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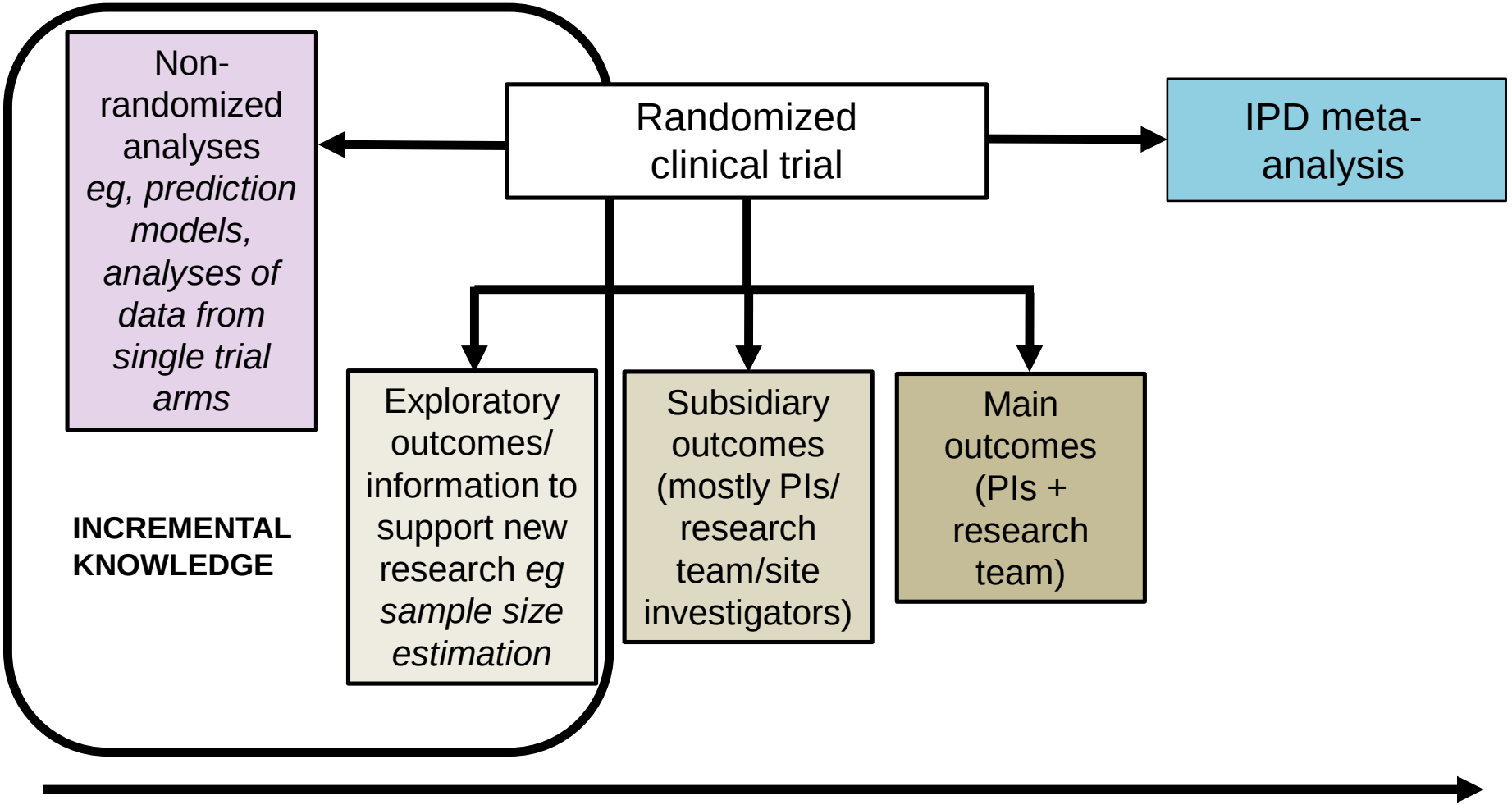
# How we learn something new and important from shared clinical trial data?



