] Compared with a noninformative prior or a traditional meta-analysis (Figure 3), an informative prior usually produces tighter intervals in the posterior inference, because the posterior borrows information from the prior.[3]

The present example illustrates strengths and limitations of Bayesian analysis. Although a conjugate-normal model is not fully Bayesian, and a narrower interval does not automatically signify a superior approach,[3] an approach based on probability distributions overcomes the reliance on P values. Additional strengths include the ability to obtain direct probability statements about the treatment hypothesis and to see how changes in existing knowledge influence the interpretation of new data. Although this may not seem novel when the Bayesian result converges with the frequentist,[19] Bayesian analysis in this instance supports the new Class I recommendation in the American College of Cardiology/American Heart Association guideline update for a preference for CABG over PCI.[33] In the next section, we show how a Bayesian mixed-treatment analysis compares treatments indirectly when direct comparisons do not exist.

What Is the Optimal Duration of Dual Antiplatelet Therapy After Drug-Eluting Stent Implantation?

Bayesian Network Meta-Analysis—Although aspirin and a platelet $P2Y_{12}$ inhibitor may prevent thrombotic complications after drug-eluting stent (DES) implantation, the combined use of 2 antiplatelet agents may increase bleeding. After an authoritative trial[34] found a borderline increase in all-cause mortality with prolonged dual antiplatelet therapy (DAPT), several investigators performed traditional meta-analyses to determine whether prolonged DAPT was associated with increased mortality using the pooled evidence from multiple RCTs, but results were mixed.[35–37] Because each individual RCT compared pairwise DAPT durations that varied widely (Figure 4),[34,38–50] with a DAPT duration of 12 months being defined as short in 4 trials[34,44–47] and long in 7 trials,[38–44] the traditional meta-analyses[35–37] contained several 12-month-versus-12-month comparisons.

Relative Differences—To compare outcomes using a coherent separation of DAPT durations, we define a network (Figure 4).[3] When the network is analyzed using methods outlined in the Table and Appendix D in the Data Supplement, we show in Figure 5 that mortality is not increased when DAPT increased from 3–6 to 12 months (OR, 1.06; 95% BCI, 0.76–1.40), from 12 to 18–48 months (OR, 1.19; 95% BCI, 0.88–1.63), or from 3–6 to 18–48 months (OR, 1.25; 95% BCI, 0.89–1.81). However, bleeding increases, and the risk of myocardial infarctions falls as the duration of DAPT increases (Figure 5).

The network findings provide reassurance that DAPT does not increase all-cause mortality. Furthermore, no differences in outcomes are seen after 3 to 6 months as compared with 12 months of DAPT in stable patients undergoing drug-eluting stent implantation (Figure 5). Together, these findings support the new Class I recommendation for using DAPT for 6 months after drug-eluting stent implantation in stable patients.[51]

Absolute Differences—To provide a practical perspective for the clinician, we calculate absolute event rates and numbers needed to treat (NNTs).[52] For every 1000 patients treated with 18 to 48 months compared with 3 to 6 months of DAPT, there are 6 more major bleeds (95% BCI, 4–14) but 9 fewer myocardial infarctions (4–16) and 4 fewer stent thromboses (3–8) for each additional 12 months of therapy.[52] As DAPT is prolonged, the corresponding NNT_{harm} for major bleeding is 165 (95% BCI, 65–537), the $NNT_{benefit}$ for preventing myocardial infarction is 117 (77–726), and the $NNT_{benefit}$ for preventing stent thrombosis is 282 (213–514). The findings support a Class IIb recommendation to prolong DAPT >12 months.[51]

The foregoing analysis uses evidence from RCTs, but in most areas of cardiovascular investigation, RCT evidence is limited or absent. In the next section, we illustrate how Bayesian methods synthesize evidence from disparate sources.

Should Noninfarct PCI Be Performed During ST-Segment–Elevation Myocardial Infarction?

