
National Academies of Science, Engineering and Medicine: Workshop on Sharing Clinical Trial Data

Looking forward: extracting value from shared clinical trial data to enhance patient care

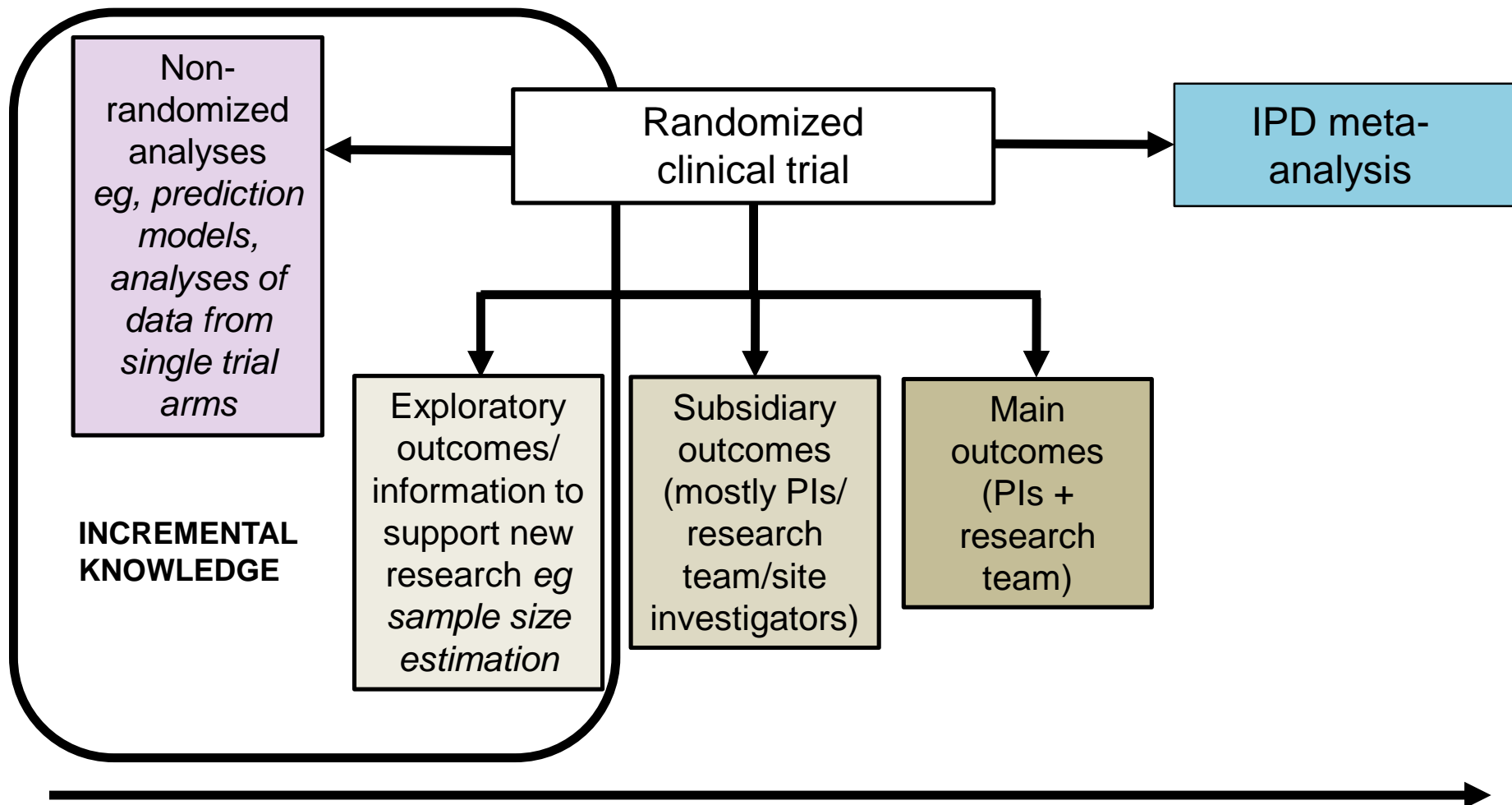
~~**incentivizing data sharing and reuse: A researcher perspective**~~

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How we learn something new and important from shared clinical trial data?



