HTA Fallbeispiele (and process – methods recommendations)

Jos Kleijnen
Kleijnen Systematic Reviews Ltd

Assessments and appraisals

- "The assessment process consists of an objective analysis of the quality, findings and implications of the (mainly research) evidence available as it relates to the appraisal question and context. The appraisal process, in contrast, is a consideration of the outputs of the assessment process within the context of additional information supplied by relevant parties such as clinical specialists and patient experts. The appraisal decision is a judgment on the importance of a range of factors that differ from appraisal to appraisal"

Assessment and appraisal

- IQWiG performs assessments and gives recommendations
- G-BA performs appraisals

- Overlap between assessment and appraisal by IQWiG giving recommendations

- Hauptverband EBM gives recommendations

- NICE performs technology appraisals
- The assessments are done in house and/or by independent academic groups

Diagnostic accuracy and outcomes of ultrasound in the first trimester of pregnancy for detection of complications relevant for Austrian population, exclusive of screening for Down syndrome: a systematic review

Recommendations

1. First trimester ultrasound can not displace second trimester organ screening
2. First trimester ultrasound screening needs the informed consent of the woman (parents). Women have to understand the limits and risks
3. If first trimester ultrasound screening is provided, CVS has to be available in an adequate way
4. First trimester ultrasound for detection of chorionicity is not a screening aim
5. First trimester screening should be presented as an option and not an obligation to all women
6. First trimester ultrasound needs to be included into a quality management system to ascertain an adequate training of the examiners

Process - Scoping

- Scoping workshop (before Berichtsplan/Protocol) to address PICOS questions – Patients, Interventions, Comparator, Outcomes, Study designs
- Scoping workshop to enable input from stakeholders, external experts, patients
- Scoping workshop enhances transparency
- Stakeholders should participate – Institute should remain responsible for all decisions : scope is an Institute decision, not a joint decision

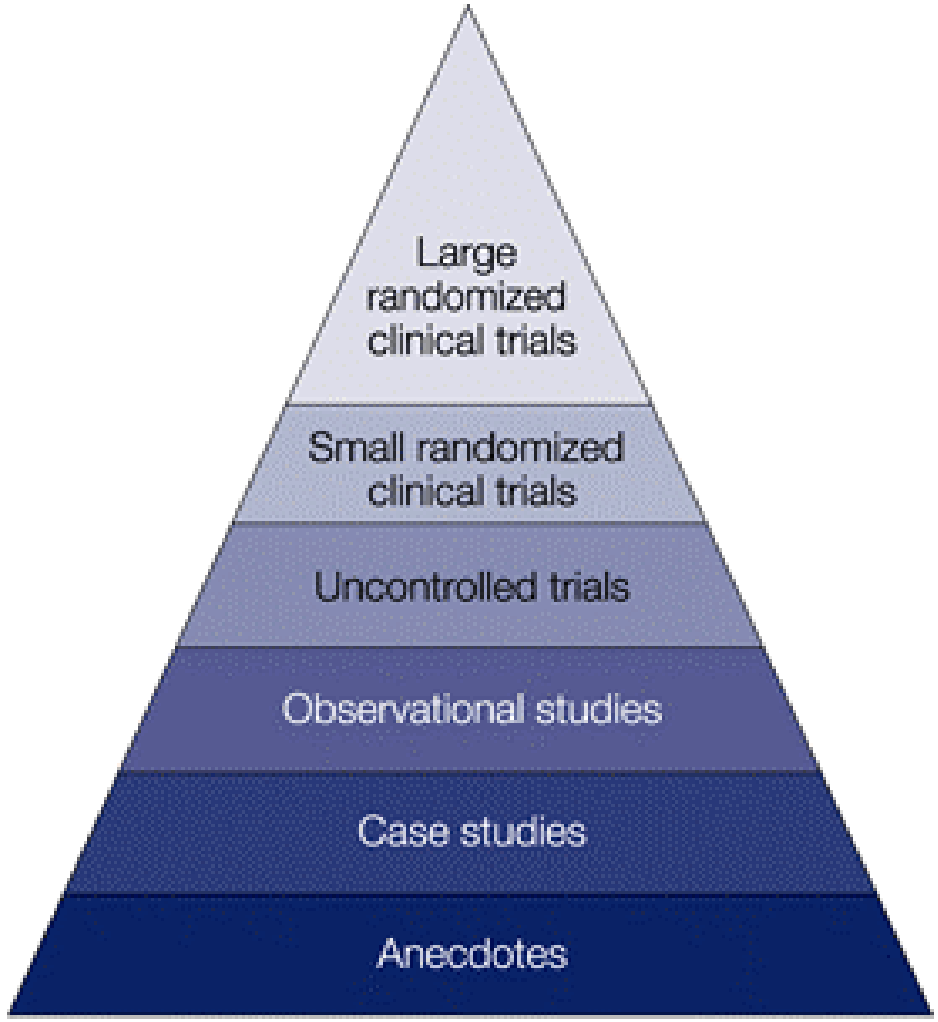
Process – open process of dealing with comments