Bayesian Cross-Design Meta-Analysis—Outcomes after culprit vessel-only or multivessel-vessel PCI in patients with ST-segment–elevation myocardial infarction and multivessel CAD have been compared in studies of multiple designs: RCTs, matched cohort, and observational studies.[53] RCTs are commonly viewed as having the highest quality, but cohort studies may be more representative of clinical practice.[10]

Traditional approaches using stratified meta-analyses can determine whether treatment outcomes are sensitive to study type. In stratified analyses,[53] observational studies tend to show that the culprit vessel-only arm has lower mortalities than the multivessel arm, although confounding cannot be excluded, whereas RCTs tend to show that the multivessel arm has lower event rates than the culprit vessel-only arm. A strategy using stratified meta-analyses may not yield a single inference for the overall treatment effect, however, because study designs are different and a power problem might arise from inclusion of small RCTs. Another approach is to use Bayesian cross-design methods.[3,30,54]

Hierarchical Model for Analyzing Evidence From Different Study Designs—To compare mortality outcomes from all sources, we create a 3-level hierarchical model illustrated in Figure 6 and detailed in Appendix E in the Data Supplement that analyzes overall outcome as a function of treatment effect and study type. In the model, we assume[3]:

$$\begin{aligned} &\log_e\left[\mathrm{OR}_{i(k)}\right] \Big| \theta_{i(k)}, s^2_{i(k)} \underbrace{\sim}_{\text{independent}} \mathrm{N}\left[\theta_{i(k)}, s^2_{i(k)}\right], \\ &\theta_{i(k)} \Big| \theta_k, \tau^2_k \underbrace{\sim}_{\text{independent}} \mathrm{N}\left[\theta_k, \tau^2_k\right], \\ &\theta_k \Big| \theta, \sigma^2 \underbrace{\sim}_{\text{independent}} \mathrm{N}\left[\theta, \sigma^2\right], \end{aligned} \qquad (3)$$

where $\theta_{i(k)}$ and $s^2_{i(k)}$ denote the study-level treatment effect and its variance, θ_k is the study-type average effect, τ^2_k is the between-study variance for each design, θ is the global

treatment effect viewed as an average across all possible studies (nested within all possible designs), and σ^2 is the between-study type variance for RCTs (k=1), matched cohort (k=2), and unmatched cohort (k=3) studies. The first 2 equations define the random-effects meta-analysis models for studies separately within each design. The last equation treats the study-type averages as random effects from a normal distribution centered at the global average. The hierarchical model assumes that the θ_{kS} are exchangeable and conditional on θ and σ^2, whereas a traditional approach would have assumed that they are fixed and independent parameters.[3,54]

Using published guidance[3,54] to select priors that provide no advantage for 1 treatment strategy or study type over another (Table), we obtain a posterior inference that shows no credible difference in the end point of all-cause mortality after culprit artery-only compared with multivessel PCI (OR, 1.10; 95% BCI, 0.74–1.51), as shown in Figure 7. When we use priors that weight RCTs over observational studies by a factor that ranges from 1 to 5, we obtain an estimate closer to 1.00 (OR, 1.05; 95% BCI 0.64–1.48).[30]

The overall findings support the decision made by members of the writing committee to replace the old Class III prohibition against nonculprit PCI[17] with a new Class IIb recommendation allowing nonculprit artery PCI.[55] The process of synthesizing RCT and observational evidence does not change the overall estimate of the mortality difference between the different strategies but rather increases the confidence that no difference likely exists.[3]

Conclusions

Analogous to making a clinical diagnosis, deciding what works in clinical investigation can be challenging. Bayesian analysis quantifies the probability that a study hypothesis is true when it is tested with new data. Although P values may ensure that trial results in which we are 95% confident are correct 95% of the time in the long run,[31] P values cannot capture the effect size or the evidential meaning of an outcome.[6] Bayesian analysis replaces the dependence on a single number and moves the interpretation of trial results into the world of probabilities based on prior knowledge.[6]

By giving writing committees tools for dealing with the uncertainty of trial results, Bayesian methods are useful for analyzing observational studies,[56] mega-trials,[6] and noninferiority trials by treating H_0 and H_A equivalently by accepting the null rather than failing to reject it. Because many experts rightly demand a higher threshold than 2 SEs in post hoc exercises like meta-analyses, Bayesian methods may raise the bar for declaring that a finding is significant.[31]

