



COMBINING EVIDENCE FROM MULTIPLE COHORTS: INDIVIDUAL-PARTICIPANT-DATA META-ANALYSES

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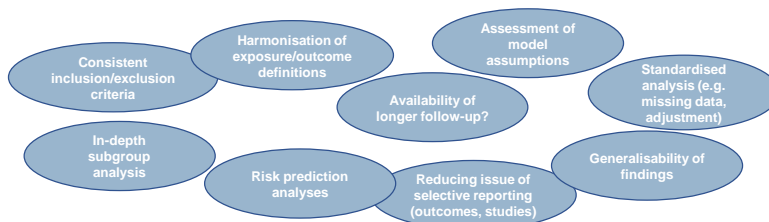
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Individual-participant-data meta-analyses



- **AIM:** To produce results on a whole body of evidence by combining findings across studies
- **APPROACH:** Raw individual data for each study are obtained and used for synthesis
- **STRENGTHS:**



- **CHALLENGES:** Complexity, time, methodology in data management and statistics

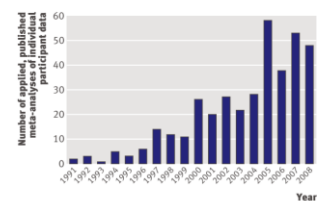


Fig 1 | Number of distinct, applied meta-analyses of individual participant data published up to March 2009,* as identified by a systematic review of Medline, Embase, and the Cochrane Library. *Six articles published in 2009 were identified up to 5 March, when the review was conducted

BMJ 2010;340:c221

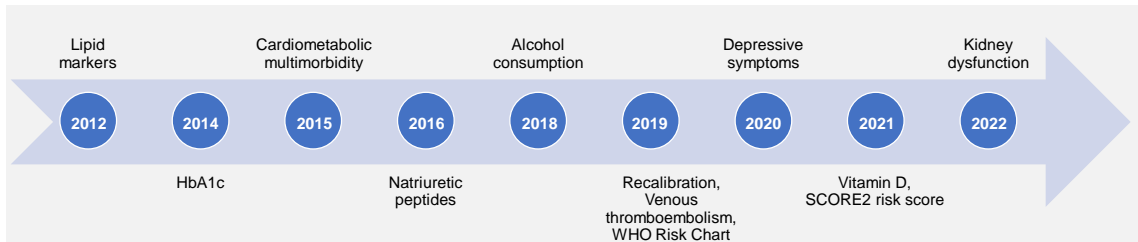
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IPD meta-analyses since 2010



- **UNIVERSITY OF CAMBRIDGE:** Emerging Risk Factors Collaboration (130 studies, n=2.5M)



- **MEDICAL UNIVERSITY OF INNSBRUCK:**

- **Lipoprotein(a) Studies Collaboration:** Residual risk on statin therapy (Lancet 2018)
- **Prospective Studies of Atherosclerosis Consortium:** Carotid IMT as surrogate marker in clinical trials (Circulation 2020)

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Proof-ATHERO consortium – Overview

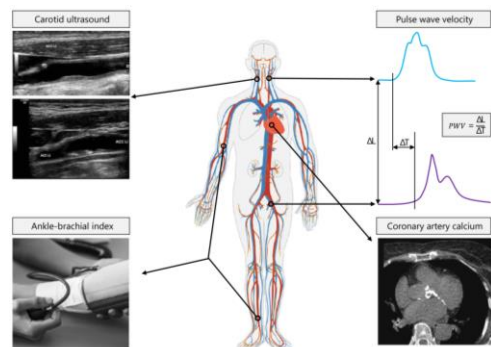


- **OVERARCHING AIM:**

To study the development of atherosclerosis over life, better understand the influence of risk factors on atherosclerosis, and investigate clinical consequences of atherosclerosis.