# 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
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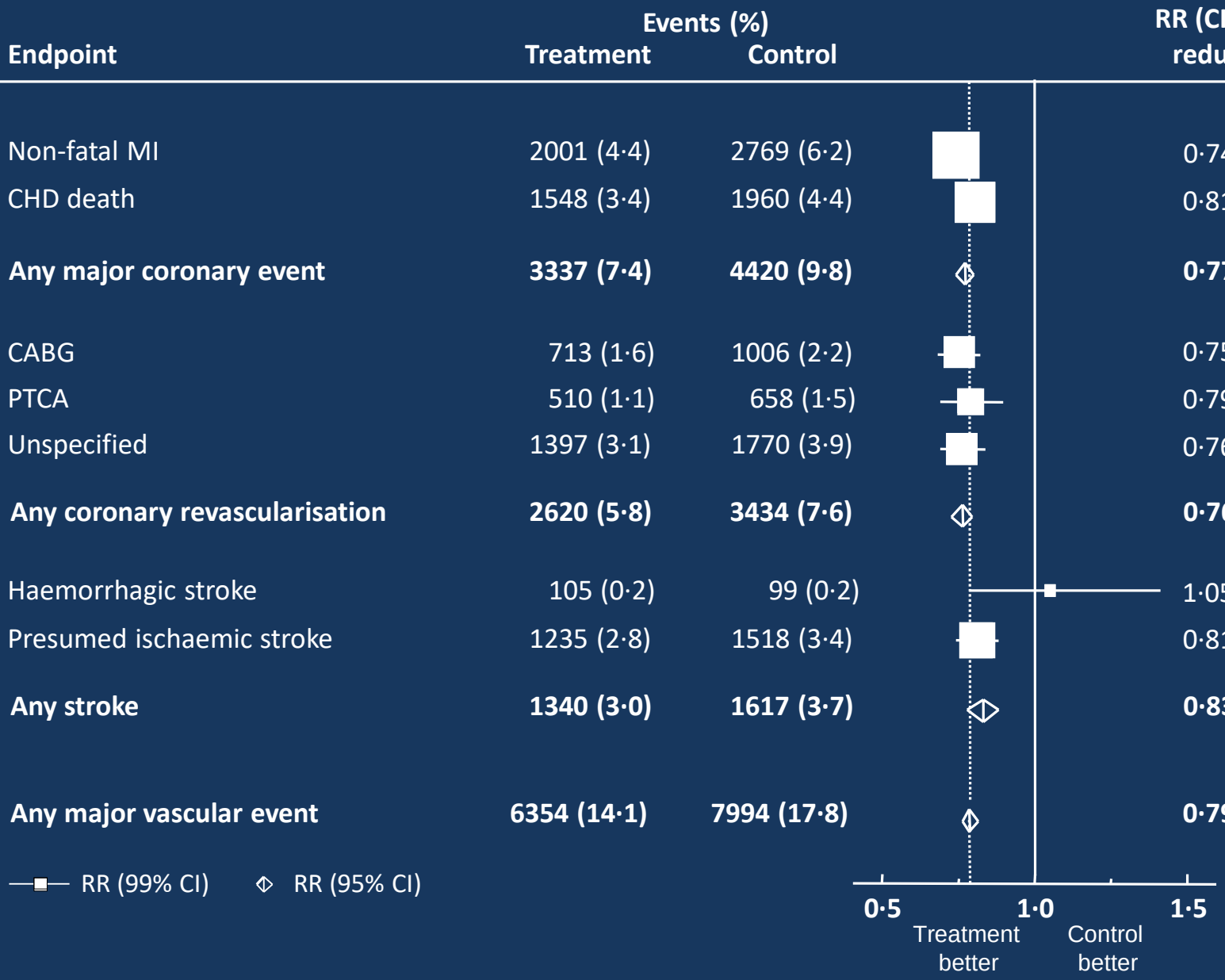
- Effects on particular outcomes