In presenting vignettes in this review that illustrate the use of Bayesian approaches for the analysis of trial results, we have tried to strike a balance between the past and the present, between the practical and the academic, and between common sense and the pedantic, in the hope that we can move the search for what works in healthcare from the realm of chance to the science of probability.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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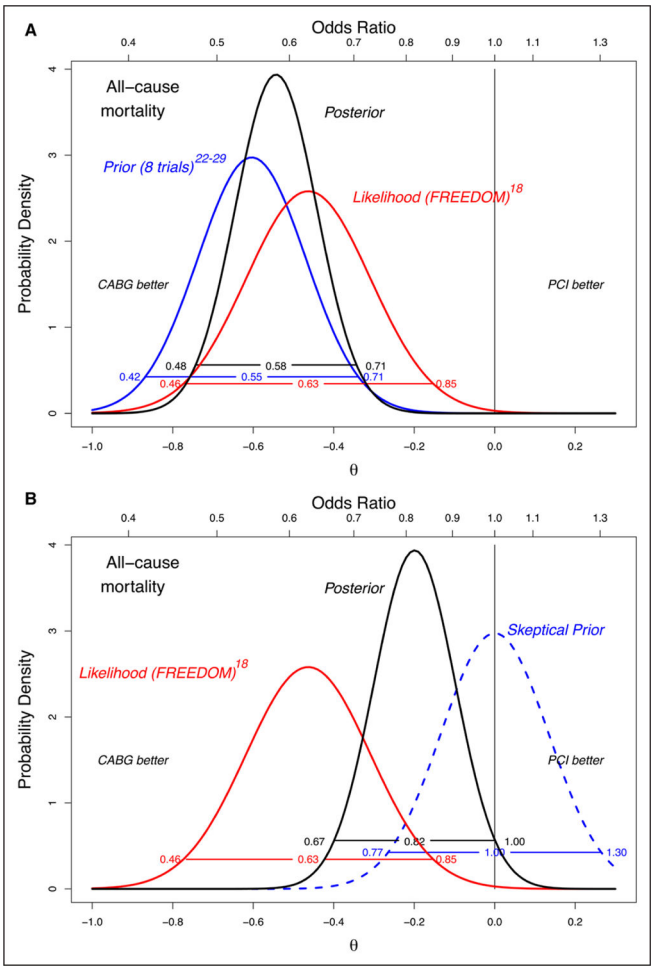

Figure 1.

Bayesian triplot of mortality risk after percutaneous coronary intervention (PCI) or coronary artery bypass graft (CABG) surgery in diabetic patients with multivessel coronary artery disease. **A**, Each triplot contains 3 normal distributions and thus illustrates a conjugate-normal analysis, plotted on the odds ratio (OR) scale and on the θ, or $\log_e$(OR), scale. The prior distribution (blue), represented by a bell-shaped curve derived from evidence from 8 older trials,[22–29] strongly suggests a mortality advantage for CABG over PCI. The likelihood (red), representing the results from FREEDOM trial (Future Revascularization Evaluation in Patients with Diabetes Mellitus: Optimal Management of Multivessel Disease),[18] still favors CABG but less so than the prior. Bayesian methods, which combine the likelihood with the prior to produce the posterior distribution (black), confirm a mortality advantage for CABG. **B**, A skeptical prior (dashed blue), which is centered on an OR of 1.00, results in a posterior distribution that shifts to the right and provides borderline support for a surgical advantage. All curves normalized to 1. Part figure (**A**) is adapted with permission from the American Heart Association.[20,21] Authorization for this adaptation has been obtained both from the owner of the copyright in the original work and from the owner of copyright in the translation or adaptation.

