Analysis of HTAs on Spinal Cord Stimulation (SCS) and Sacral Neuromodulation (SNM) Therapies, and Identification of Patient-Reported-Outcome (PRO) use and assessment for sustainable and evidence-based decision-making.

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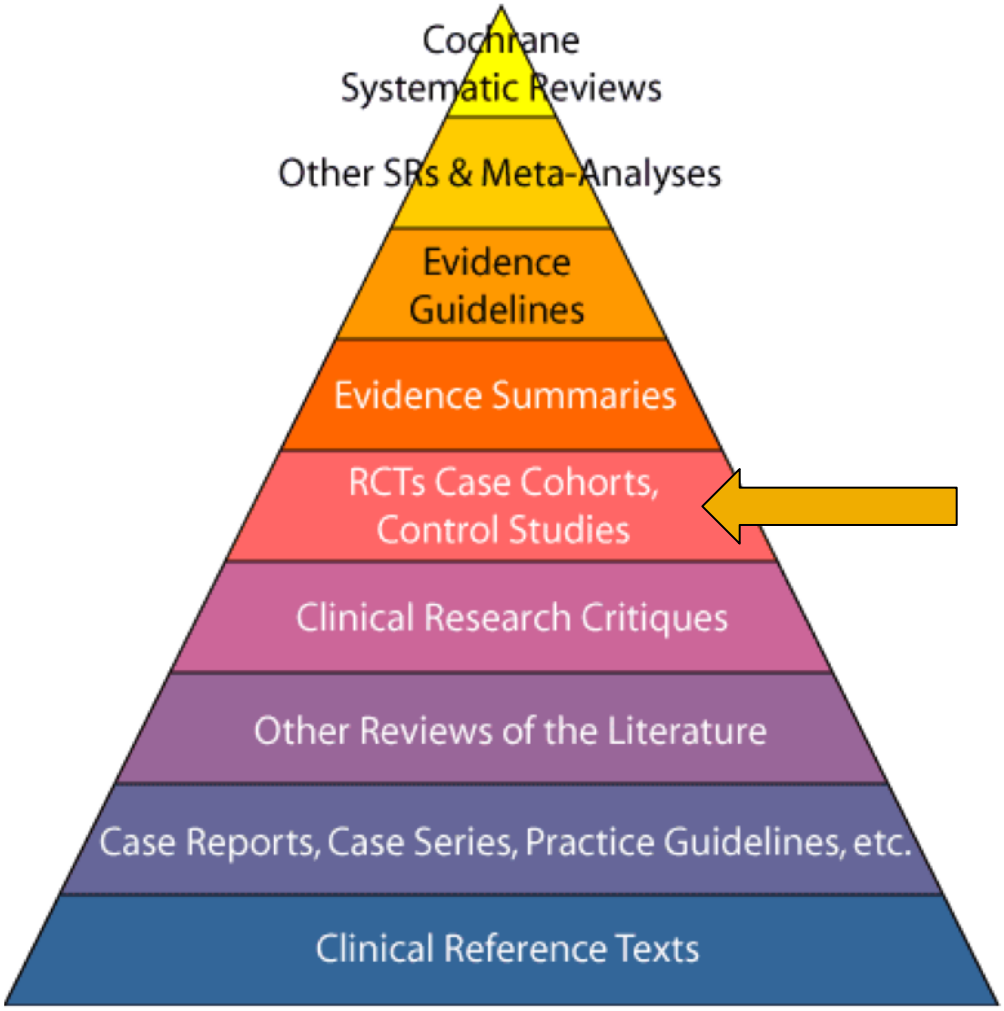
Outline of presentation

- Background: EBM, patient experiences, PROs and sustainable decision-making
- Methodology
- Findings
- Opportunities for the future: comparable and evidence-based decision making