What can IPD meta-analysis provide that is new and important?

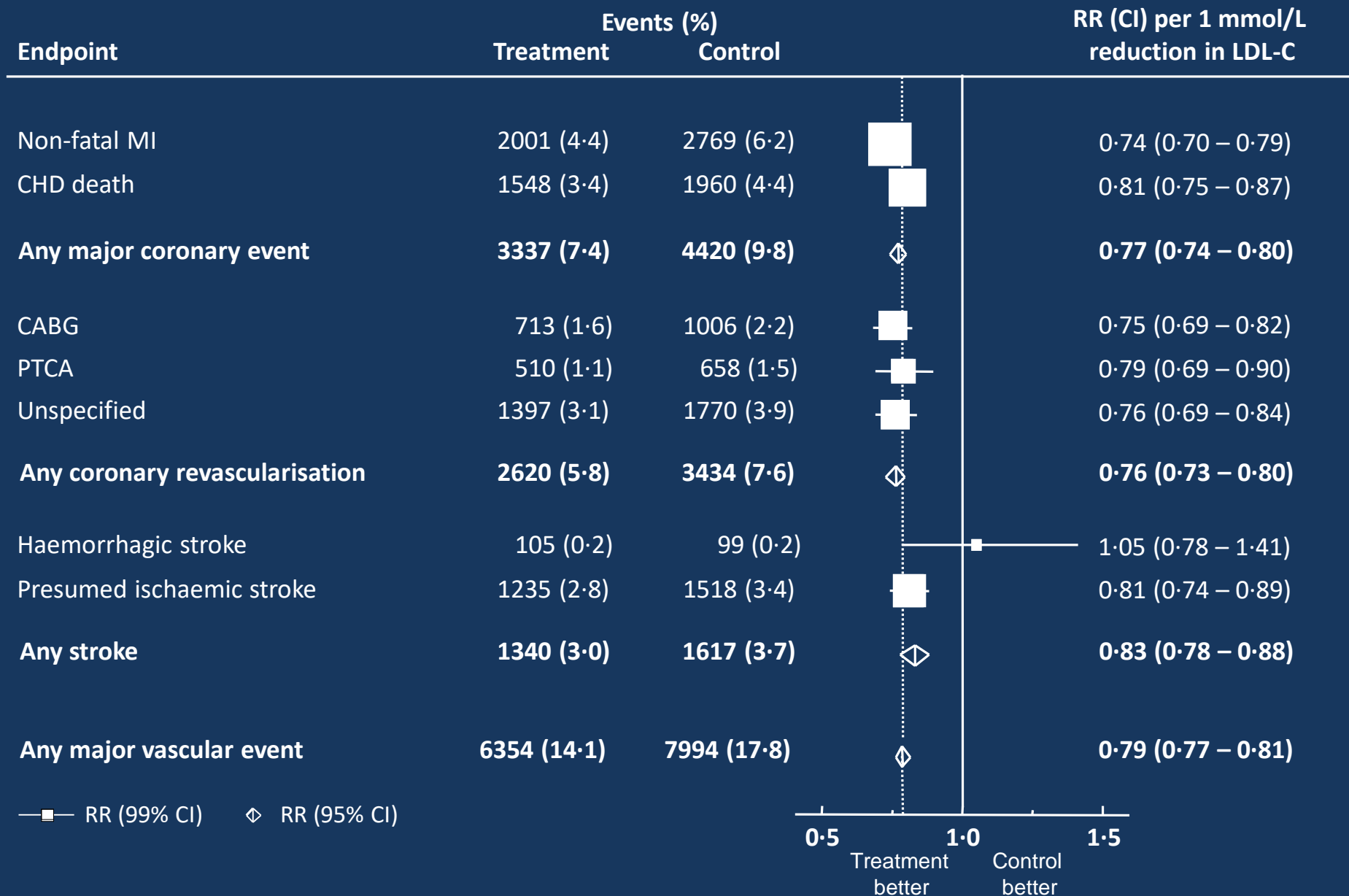
EXAMPLE: Cholesterol Treatment Trialists' (CTT) Collaboration

- Long-term project: CTT established 1994; initial protocol published 1995
- Individual participant data (IPD) from statin trials with ≥ 1000 participants; ≥ 2 years scheduled follow-up
 - Standardised data request: baseline data, major vascular events, cancer, all cause mortality, demographics, lipid subfractions at baseline, 1 year, final visit
- 28 included statin trials (~175,000 participants)
- 10 major publications (6 in Lancet): >10,000 citations

What can IPD meta-analysis provide that is new and important?