- **INCLUSION CRITERIA:**

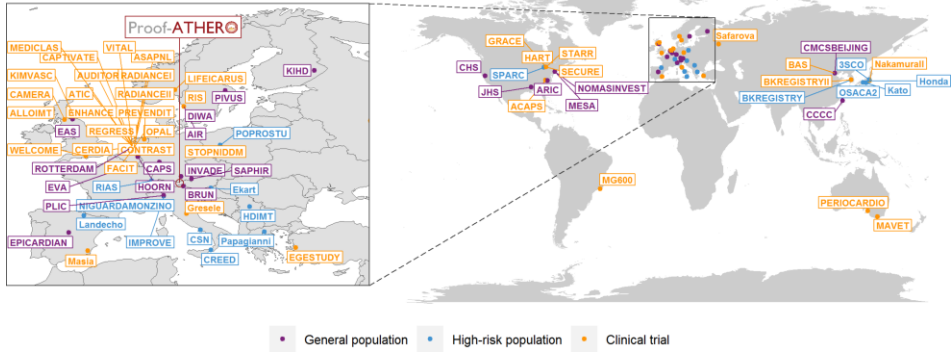
- Prospective design
- Repeat assessment of atherosclerosis measures
- Concomitant assessment of cardiovascular risk factors
- Assessment of incident cardiovascular outcomes



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Proof-ATHERO consortium – Data



- **SUMMARY OF DATA:** 74 studies, 106K participants, mean age 59 years (SD 10), 50% female, 17270 incident cardiovascular events and 13270 deaths over 830K person-years of follow-up.

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Proof-ATHERO consortium – Example



- **PROJECT AIM:**

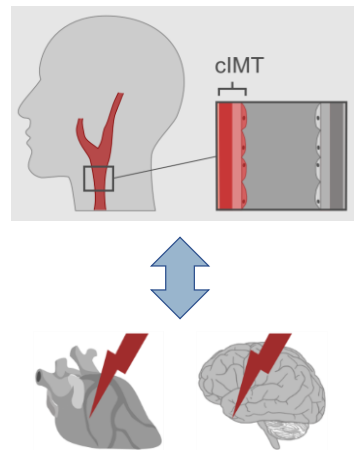
To study whether the intervention effects on progression of carotid intima media thickness (cIMT) are associated with intervention effects on cardiovascular risk.

- **RATIONALE:**

From a clinical and trialist's perspective, a surrogate marker could:

- allow for more efficient clinical trial designs
- save costs
- speed up development and licensing of new therapies.

- **FULL PAPER:** See Circulation 2020;142:621-642.



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Proof-ATHERO consortium – Example

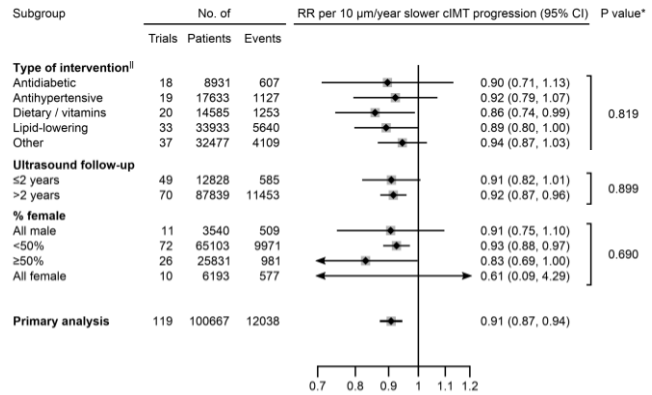


● METHODS:

- Added literature data
- Assessment of intervention effects in each trial
- Pooling across studies using a Bayesian meta-regression approach

● FINDINGS:

- A 10 $\mu\text{m}/\text{year}$ reduction in cIMT progression was associated with a relative risk for CVD of **0.91 (95% CI 0.87-0.94)**.
- No evidence for differences by type of intervention, duration of follow-up, or proportion of females.



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IPD meta-analyses – Conclusion



● SUMMARY:

- The use of individual-participant data instead of aggregate data in meta-analysis has **many potential advantages**, but such meta-analyses are long-term endeavours.
- At the Medical University of Innsbruck, we are coordinating consortia focusing on **cardiovascular epidemiology**.
- In the Proof-ATHERO consortium, we showed that cIMT progression can serve as a **useful surrogate marker in clinical trials** and thereby enhance their efficiency.

● (FURTHER) NEEDS:

- **Additional funding:** currently funded by FWF (P 32488)
- **Additional staff:** recruiting individuals with the required know-how
- **Additional eligible studies:** in Austria, currently restricted to SAPHIR

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