Evidence-based decision-making – I
EBM principles and the PICO approach



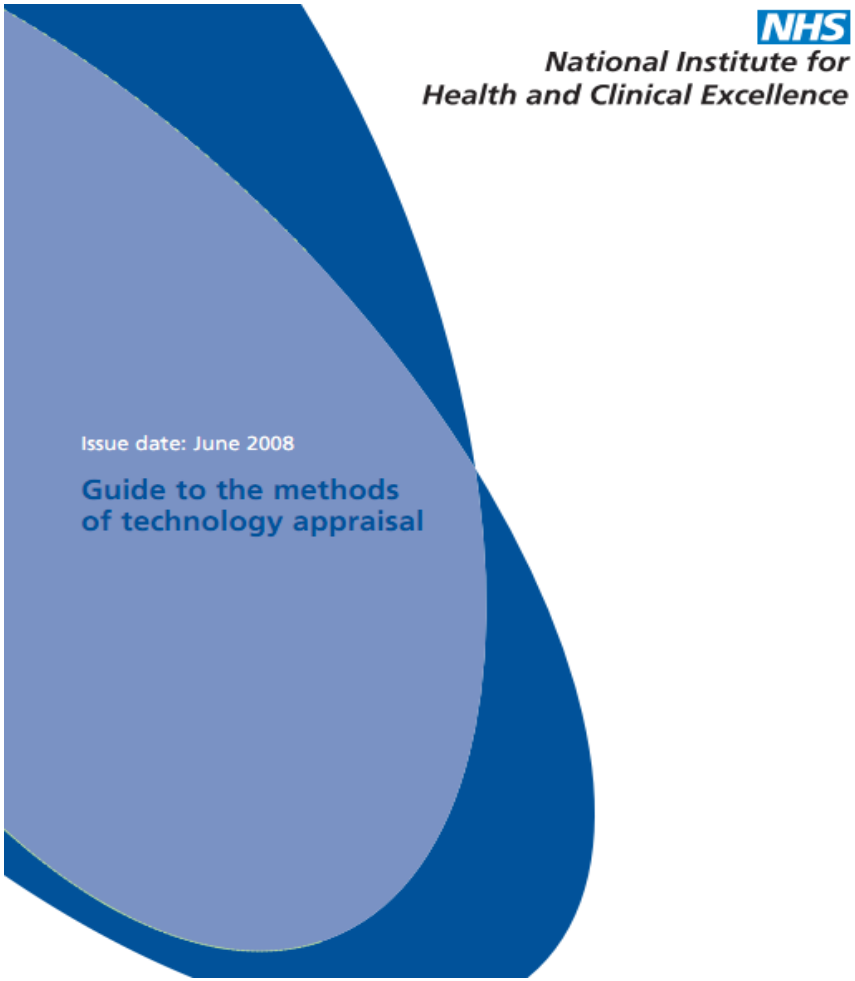
Pyramid modified from: Information Mastery: Navigating the Maze. 2009. University of Virginia, Claude Moore Health Sciences Library

- Frame patient scenario into a clinical question
- Systematically retrieve best evidence available
- Clinically appraise the evidence
- **P**atient or **P**opulation*
- **I**ntervention
- **C**omparator
- **O**utcome

*Subpopulations and selection/matching of/to relevant outcomes

Evidence-based decision-making – II
Shifting from RCTs to "Relevant Data"

3.2.3 The potential for bias, including performance, measurement and attrition bias, is greater in studies lower in the ranking. However, it is important to recognise that, even for the analysis of relative treatment effects, RCT data are often limited to selected populations and may include comparator treatments and short time spans that do not reflect routine or best NHS practice. Therefore, **good-quality non-randomised studies may be needed to supplement RCT data.** In addition, the **value of evidence** from anywhere in the ranking will depend on its **quality and relevance** to the appraisal (as defined in the scope).*



*Guide to the methods of technology appraisal. 2008. NICE

The purpose of the tracker - I

To compile a matrix for comparing and contrasting published international HTAs on device therapies

*…with specific emphasis on **tracking**:*

- the methods used
- the processes undertaken
- the outcomes and decisions made

The purpose of the tracker - II

- Product-specific international comparison of protocols and methodologies
- Degree of HTA value for money assessment for new and established therapies
- Best practices and convergence

