NICE National Institute for Health and Care Excellence

SAPs and HEAPs – The NICE View

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Aims for the day (mine)

- Admission: use of SAPs and HEAPs ranges from uncommon to non-existent across our programmes

- What could/should change about this and why?
  - Given that: NICE carry out very little analysis of raw data; would expect trial reporting methods (including adherence to SAPs) to be appraised by the regulator separately – perhaps not if being used outside indication

Plan for this talk

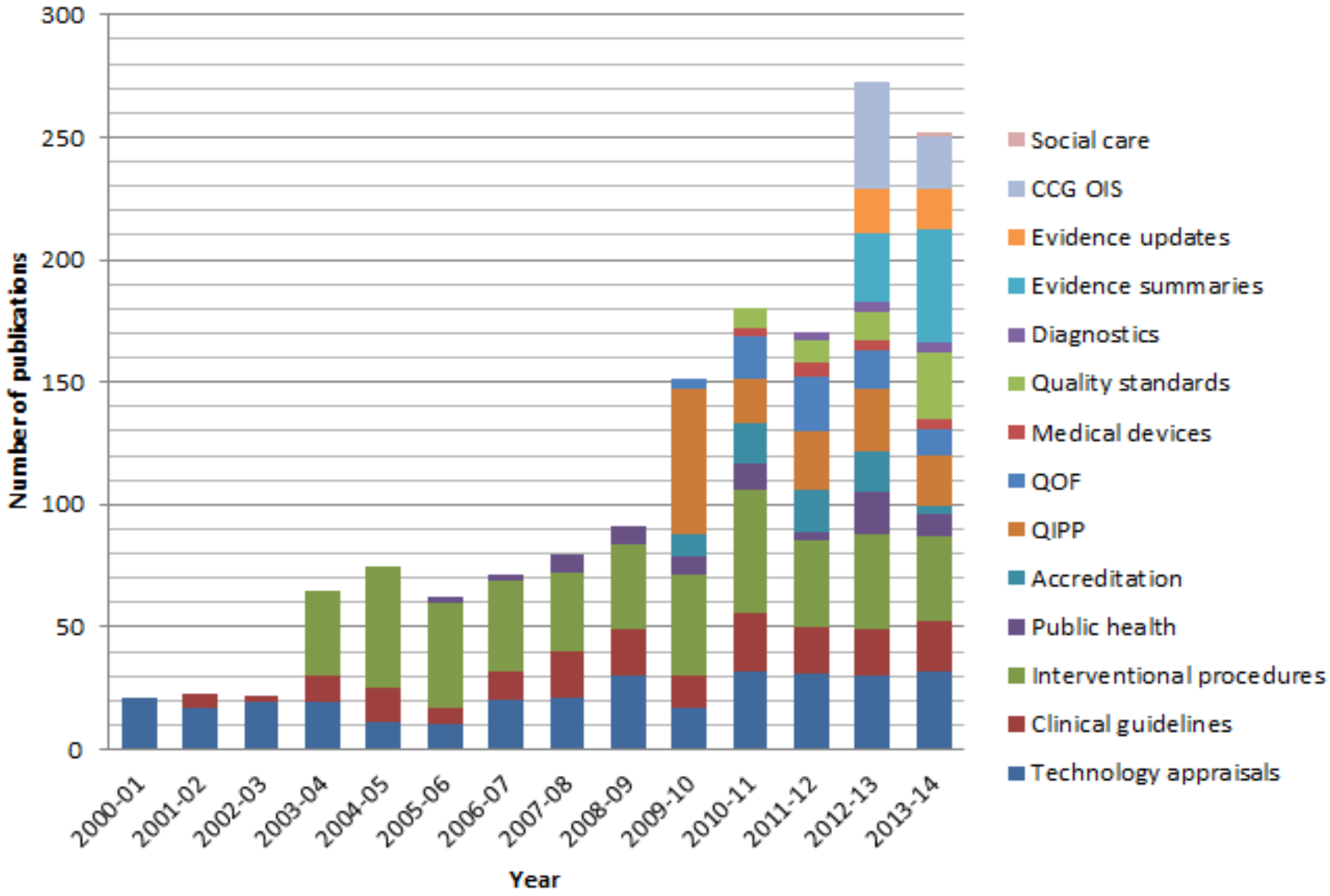
- About NICE
- NICE's Programmes
  - Technology Appraisals
  - Guidelines (Clinical, Public Health, Social Care)
  - Standards and Indicators
  - Others
- Areas for the future
- Discussion

NICE's Remit (1999)

Aim: to reduce variation in the availability and quality of treatments and care (the so called 'postcode lottery')

NICE guidance to resolve uncertainty about which medicines and interventions work best and which represent best value for money for the NHS and PSS.

