PredictSURE-IBD and IBDX to guide personalised treatment of Crohn's disease in adults

DIAGNOSTIC ASSESSMENT REPORT

1 Appendix

The details provided in this Appendix are to supplement the External Assessment Group's (EAG's) comments on the National Institute for Health and Care Excellence's (NICE) Overview of the Diagnostic Assessment Review (DAR). The Appendix focuses on the reasons for exclusion of studies from the EAG's review of the comparative clinical effectiveness of the step-up (SU) and top-down (TD) strategies to inform the economic evaluation.

As outlined in Section 4.2.4.3 of the DAR report submitted by the EAG, the EAG carried out a search of electronic databases to identify systematic reviews of SU or TD treatments for Crohn's disease (CD). After appraisal of the systematic reviews identified, the EAG selected the review by Tsui et al.[1] as the source of randomised controlled trials (RCTs) for SU versus TD. Additionally, the EAG used TA352[2] (vedolizumab) and TA456[3] (ustekinumab) as sources to identify studies evaluating clinical effectiveness of non-anti-tumour necrosis factor (TNF) biological therapies, and also as a supplementary reference on anti-TNF therapies as used in SU treatment.

The EAG's electronic search retrieved the article by Chen *et al*. (2014)[4] highlighted by NICE as a potential source of studies. Two reviewers independently excluded the article at appraisal of titles and abstracts, citing a reason for exclusion that the study was not a systematic review. The EAG has assessed the studies included in the review by Chen et al.[4] Of the four studies identified by the authors as comparing SU versus TD, the EAG independently reviewed one of the studies as part of its literature review.[5] The EAG's assessment of the studies for relevance to inform the clinical effectiveness of SU versus TD are presented in Table 1.

Table 1. Summary of EAG's assessment of studies identified by Chen et al. for SU versus TD.

Study	EAG assessment
D'Haens[5]	Excluded from initial review: included those with mild Crohn's disease, and unclear whether people received corticosteroid induction therapy.
Kim[6]	Not identified in Tsui et al. EAG would exclude as study enrols a paediatric population.[a]
Xiao[7]	Not identified in Tsui et al. EAG would exclude as study is not an RCT and has different inclusion criteria for those allocated to SU versus those selected for TD treatment strategies.
Yang[8]	Not identified in Tsui et al. EAG would exclude as study enrols a paediatric population.[a]

[a] The protocol for the project indicates that the economic evaluation will focus on adults.
Abbreviations: EAG, External Assessment Group; SU, step up; TD, top down.

As outlined in Section 4.4.2 of the DAR report, other than the individual patient data supplied by PredictImmune, the EAG posits that the RCT by D'Haens et al.,[5] and the subsequent study reporting follow-up at 10 years,[9] together represent the best available evidence on SU versus TD treatment strategies. The EAG considers that the PROFILE RCT, which is in progress, was designed to compare

the relative efficacy of TD and accelerated SU therapy within the subgroups of high and low risk of following a severe course of CD, and thus shed light on whether early treatment with biologics is effective.

The EAG draws attention to a systematic review from the Canadian Agency for Drugs and Technologies in Health (CADTH) on the comparative clinical and cost effectiveness of early treatment with biological therapy compared with conventional treatment, which retrieved the same studies as the EAG and reached the same conclusions on the evidence underpinning use of early biological therapy.[10] The authors of the report commented, "*The clinical effectiveness of early biologic therapy compared to conventional therapy for Crohn's disease in adults is unclear based on available evidence, due to a limited number of studies and heterogeneity of existing studies*". The authors did go on to say that, although the evidence did not suggest consistent benefit associated with early biologic therapy, possible benefits were observed that warranted further research.

2 References

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