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

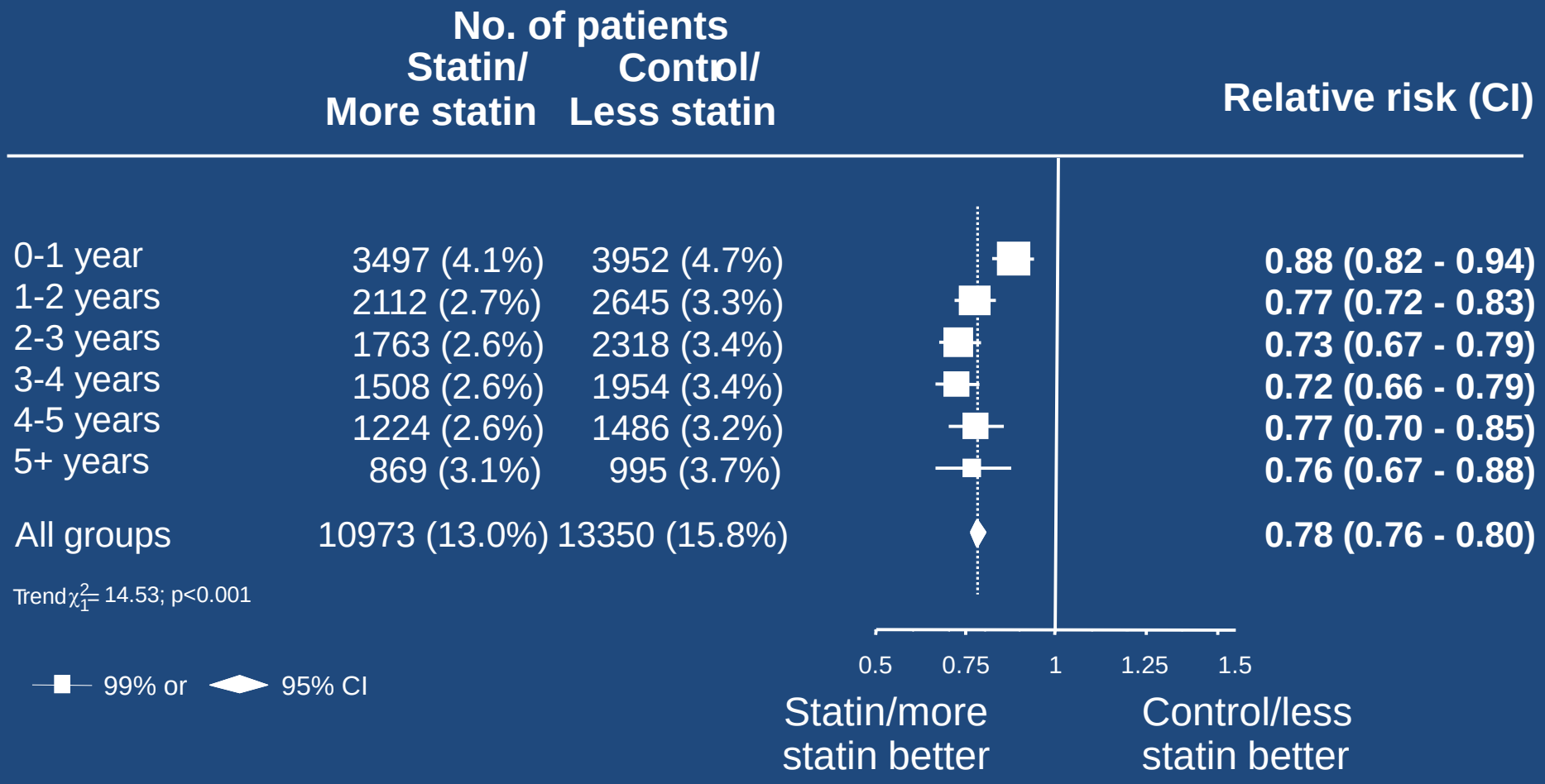
| Endpoint | Events (%) Treatment | Events (%) Control | RR (CI) per 1 mmol/L reduction in LDL-C |
|---|---|---|---|
| Non-fatal MI | 2001 (4·4) | 2769 (6·2) | 0·74 (0·70 – 0·79) |
| CHD death | 1548 (3·4) | 1960 (4·4) | 0·81 (0·75 – 0·87) |
| **Any major coronary event** | **3337 (7·4)** | **4420 (9·8)** | **0·77 (0·74 – 0·80)** |
| CABG | 713 (1·6) | 1006 (2·2) | 0·75 (0·69 – 0·82) |
| PTCA | 510 (1·1) | 658 (1·5) | 0·79 (0·69 – 0·90) |
| Unspecified | 1397 (3·1) | 1770 (3·9) | 0·76 (0·69 – 0·84) |
| **Any coronary revascularisation** | **2620 (5·8)** | **3434 (7·6)** | **0·76 (0·73 – 0·80)** |
| Haemorrhagic stroke | 105 (0·2) | 99 (0·2) | 1·05 (0·78 – 1·41) |
| Presumed ischaemic stroke | 1235 (2·8) | 1518 (3·4) | 0·81 (0·74 – 0·89) |
| **Any stroke** | **1340 (3·0)** | **1617 (3·7)** | **0·83 (0·78 – 0·88)** |
| **Any major vascular event** | **6354 (14·1)** | **7994 (17·8)** | **0·79 (0·77 – 0·81)** |



