

Evidence of biomarker validity: what do we need?



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What Is A Biomarker?

A biomarker is “**a characteristic that is an indicator of normal biological or pathogenic processes, or pharmacologic responses to a therapeutic intervention**”

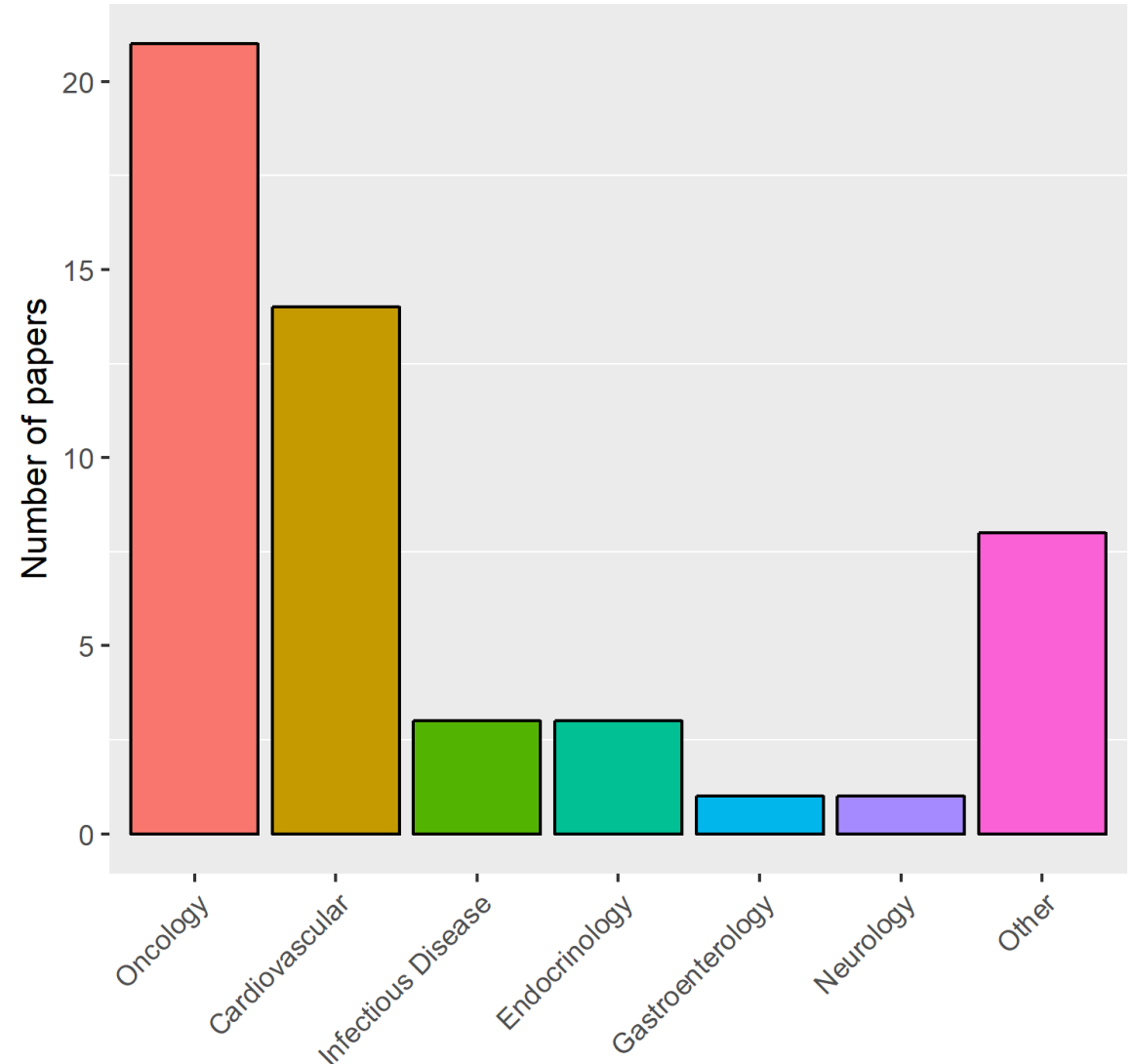
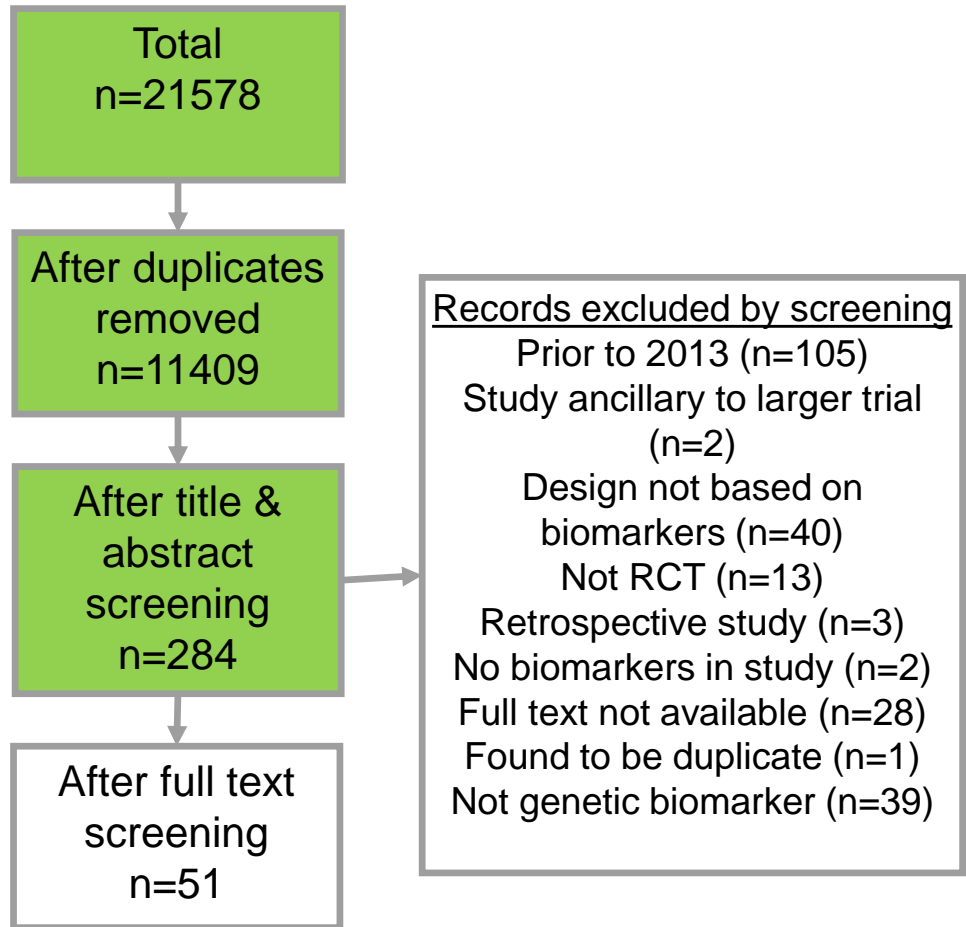
- Several are in clinical use right now – e.g. BRCA1 /2, VKORC1
- Not clear what evidence is needed to show biomarker validity before proceeding to an RCT