- Effects on particular outcomes

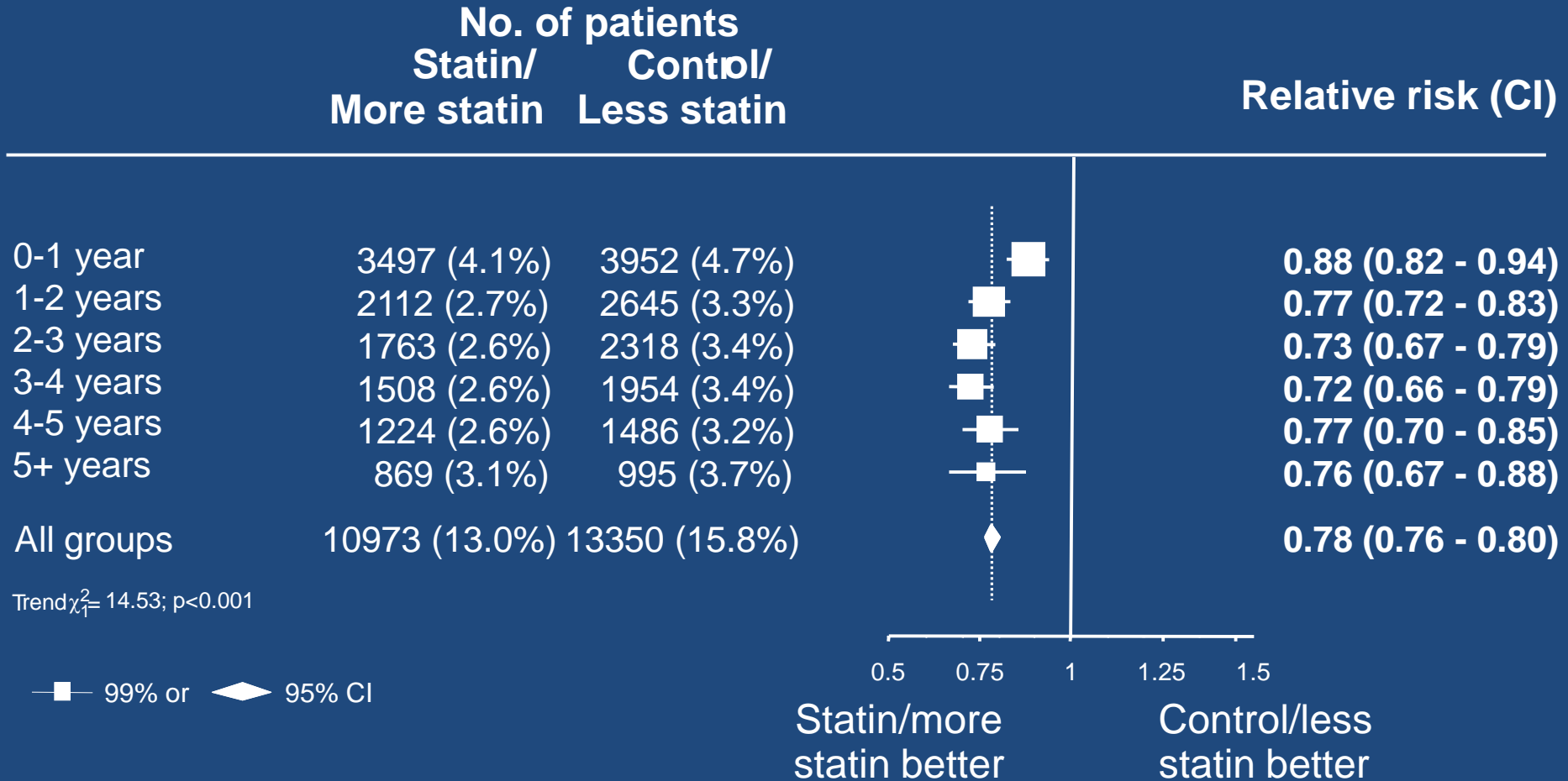
First CTT cycle: Effects on MAJOR VASCULAR EVENTS per mmol/L LDL cholesterol reduction



What can IPD meta-analysis provide that is new and important?