Methodology - I

- **Databases searched:** CRD York; PubMed, EMBASE; Cochrane; HTA agency sites (e.g. NICE, MSAC, etc.)
- **Search terms:** spinal cord stimulation; sacral neuromodulation, sacral nerve stimulation (various algorithms for cross-checking findings by using MESH Terms for multiple indications)
- **Search dates:**
  July 2010 (1st); January 2011 (2nd): to cross-check existing data
- **Approach:** Study selection and data extraction were performed by 2 reviewers independently, according to predefined and detailed criteria. Various data analyses methods were used to interpret results and highlight similarities and differences between agencies. Other relevant material was identified (Hayes and ECRI report) but not included in this analysis (proprietary data not publicly available)
- No language and date restriction filters were applied; material retrieved up to **June 2010**

Methodology – II

Inclusion Criteria:

- For target (human) population, with main intervention evaluated the device of interest.
- Full health technology assessments, IPGs, horizon scanning reports and rapid reviews.
- Latest updated or original publication by national/regional/local HTA authority or qualified contracted body.
- Any outcome reported.
- Only full published/public or government HTAs were included.

Exclusion Criteria:

- Systematic reviews, clinical trials report, economic evaluations, meta-analyses, editorials, letters, and opinion pieces.
- Non-human studies
- HTA reports from private groups (e.g. Hayes and ECRI in the USA)

The tracker: Elements of the data extraction framework

- Region/Country/Agency/Year, Authors, Objective/Title, etc.
- Conflicts of Interest/Stakeholder involvement/Transparency/Language, Dates (submission/Publication)

Scope of HTA

- Device
- Comparator
- Clinical need/Burden of disease
- Analysis perspective
- Study population
- Setting
- CEA Threshold

Methods

- Search strategy/Inclusion criteria/# studies included
- Level of evidence/Grading system
- # of reviewers
- Clinical evidence considered & data source
- Costs/CE evidence & data source
- QALYs assumptions
- BI analysis
- Threshold analysis
- Psychosocial/Ethical impact
- Others
- Meta-analysis

Results

- Safety Risks
- Effectiveness
- Cost/Cost-effectiveness
- Budget impact
- Quality of Life

Reliability & Robustness

- Methodological challenges
- Sensitivity analysis
- Uncertainty analysis
- Other
- Comparison with other countries

Conclusions

- From assessment
- From appraisal
- Funding decision
- Market access implications
- Date of reappraisal
- Additional comments

The tracker: SCS and SNM therapies

14 HTAs of **2** therapies were evaluated by **6** agencies in **5** different countries

Methodology – III
EBM Principles and the PICO approach

Evidence-Grading Systems

- Identify evidence-grading system (examine convergence, intra-agency variation, etc.)
- Determine PICO use (appraisal and/or re-appraisal)
- Examine population/comparator/outcome grouping
- Determine QoL measures use (generic vs specific)

Findings - I

Studies

- 14 published HTAs: 10 for SNM, 4 for SCS
- Six different agencies, in 5 different countries

Evidence-grading systems

- Used by all SCS HTAs
- Only by 50% of the SNM HTAs
- Only the most recent one used the PICO approach

PRO research

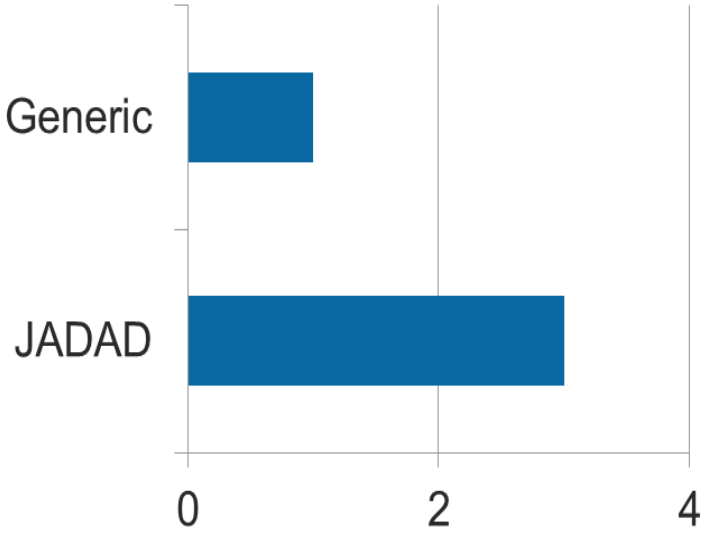
- Most HTAs evaluated PRO research
- Disease-specific tools: Limited amount of data reported (only seen in two HTAs)