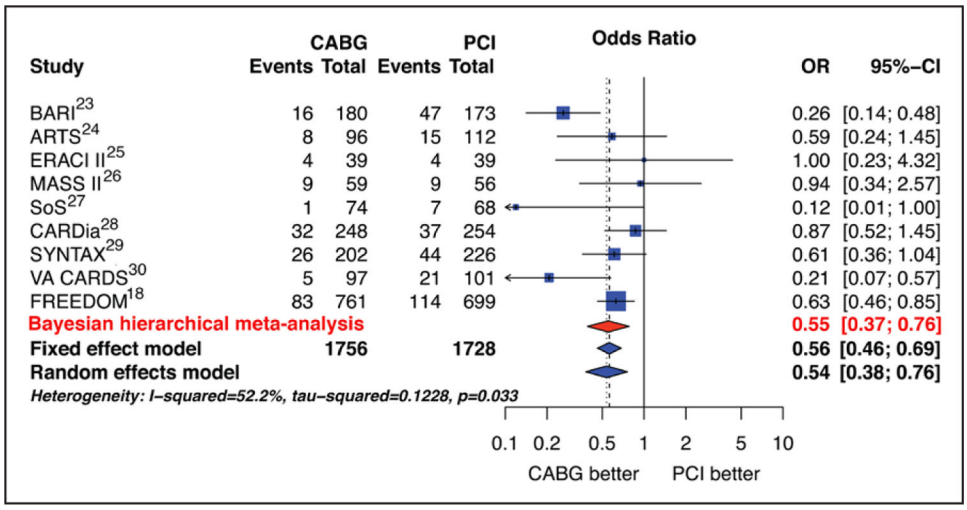

Figure 2.

Traditional and Bayesian hierarchical meta-analysis of subgroup and trial evidence comparing percutaneous coronary intervention (PCI) or coronary artery bypass graft (CABG) surgery in diabetic patients with multivessel coronary artery disease. Adapted with permission from the American Heart Association.[21] Authorization for this adaptation has been obtained both from the owner of the copyright in the original work and from the owner of copyright in the translation or adaptation. CI indicates confidence interval; and OR, odds ratio.

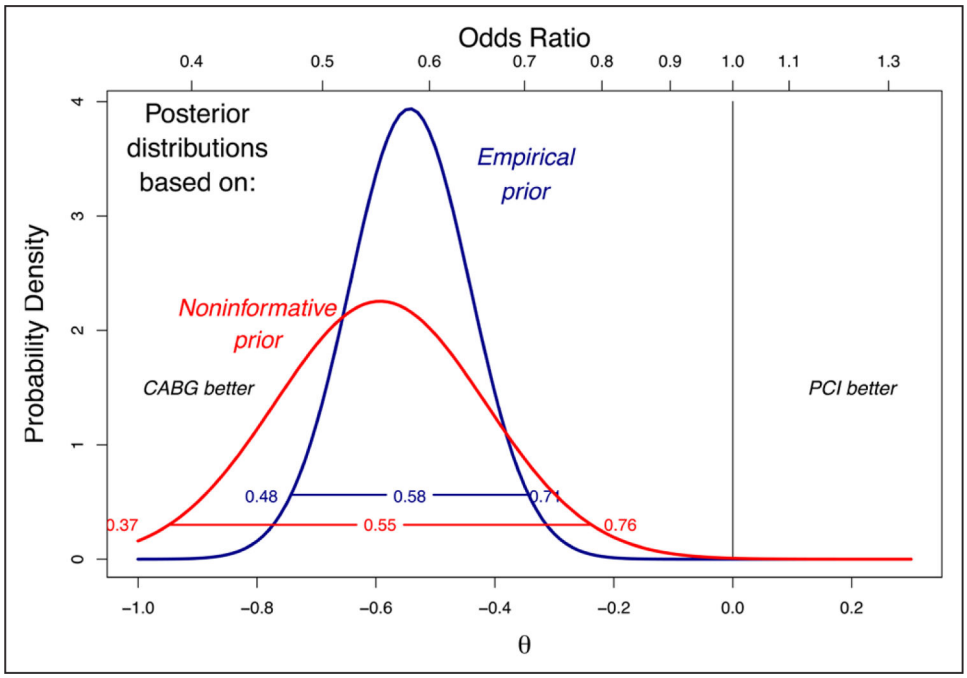

Figure 3.

Comparison of posterior probability distributions derived from different prior probabilities distributions. CABG indicates coronary artery bypass graft; and PCI, percutaneous coronary intervention.