- Effects on particular outcomes
- Timing of treatment effects

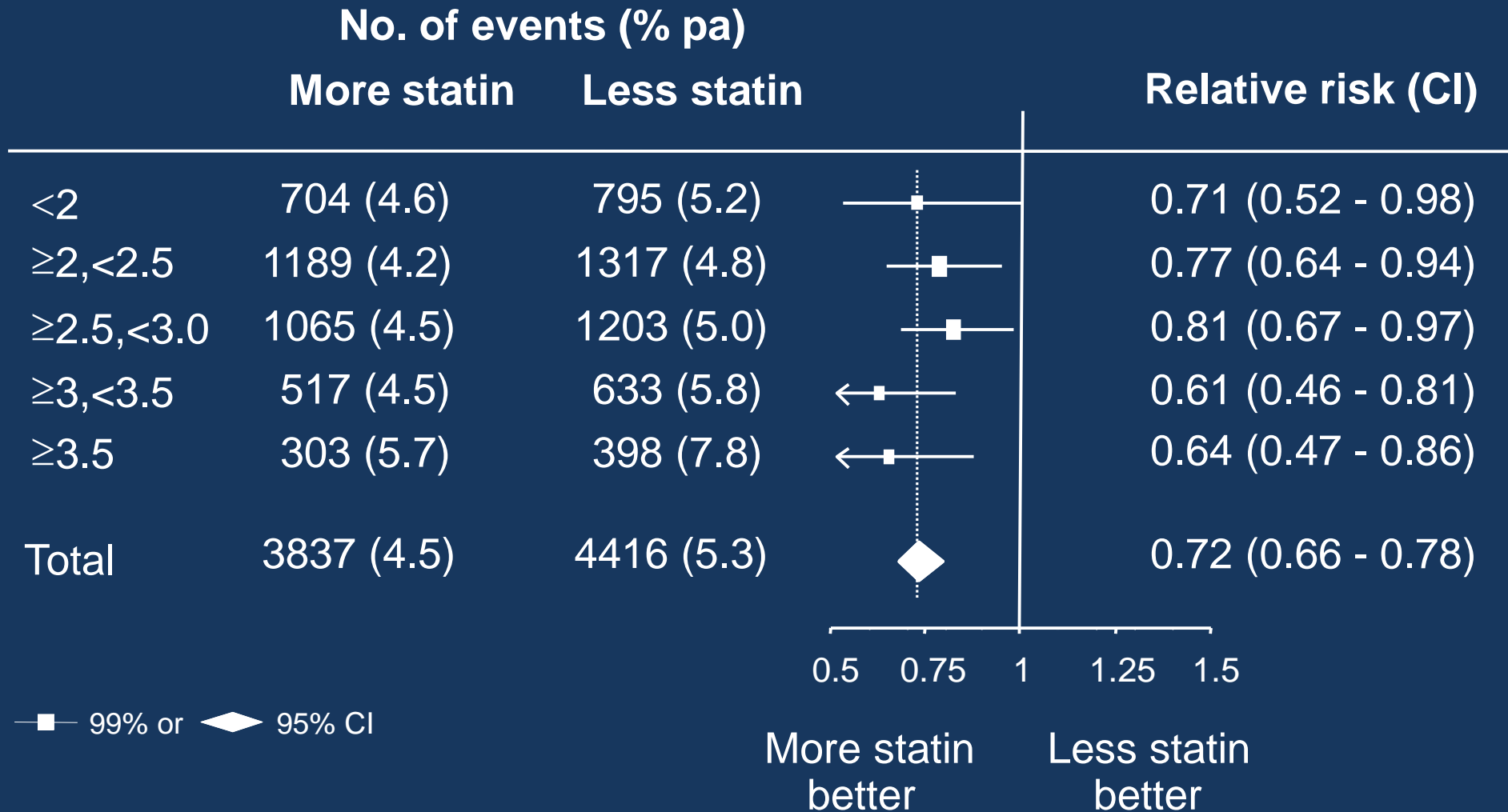
CTT meta-analysis: Effects on MAJOR VASCULAR EVENTS per mmol/L LDL-C reduction, by year