Sensitivity analysis

- Only the 3 most recent HTAs tackled uncertainty through sensitivity analysis

Clinical Evidence – I
What Evidence-Grading Systems were used?

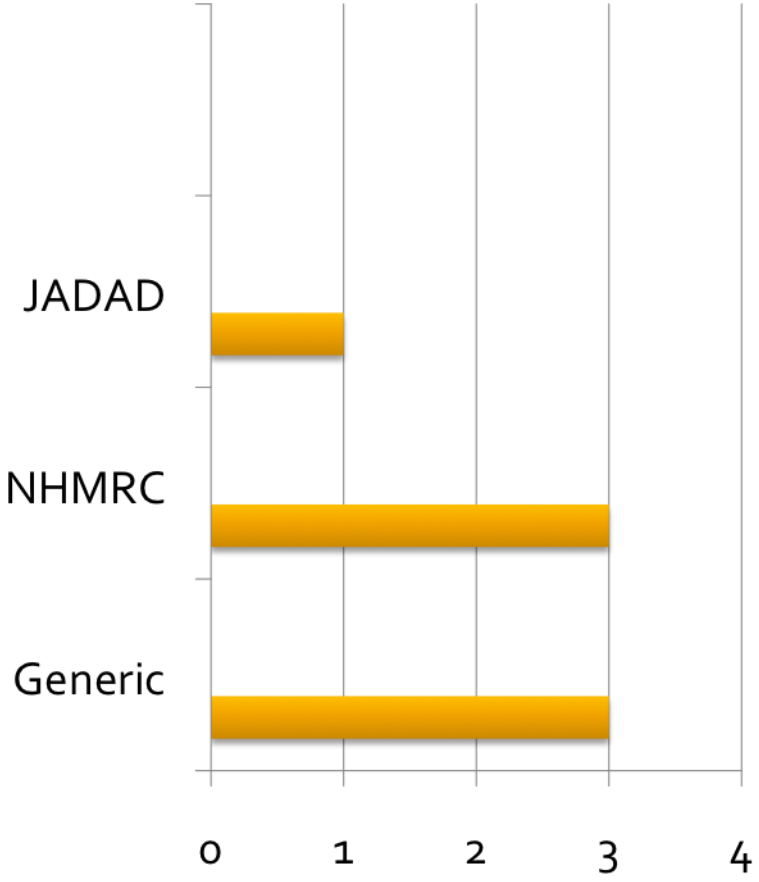
Health Technology Assessments on Spinal Cord Stimulation (SCS) for chronic, neuropathic or ischaemic pain



Country	Agency	Evidence Grading system	Year
Australia	ASERNIP-S	JADAD	2003
Canada	OHTAC	Generic based on GRADE	2005
Netherlands	CVZ	JADAD	2006
UK	NICE	JADAD	2009

Clinical Evidence – II
What Evidence-Grading Systems were used?

Health Technology Assessments on Sacral Neuromodulation therapies (SNM) for faecal and/or urinary incontinence



Country	Agency	Evidence Grading system	Year
Australia	MSAC	NHMRC 4-point (I-IV) scale	2000
Spain	CAHIAC	None	2000
UK	NICE	Multiple generic	2003
Australia	RACS/ ASERNIP-S	None	2003
Australia	RACS/ ASERNIP-S	None	2003
UK	NICE	Multiple generic	2004
Australia	MSAC	NHMRC 4-point (I-IV) scale	2005
Canada	OHTAC	Generic based on GRADE	2005
Australia	MSAC	NHMRC 4-point (I-IV) scale	2008
Netherlands	CVZ	JADAD	2008

Clinical Evidence – III

What Evidence-Grading Systems is used within a single agency?