# 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




Lancet 2010

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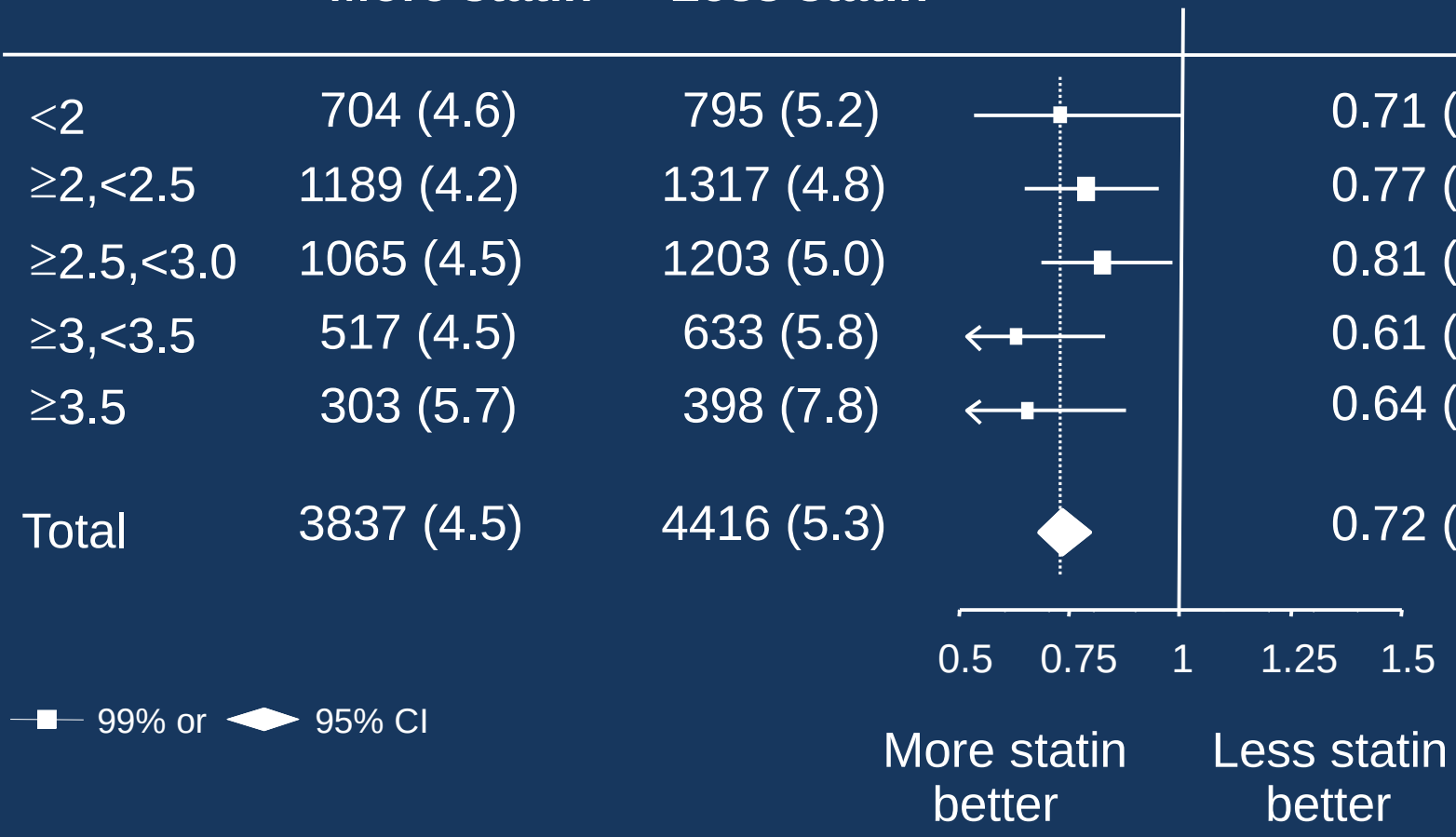
- Timing of treatment effects
- Definition of whom to treat