What can IPD meta-analysis provide that is new and important?

- Effects on particular outcomes
- Timing of treatment effects
- Definition of whom to treat

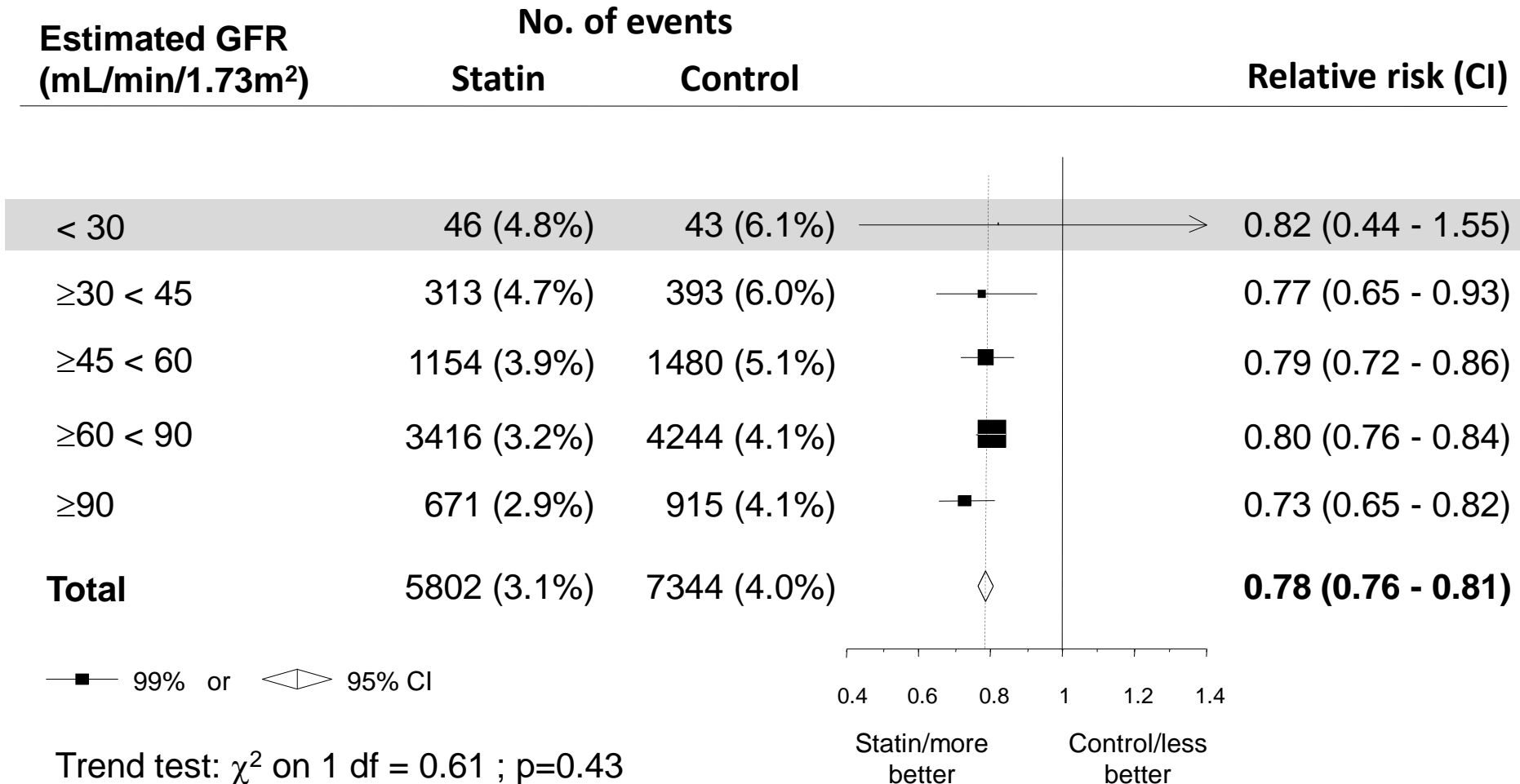
More vs less trials: Proportional effects on MAJOR VASCULAR EVENTS per mmol/L reduction in LDL cholesterol, by baseline LDL cholesterol