NICE (UK)

Therapy	Year	Evaluator	Evidence Grading System
SNM	2003	Aberdeen University, UK	Multiple generic: -Modified version of Delphi list (& Verhagen et al., 1998) -CRD quality checklist (& Downs & Black, 1998)
SNM	2004	Sheffield & Aberdeen University, UK	Multiple generic: -Modified version of Delphi list (& Verhagen et al., 1998) -CRD quality checklist (& Downs & Black, 1998)
SCS	2009	Sheffield University	JADAD

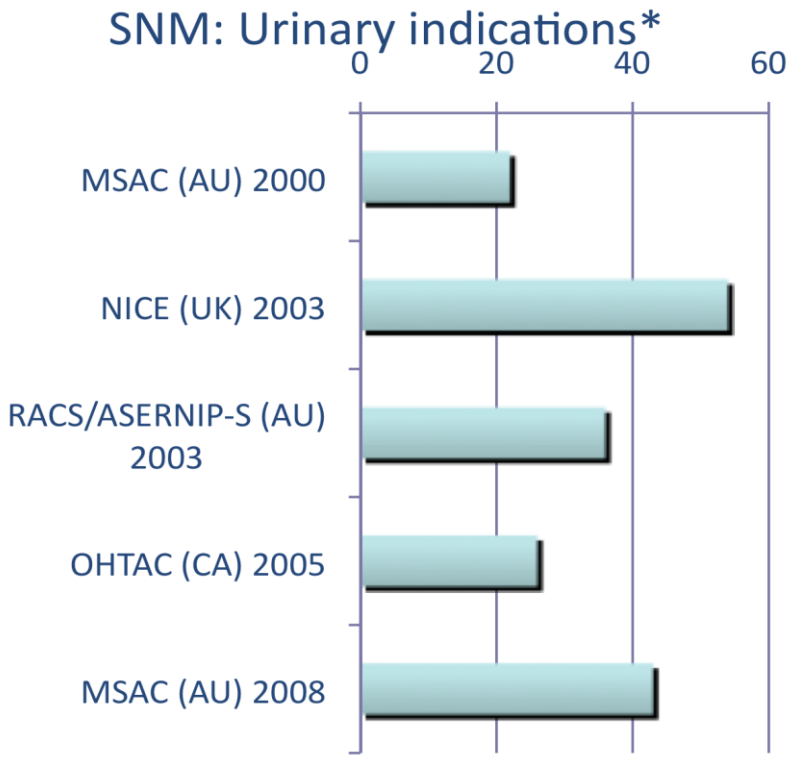
Clinical Evidence – IV

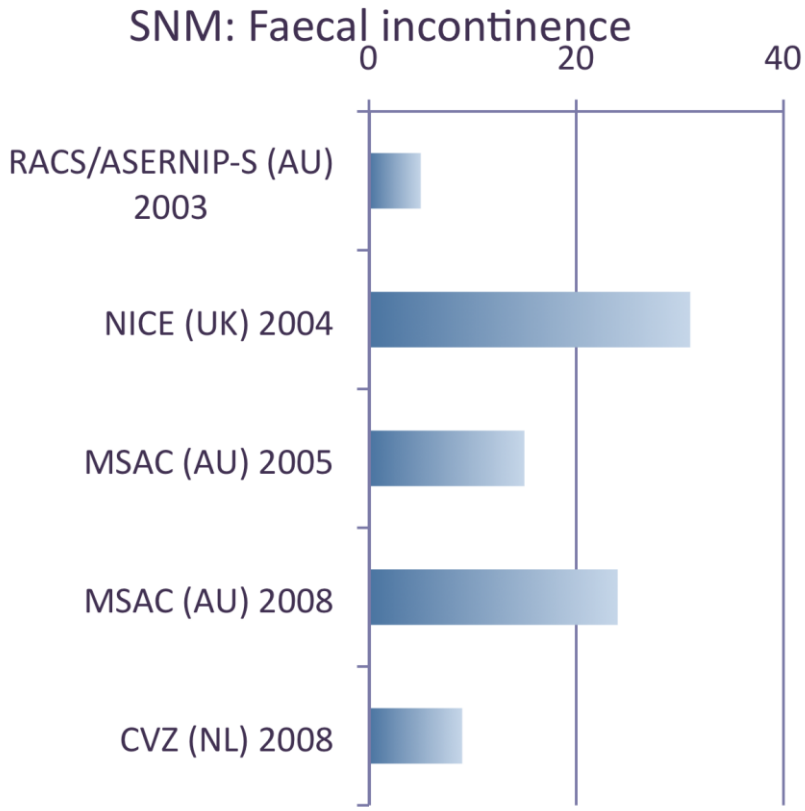
How many studies did each agency review in their HTA on SCS therapies?

Agency	Year of publication	Indication	Type of evaluation	# studies included
ASERNIP-S	2003	Chronic, neuropathic pain	Accelerated systematic review	9
OHTAC	2005	Chronic, neuropathic pain	HTA	16
CVZ	2008	Chronic pain	Systematic review	19
NICE	2009	Chronic, neuropathic, ischaemic pain	HTA	10

Clinical Evidence – V

How many studies did each agency review in their HTA on SNM therapies?





**urinary urge incontinence, urinary retention, urgency frequency, PBS*

Findings – I

MSAC Methodology

Agency	Year of publication	Indication	Search strategy / Research question, Comparator and Outcome measures	Decision outcome
MSAC	2000	Urinary indications	Multiple search strategies for safety, effectiveness, SR; **Comparator: Standard clinical management (supportive care)**; results arranged according to indication	Not recommended for adoption
MSAC	2005	Faecal incontinence	Boolean operators and searching with filters -SR; lack of comparator noted	Conditional positive
MSAC	2008/9	Urinary indications (however, assessment of evidence on fecal incontinence)	**PICO** approach; **Detailed comparators and outcomes according to patient grouping** (e.g. six reported outcomes for PBS patients)	**Recommendations according to each population searched and linked to outcome for expanded indications**