- Comments from stakeholders and referees should be published
- Institute’s decision about whether or not to take up the comments should be documented and be made public
- Names of all commentators should be published

Process – consequences for stakeholders

- Participation also comes with requirements:
  - Stakeholders need to make patient based data public, only confidentiality of economic data can be justified
  - A registry of all clinical trials is inevitable in the long term, best to put it in place as soon as possible

Study designs



Methods – principle of best available evidence

- Scoping workshop will be crucial in defining the objectives of the assessment
- Decisions must be taken, therefore best available evidence, whatever its level, needs to be summarised
- Needs differentiated approach to accepting study designs for sub-questions

Methods – Use of different study designs

- Applying the principle of best available evidence means that one cannot strictly always demand certain study designs such as randomised trials
- This needs to be addressed during scoping and decisions about the approach to be taken need to be made on a case-by-case basis, and possibly also within projects individually per different outcomes (categories)

Objectives

1. Determination of the accuracy of ultrasound examination in the first pregnancy trimester (incl. 12th week) in diagnosing the following disorders:

2. Determination of the outcomes after ultrasound examination in the first trimester of pregnancy versus ultrasound examination in the second and/or third trimester for the following target disorders:

- Chromosomal anomalies other than Down Syndrome (Chimera 46,XX/46,XY, Chimera 46,XX/46,XY true hermaphrodite, 46,XX with streak-gonads, 46,XY with streak-gonads, pure gonadal dysgenesis, Fragile X-Chromosome, Fragile X-syndrome) (ICD 10 Q99)
- Detection of chorionicity with ultrasound in the first trimester of pregnancy
- Increased risk of preterm birth (ICD 10 P 07)
- Gestational diabetes (ICD 10 O24)
- Determination of gestational age

- accuracy studies
- studies that contain early screening vs. later screening
- screening population
- scan in the first trimester, transvaginal + abdominal
- date of publication as of 1.1.1996
- comparison of screening with confirmation of the findings post partum/post abortum/post AC/CVS

Head to head comparisons

Methods - comparators

- Needs to be addressed in scoping workshop – careful decisions needed about:
  - Head to head comparisons
  - Comparisons with placebos
  - Co-interventions that are allowed
  - Indirect comparisons (inevitable when economic evaluations are done)

- The decisions should again be taken on a case-by-case basis

Subgroup analysis

Methods - Subgroups

- Information about subgroups will be increasingly demanded by decision makers of all kinds
- These should be addressed in scoping workshop, preferably be defined in advance and included in protocol
- Trials give average effects in large widely defined groups, but need for knowledge of effects in very small strictly defined groups
- Doctors and patients ideally want to know whether an individual patient will have the benefits from a treatment and whether she will have the adverse effects

Methods - Outcomes

- Adverse effects traditionally under-addressed
- Patient relevant outcomes
- Patient reported outcomes
- QALYs (needs e.g. EQ-5D)

"Listen, when the side effects of this medication kick in, you'll forget what was wrong in the first place!"