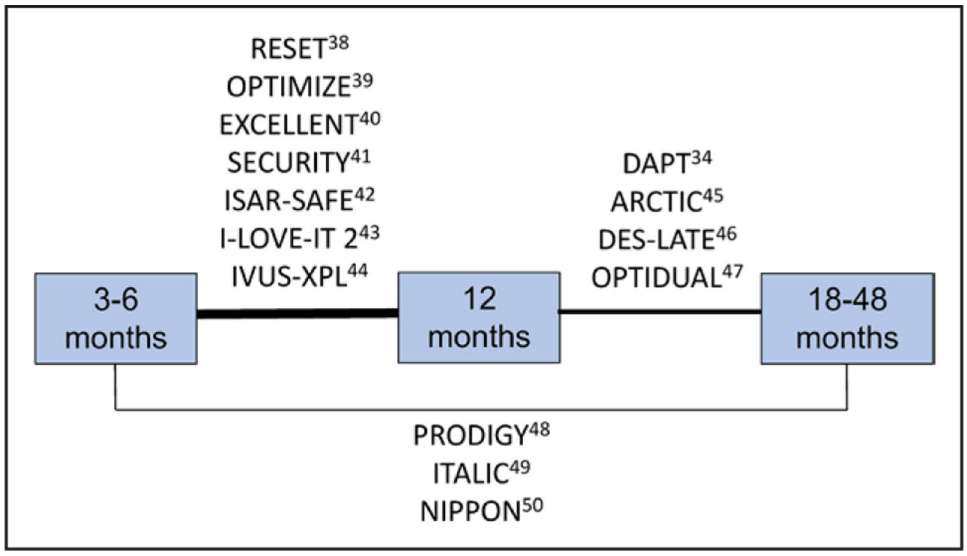

Figure 4.
Network meta-analysis of dual antiplatelet therapy (DAPT). Each node represents a different DAPT duration and each line a different pairwise comparison.

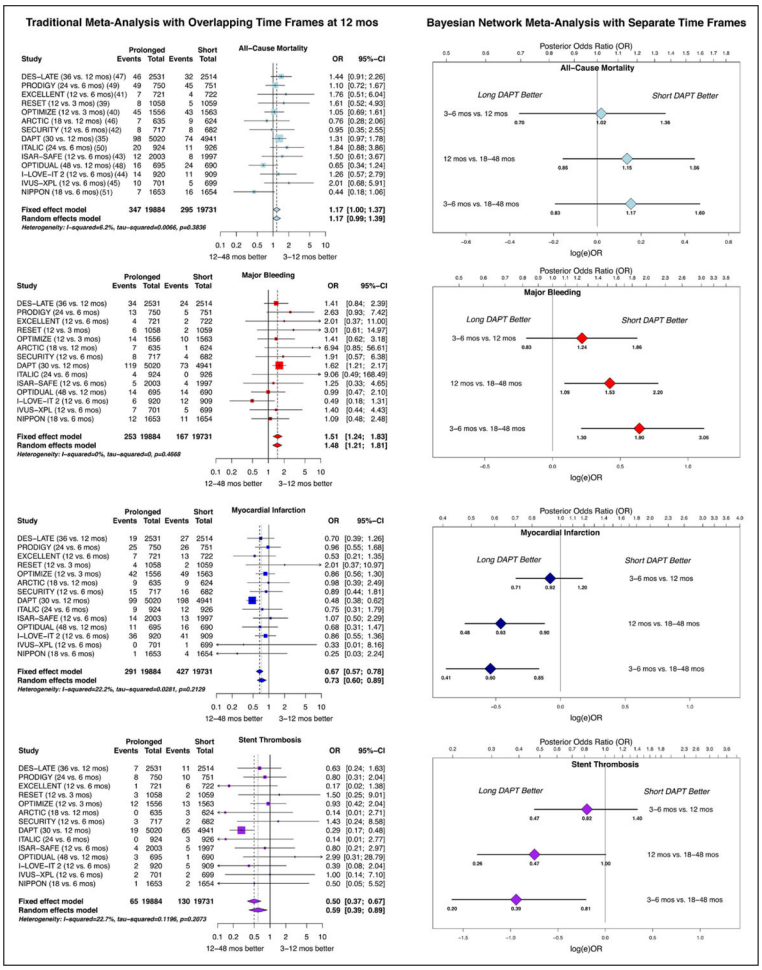

Figure 5.