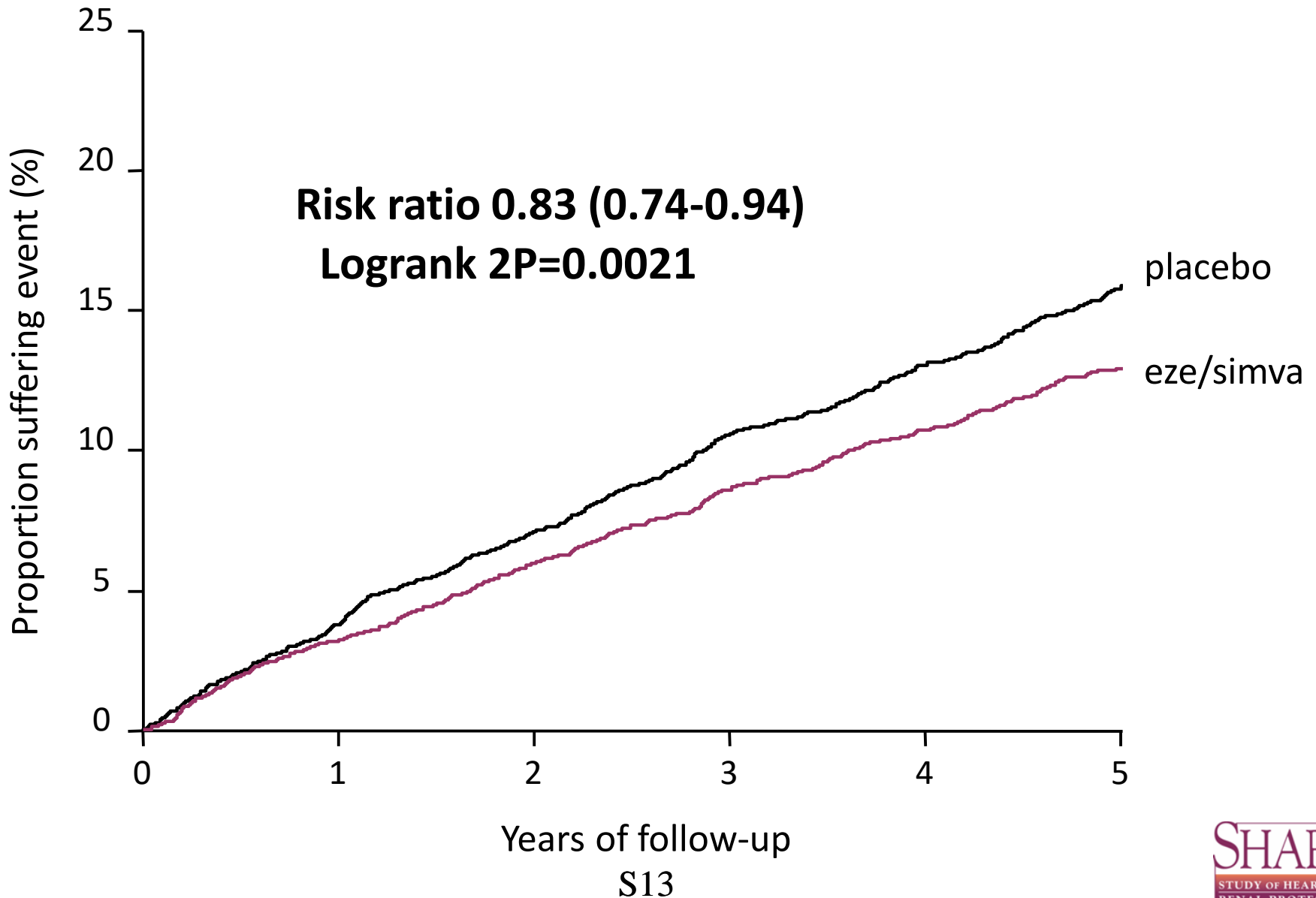
What can IPD meta-analysis provide that is new and important?