Patient reported outcomes

IQWiG Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen

Vergleichende Nutzenbewertung verschiedener antihypertensiver Wirkstoffgruppen als Therapie der ersten Wahl bei Patienten mit essentieller Hypertonie

Vorbericht (vorläufige Nutzenbewertung)

Auftrag A05-09
Version 2.0
Stand: 09.09.2008

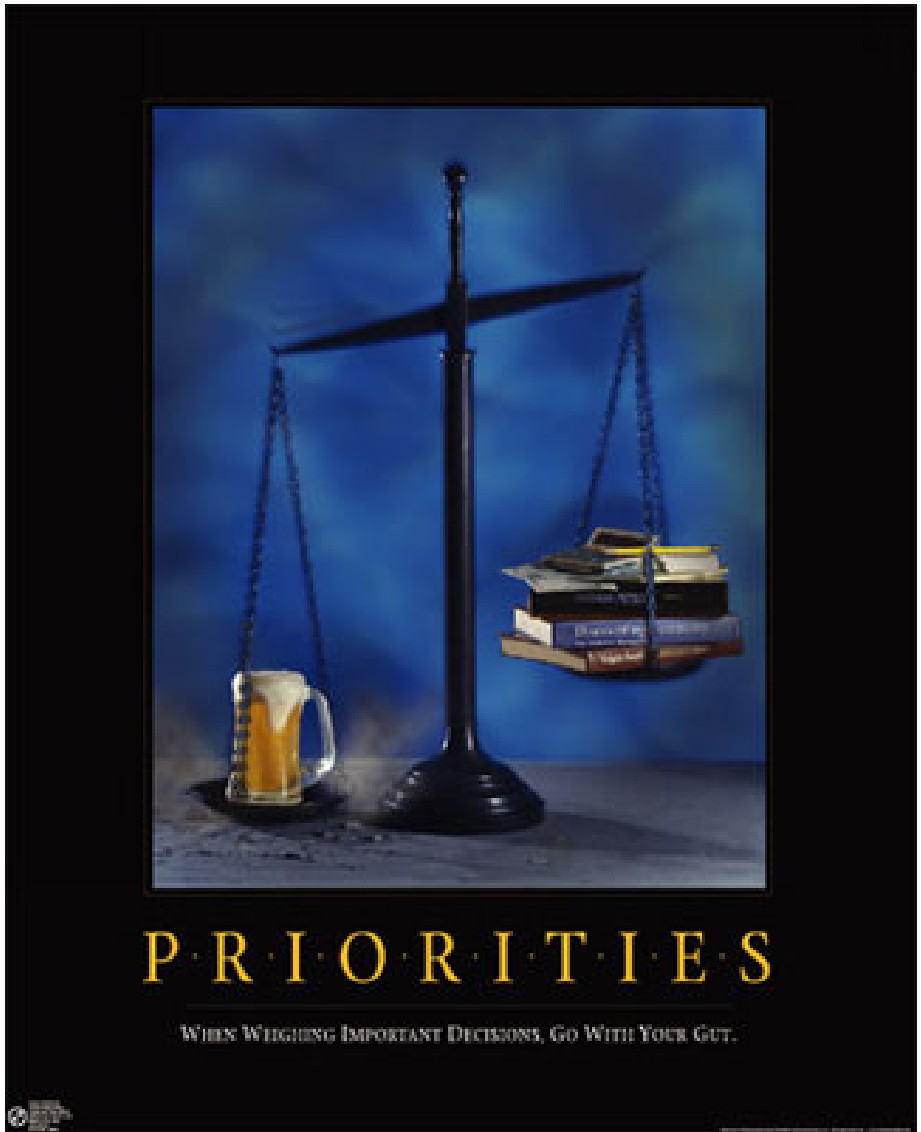
Main issues

- Systematic review methods of version 2.0 as such are sound, this is a good systematic review within its scope
- Only direct comparisons, no placebo controlled trials, this is defensible but it limits indirect comparisons – network meta-analyses
- Limited scope concerning trials also limits analyses in sub-groups (e.g. placebo controlled trials of beta-blockers in black people)
- Interpretation of results – emphasis on diabetes; treatments for heart failure not discussed!
- Shouldn’t patient risk profile and patient preferences play a role?

What evidence-based medicine is:

Evidence-based medicine is the conscientious, explicit and judicious use of current best evidence in making decisions about the care of individual patients. Its philosophical base dates back to the sceptics of post-revolutionary Paris (Bichat, Louis, Magendie).

Priorities, values, needs, preferences



Conclusions

- Transparency is important, openness of processes should be optimised
- Scoping workshop with all parties involved is crucial
- Principle of best available evidence should be consistently applied
- Differentiated approach needed for use of study designs
- Comparators and subgroups need careful consideration
- Trials register is needed, patient data should not be confidential