Traditional network meta-analyses of prolonged dual antiplatelet therapy (DAPT). The forest plots (**left**) contain several 12-mo-versus-12-mo comparisons of outcomes, whereas the caterpillar plots (**right**) compare outcomes after DAPT durations that do not overlap. All studies identified and referenced in Figure 4. CI indicates confidence interval.

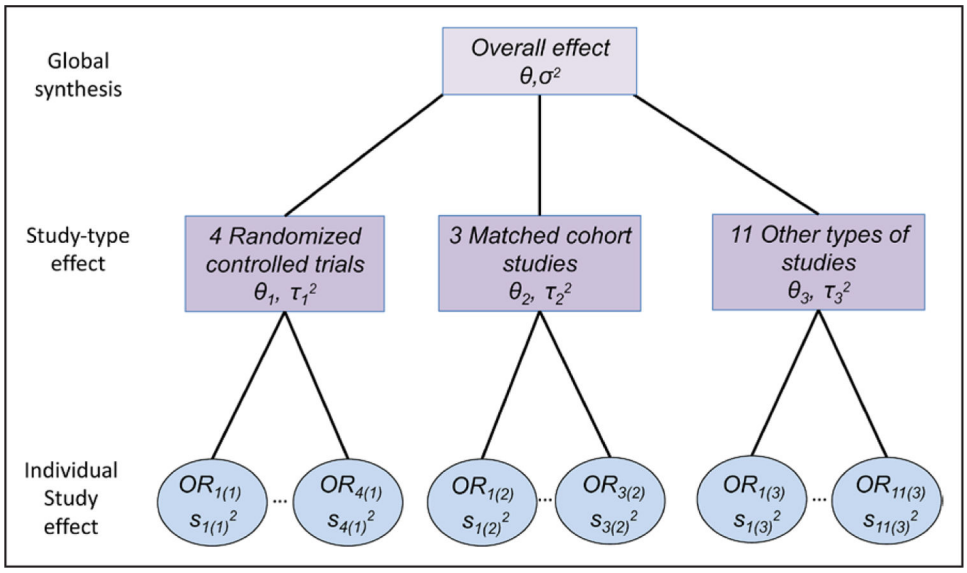

Figure 6.

Hierarchical model. At the individual study level in the **bottom** row, the parameters include $OR_{i(k)}$ and variances s^2 from each study $i=1,\ldots, 18$; in the **middle** level, the mean study-type effects θ_i and variances τ_k^2 from each study type $k=1,\ldots, 3$; and, in the **top** level, the overall treatment effect θ and its variance σ^2. OR indicates odds ratio. Adapted with permission from John Wiley and Sons.[30] Authorization for this adaptation has been obtained both from the owner of the copyright in the original work and from the owner of copyright in the translation or adaptation.