NICE's remit has expanded



A list of documents…

- …that do not currently mention SAPs or HEAPs
  - (but could/should?)

- Guide to the methods of technology appraisal
- User guide for company evidence submission
- Developing NICE guidelines: the manual

Simplified Technology Appraisal Process

- Company is either seeking or has obtained marketing authorisation from MHRA or other regulator
- Topic referred to NICE, Scope produced
- **Decision Problem** Meeting
- Company submits evidence (others comment)
- Evidence Review group critique (maybe extra analysis)
- Decision making process ensues

Examples from TAs

- I tried…
- vemurafenib for melanoma – SAP changed – additional primary outcomes added at request of regulator (seems reasonable – no effect on decision)

Clinical Guidelines

- Referred by NHS England
- Cover a whole clinical area, examples:-
  - Type 1 diabetes in adults
  - Coeliac disease
  - Dementia
  - Psychosis and Schizophrenia in Children and Young People
- May include more than 100 clinical questions
- Produced by committee of experts and development team (reviewers, HE, clinical advisors, editors etc.)
- Timeline is approximately 2 years (~12 meetings)
- CCP has 60 guidelines in train at any one time

The Manual

- Guidelines are produced in line with The Manual
- Reference Case
- Methods specified in broad terms
- Hierarchy of evidence
  - What can and cannot be considered and what carries more weight

Simplified Guidelines Process

- Topic referral
- Scoping workshop and refinement
  - RQs determined with inclusion/exclusion criteria
  - Recruitment of committee
- Reviews start
- HE analysis prioritisation (3rd Meeting)
- Reviews
- HE plan formulated and sent to NICE for sign off
- More reviews
- Even more reviews
- HE modelling takes place (fairly late in process)
- HE plan updated post-hoc to reflect any deviations
- HE Analysis and reporting
- And so on…

Examples of HEAPs in Guidelines

- Followed by what we actually did!

- Reasons for deviation
  - Intervention found to be ineffective
  - no available evidence at all (quite common)
  - heterogeneous outcomes reported (no MA/NMA)
  - serious un-generalisability
  - very low quality study design (lack of adherence to SAP *may* be considered in Risk of Bias GRADE assessment *if* it was reported in the published paper)

