A Methodological Framework to Account for the Impact of Non-Adherence on the Cost-Effectiveness of Chronic Medications

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BACKGROUND

- Non-adherence to medications is a major and intractable issue in health care, with significant negative consequences for both clinical outcomes and costs.
- Evidence suggests that adherence levels in the real world are likely to differ from clinical trials[1] – this leads to uncertainty in the actual effectiveness of treatments.
- The research investigates the problem of estimating the effectiveness and cost-effectiveness of treatments in the presence of patient non-adherence, which is a major issue when making reimbursement decisions.
- Poor reimbursement decisions can have a significant negative consequences for both patient outcomes and costs.

OBJECTIVES

- The aim was to develop a methodological framework to account for the impact of non-adherence on the cost-effectiveness of chronic medications in the context of health technology assessments (HTA) using time-to-event outcomes.
- The focus was on methods that allow for adjusting estimates of effectiveness for real-world non-adherence, that could then be used to inform parameters in an economic model.

METHODS

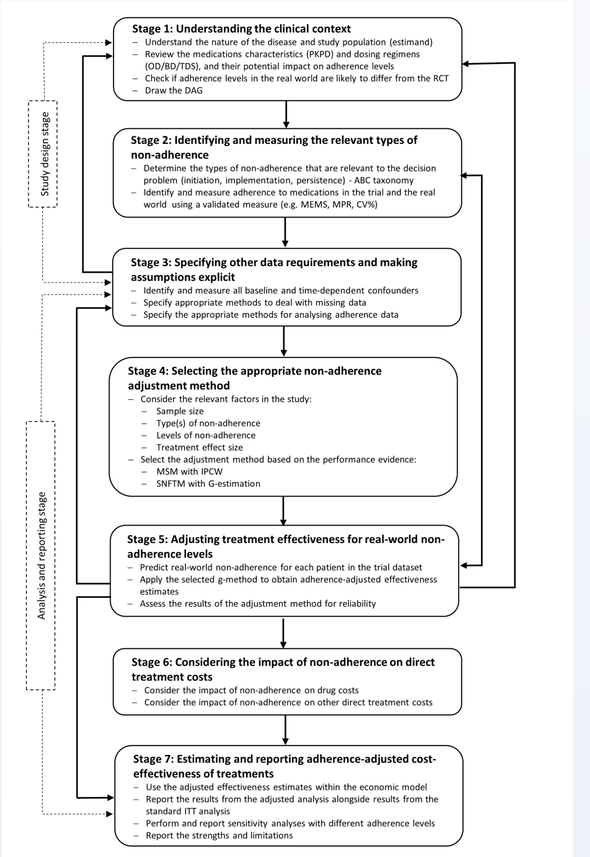
The framework was informed by four linked stages of this research:

1) A systematic review of methodological papers that identified 12 methods that could be used to adjust for non-adherence and assessed their suitability for use in HTA.[2]
2) A simulation study that assessed the performance of four adjustment methods in 90 scenarios.
3) A case study that applied two g-methods[1,3] to a trial of maintenance immunosuppressants in kidney transplantation in order to produce cost-effectiveness estimates based on external 'real-world' non-adherence data.
4) The development of an analytical framework for incorporating non-adherence into cost-effectiveness models.

RESULTS

- We put forward a seven-stage methodological framework to produce adherence-adjusted effectiveness and cost-effectiveness estimates (Figure 1).
- Based on the review, the case study and the simulation study, the framework made 17 supplementary recommendations and considerations for study design and analysis.

Figure 1: A seven-stage methodological framework



PKPD=pharmacokinetics and pharmacodynamics, ITT=intention-to-treat, OD=once daily, BD=twice a day, TDS=three times a day, RCT=randomised controlled trial, DAG=directed acyclic graph, ABC=ascertaining barriers to compliance, MEMS=medication event monitoring system, MPR=medication possession ratio, CV=coefficient of variation, MSM=marginal structural model, SNFTM=structural nested failure time model, IPCW=inverse probability of censoring weighting

CONCLUSIONS

- The framework provides guidance on the steps that could be followed to account for real-world non-adherence when undertaking cost-effectiveness analyses.
- Future research is recommended to use the framework in different case studies for evaluation.
- The framework could be used as a starting point for the development of wider good practice recommendations on non-adherence adjustment.

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