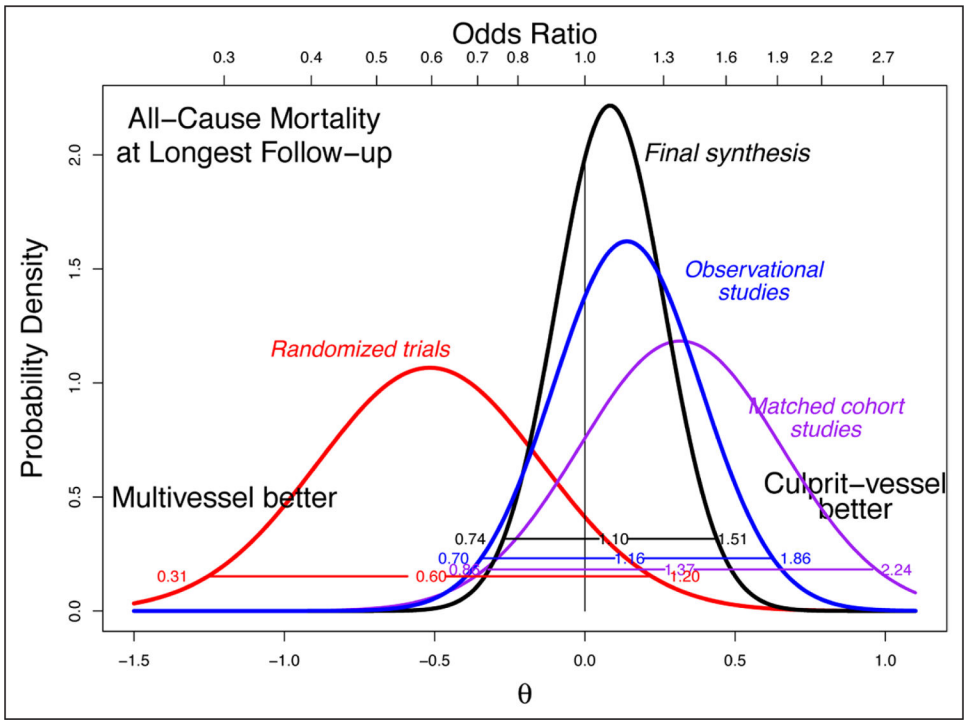

Figure 7.

Mortality after multivessel or culprit vessel-only intervention for ST-segment–elevation myocardial infarction. Information sources segregated by study type are plotted on the odds ratio (OR) scale and on the θ scale, which is equivalent to $\log_e$(OR). Data from randomized controlled trials (red), which are represented by a bell-shaped curve to show the distribution of all possible ORs, tend to favor the strategy of multivessel intervention, whereas data from matched cohort studies (purple) and from the unmatched observational studies (blue) tend to favor the strategy of culprit vessel-only intervention. The final synthesis (black), which combines the data from all studies and generates the posterior median OR and 95% Bayesian credible interval (data labels), suggests no plausible difference in mortality rates after a strategy of multivessel or culprit artery-only intervention at the time of primary intervention. All curves are normalized to 1. Adapted with permission from John Wiley and Sons.[30] Authorization for this adaptation has been obtained both from the owner of the copyright in the original work and from the owner of copyright in the translation or adaptation.

Table.

Components of Analysis

	Clinical Example		
	Revascularization Choices in Diabetic Patients	**Duration of DAPT After DES Implantation**	**Primary PCI Strategies in Patients With STEMI**
Intervention	CABG vs PCI	DAPT for 3–12 mo, 12 mo, or 18–48 mo	Culprit vessel-only vs multivessel PCI
Population	Diabetic patients with multivessel CAD	Patients undergoing DES implantation	Patients with STEMI and multivessel CAD
Evidence source	RCT and RCT subgroups	RCTs	RCTs and observational studies
Outcome measure	Mortality at longest follow-up	Mortality, bleeding, MI, and ST	Mortality at longest follow-up
Prospective analysis?	No	No	No
Bayesian model	Conjugate normal	Network meta-analysis	Cross-design meta-analysis
Data tables and programming code	Appendix C in the Data Supplement	Appendix D in the Data Supplement	Appendix E in the Data Supplement
Prior specification	External evidence	Noninformative: N [0, 10^3]	Vague: θ~N[0,10], τ_k~HN [0.36^2], and σ~ HN [0.18^2]
Statistical model	Approximate normal distribution of $\log_e$(OR)	3-node network	3-level hierarchical
Estimation approaches	Conjugate normal[3]	MCMC modeling[3,13]	MCMC modeling[3,13]
Interpretation	Confirmatory for a preference of CABG over PCI	Reduced concern for increased mortality with prolonged DAPT	Reduced concern for mortality difference between strategies
Sensitivity analysis	Skeptical and noninformative prior[21]	None	Different weights for RCTs and observational studies[30]

CAD indicates coronary artery disease; DAPT, dual antiplatelet therapy; DES, drug-eluting stent; HN [0.18^2], half-normal distribution, based on a 95% belief that the underlying risk ratio for a particular study type will <2× or >½ the overall population effect[3]; HN [0.36^2], half-normal distribution, based on 95% belief that the true underlying OR for a study of a particular type will be <4x or >1/4 the overall OR of that type[3], MCMC, Markov chain Monte Carlo; N [0.10^3], normal distribution centered on 0 with variance (1/precision) of 10^3; OR, odds ratio; PCI, percutaneous coronary intervention; RCT, randomized controlled trial; ST, stent thrombosis; and STEMI, ST-segment–elevation myocardial infarction.

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