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

| | No. of events (% pa) | | |
|---|---|---|---|
| | More statin | Less statin | Relative risk (CI) |
| <2 | 704 (4.6) | 795 (5.2) | 0.71 (0.52 - 0.98) |
| ≥2,<2.5 | 1189 (4.2) | 1317 (4.8) | 0.77 (0.64 - 0.94) |
| ≥2.5,<3.0 | 1065 (4.5) | 1203 (5.0) | 0.81 (0.67 - 0.97) |
| ≥3,<3.5 | 517 (4.5) | 633 (5.8) | 0.61 (0.46 - 0.81) |
| ≥3.5 | 303 (5.7) | 398 (7.8) | 0.64 (0.47 - 0.86) |
| Total | 3837 (4.5) | 4416 (5.3) | 0.72 (0.66 - 0.78) |

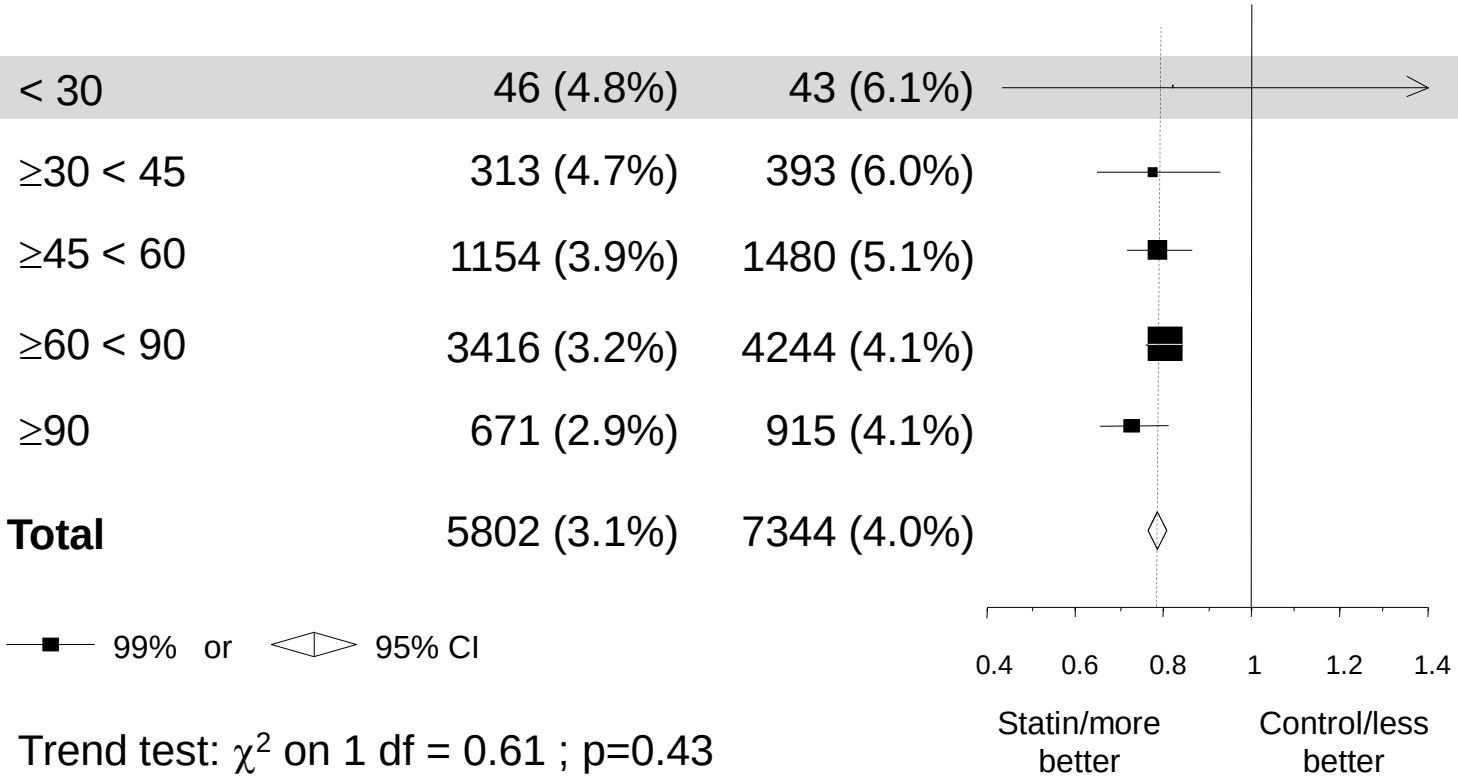


# What can IPD meta-analysis provide that is new and important?

- 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/1.73m$^2$

| Estimated GFR (mL/min/1.73m$^2$) | No. of events: Statin | No. of events: Control | Relative risk (CI) |
|---|---|---|---|
| < 30 | 46 (4.8%) | 43 (6.1%) | 0.82 (0.44 - 1.55) |
| ≥30 < 45 | 313 (4.7%) | 393 (6.0%) | 0.77 (0.65 - 0.93) |
| ≥45 < 60 | 1154 (3.9%) | 1480 (5.1%) | 0.79 (0.72 - 0.86) |
| ≥60 < 90 | 3416 (3.2%) | 4244 (4.1%) | 0.80 (0.76 - 0.84) |
| ≥90 | 671 (2.9%) | 915 (4.1%) | 0.73 (0.65 - 0.82) |
| **Total** | 5802 (3.1%) | 7344 (4.0%) | **0.78 (0.76 - 0.81)** |