- Effects on particular outcomes
- Timing of treatment effects
- Definition of whom to treat
- Unanswered questions needing new trials

CTT: Previous lack of evidence for reduction in MVE risk in people with eGFR below 30 mL/min/1.73m²



Key outcome: Major Atherosclerotic Events



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- Current project → existing CTT dataset extended to include all recorded adverse events plus other complementary data (eg, laboratory data, co-medication, reasons for stopping)

CONCLUSIONS AND PROPOSALS

- IPD meta-analyses can yield new and important insights, yet data-sharing platforms may be impractical for such research – data held locally provide the necessary flexibility
- We need new research that classifies and evaluates data-sharing outputs to date → let's move from anecdote to rigour
- The focus should switch from trying to make all trial data available to a focus on providing the most informative data (eg pivotal studies)
 - Many trials in data-sharing platforms will never be requested
 - Many sub-analyses eg, analyses of data from a single trial arm, may be seriously biased, and are of dubious value

More information at www.cttcollaboration.org

The screenshot shows a web browser window with the address bar displaying <https://www.cttcollaboration.org/>. The browser tabs include "Colin Baigent - Outlook We" and "CTT Collaboration". The website header features the "CTT Collaboration" logo and the text "Cholesterol Treatment Trialists' Collaboration". Navigation links include "HOME", "ABOUT", "INDEPENDENT OVERSIGHT", "PARTICIPATING TRIALS", "EFFICACY", "SAFETY", "NEWS", "CONTACT", and "MORE...". A search bar is located on the right. The main content area is titled "UPDATE:" and contains a list of recent events and trials. To the right of the text are two video thumbnails featuring Dr. Roger Blumenthal and Chris Cannon. A red banner at the bottom contains a "Cookies on this website" message with a "Continue" button. The Windows taskbar at the bottom shows the search bar, task view button, and several open applications.

CTT Collaboration
Cholesterol Treatment Trialists' Collaboration

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UPDATE:

- January 2019 **Statin therapy reduces cardiovascular disease risk in older people.**
- December 2018 **Statin Safety and Associated Adverse Events: A Scientific Statement from the American Heart Association**
- July 2018: **LENS trial** of fibrates in patients with diabetes and observable retinopathy commences
- April 2018: **Article published in EHJ by European Atherosclerosis Society**

The Cholesterol Treatment Trialists' (CTT) Collaboration was established in 1994, with its initial **protocol** being published in 1995. It was set up after it was recognized that no single lipid intervention trial would be likely to have a sufficient number of trial participants (and hence statistical power) to reliably assess mortality outcomes or look at events in particular types of patient. Its aim is to conduct periodic meta-analyses of large-scale (≥ 1000 participants), long-term (≥ 2 years scheduled treatment duration) unconfounded, randomized controlled trials of lipid intervention therapies.

The Collaboration's work to date has largely focused on statin therapy, with individual participant data on major vascular events, cancers and mortality having been collected from about 30 major statin trials (equating to approximately 175,000 trial participants). The analyses of such data have been published in a series of publications, sequentially adding to the body of evidence for the **efficacy** and **safety** of statins. These analyses have shown that:

- Reduction of LDL cholesterol using statin therapy substantially reduces the risk of major vascular events (major coronary events, strokes or the need for coronary revascularization) and vascular mortality by about one fifth for each 1 mmol/L reduction in LDL cholesterol achieved
- Further reductions in LDL cholesterol with more intensive statin therapy produce

Dr Roger Blumenthal, Professor of Medicine and Director of Johns Hopkins Ciccarone Center for the Prevention of Heart Disease

Chris Cannon

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