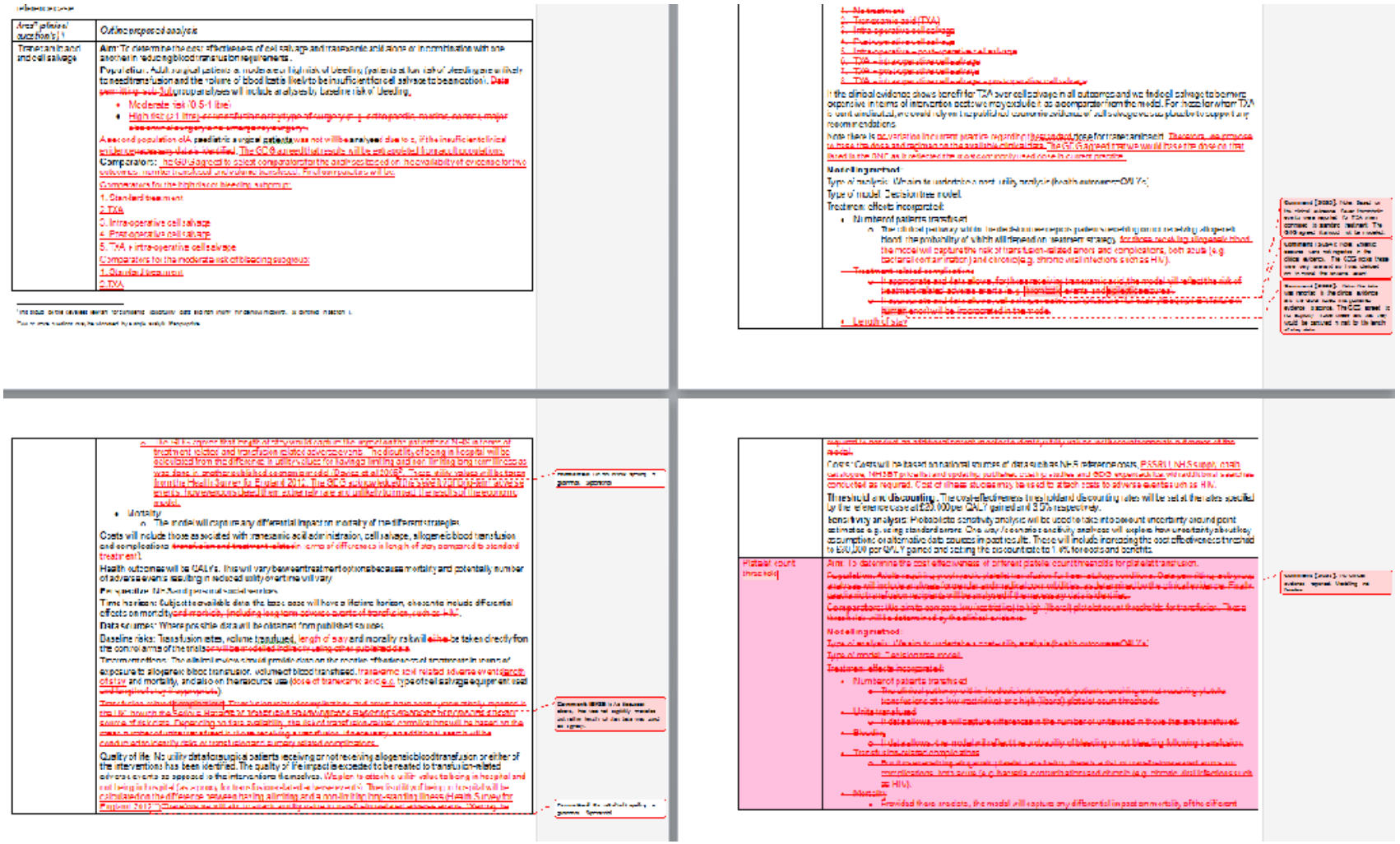
Lack of Evidence: Coeliac disease

(an example of high adherence to the plan)

- One subgroup dropped from case finding model. No recommendation made for this.
- No other changes but:-
  - Complete range of serological tests was not pre-specified
  - Other models were not described in detail as they were aspirational (but produced in the end)

Lack of evidence: Transfusion

(an example of medium adherence to the plan)



Lack of Evidence: Transfusion

- Post-hoc changes to the plan:-
  - Unable to find evidence on certain combination interventions (TXA+PCS, for example)
    - Solution: Research Recommendations
  - Some outcomes dropped (long term AEs, acute events – thrombotic e.g.) as homogenous data needed for NMA and modelling
  - Proxy of LOS used to capture major costs and health effects
  - One entire model (platelet count) dropped due to lack of evidence
    - Solution: consensus recommendation on minimum and maximum thresholds and room clinical judgement in between

Lack of Evidence: Bronchiolitis

(an example of low adherence to the plan)

- 7 (!) areas prioritised for economic modelling
  - 1 dropped because found not to be clinically effective (chest physio)
  - 1 dropped because not available in the UK and poor evidence (heliox)
  - 1 dropped because of low quality evidence that did not include all comparators of interest. A simple costs analysis produced instead
  - 1 dropped because there was no published evidence at all. A simple costs analysis produced instead
  - 3 analysed in an economic model but QALYs and longer term part of model dropped. Cost effectiveness too uncertain to make positive re. Evidence was from a subgroup analysis not included in trial design so underpowered – research rec made.

Other Guidelines

- Colleagues in Public Health and Social Care report a similarly flexible approach to HEAPs

- Other areas of NICE (Standards and Indicators, Scientific Advice, Implementation, Medicines Prescribing etc.)
  - Not really relevant but scientific advisors and new OMA would likely advise on production of and adherence to SAP as good practice. Unclear what the position on HEAPs is.

Purpose of SAPs and HEAPs

- Primarily to reduce bias in the analysis
  - NICE has less to gain from deliberately introducing bias when we undertake our own analysis
  - But considers adherence to SAP a mark of quality when assessing studies using GRADE (if mentioned at all!)
  - Technology Appraisals sometimes mention SAPs in this context
- Also useful as a write up of the methodology
  - NICE often does not know a great deal about what evidence will be identified in the reviews and the methods used to explore the RQ may change from what is planned

Conclusion

- Potential reasons why NICE doesn't routinely consider SAPs and HEAPs:-
  - Wary of being locked into methods that are too prescriptive or may become outdated
  - So have developed a set of general principals or framework to work to
  - Achieving a balance between purity of methodology with what is 'good enough' to make a decision

The Future

- Methods for Technology Appraisal
  - Should the ERG explicitly consider when critiquing the company's application?
- Guideline Manual
  - Should the reviewers explicitly consider as part of GRADE where SAP/HEAP not mentioned?

Discussion/Questions

- If you think of something later….
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