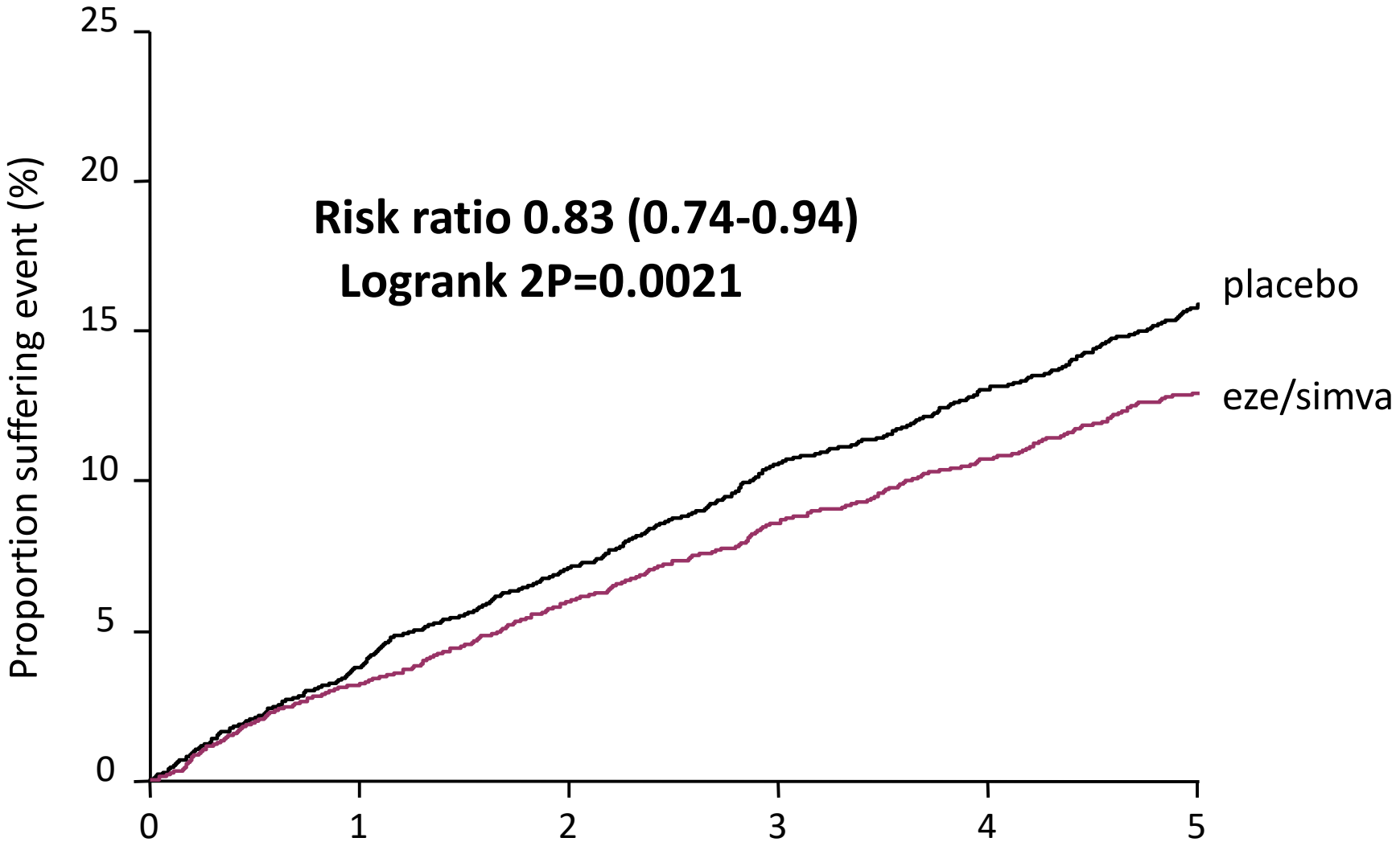

Trend test: $\chi^2$ on 1 df = 0.61 ; p=0.43

CTT Collaboration *Lancet* 2010



SHARP STUDY OF HEART AND RENAL PROTECTION

# Key outcome: Major Atherosclerotic Events






SHARP
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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