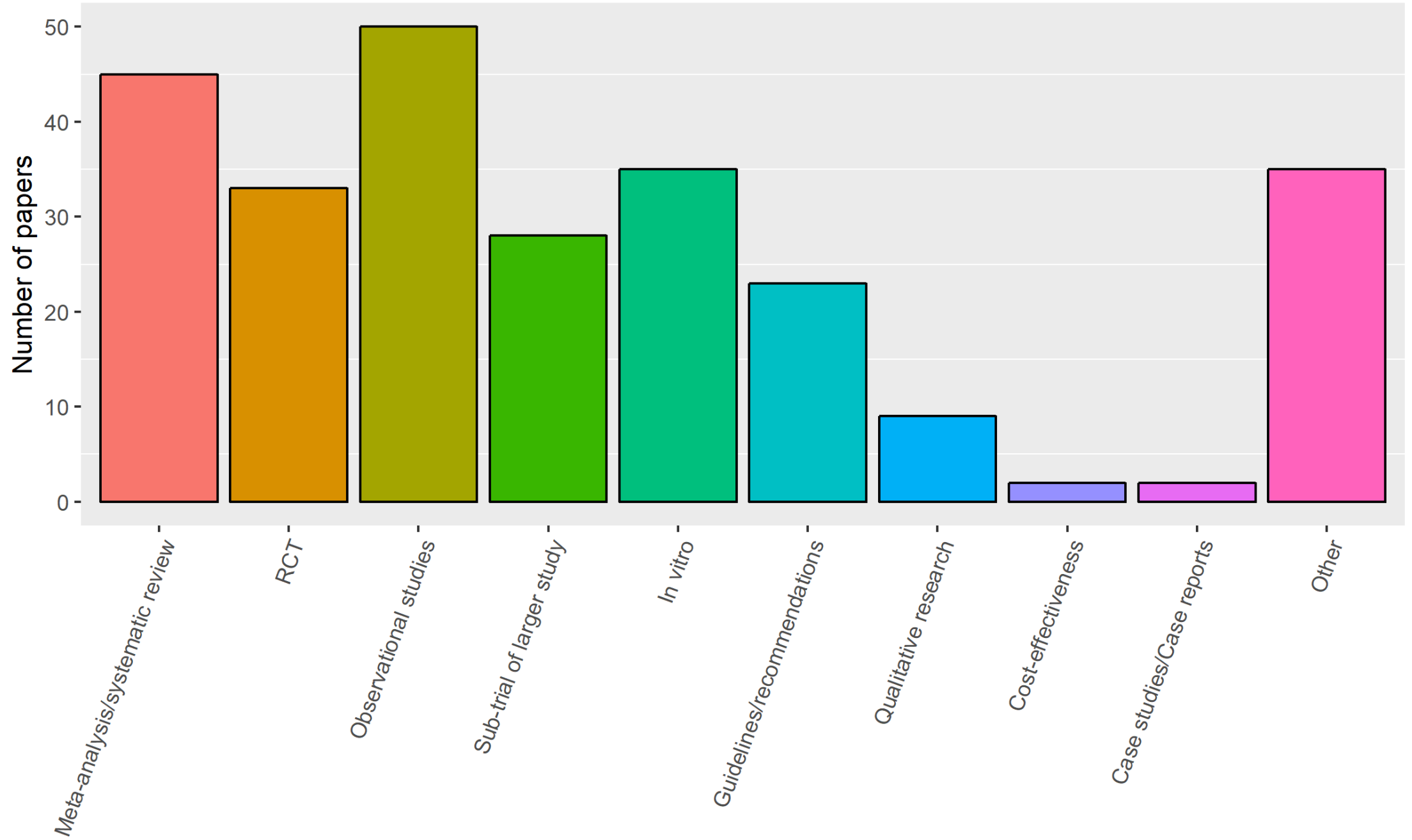


Aims and objectives

- Evaluate the evidence used by current and past biomarker guided RCTs to justify biomarker inclusion
- Compare to published regulations and guidelines for this

How have trials validated biomarkers?





TOPIC trial

- Justification for use of thiopurines [1-3].
- Studies showing prevalence of *TPMT* gene variations and the effect of these [4]. Patients discontinue treatment [5,6].
- Higher risk of death if bone marrow suppression experienced [1,7].
- Data showing effectiveness of *TPMT* genotyping is lacking [8].

To date, 2 *TPMT*-related, randomized, controlled trials have been performed, one including patients with a range of inflammatory conditions, but mainly IBD (85% of the patients included), the other study including 29 IBD patients. Definitive conclusions could not be drawn from either study.^{9,10} A recent meta-analysis (n = 4306 patients) suggested that IBD patients with decreased *TPMT* activity are indeed at increased risk of developing leukopenia compared with patients with normal *TPMT* activity.³

Meta-analysis

RCT

RCT

Conclusions from literature review

- Majority of trials are in oncology
- Variability – some trials had very little evidence for their biomarker use, others had lots of high quality evidence like meta-analyses and RCTs
- No standard approach exists

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