Findings – II
EBM: PICO Approach (2008, MSAC)

Population	Intervention	Comparator	Outcome
Patients with refractory detrusor overactivity	Chronic therapeutic sacral nerve stimulation	Standard non-surgical management (best supportive care) Bladder denervation Bladder reconstruction Urinary diversion +/- cystectomy Augmentation cystoplasty	*Effectiveness*: Response rate, Voids/day, Volume/void, Incontinence episodes/day, Leakage severity, Pad use/day Parameter adjustments Quality of life measures Parameter adjustments Quality of life measures *Safety*: Adverse event rates Revision/explant rates Mortality
Patients with refractory non-obstructive urinary retention	Chronic therapeutic sacral nerve stimulation	Clean intermittent self-catheterisation Indwelling catheter Urinary diversion +/- cystectomy	*Effectiveness*: Response rate Voids/day Volume/void Catheterisations/day Volume/catheterisation Parameter adjustments Quality of life measures *Safety*: Adverse event rates Revision/explant rates Mortality
Patients with refractory painful bladder syndrome	Chronic therapeutic sacral nerve stimulation	Standard non-surgical management (best supportive care) Bladder denervation Bladder reconstruction Urinary diversion +/- cystectomy Hydrostatic dilation/bladder instillation therapies	*Effectiveness*: Response rate Voids/day, Volume/void Parameter adjustments Quality of life measures *Safety*: Adverse event rates Revision/explant rates Mortality

Evidence-based health care (EBHC) and Evidence-based medicine (EBM)

Sustainable decision-making necessitates…

- Patient-centric approach
- Harmonization at the level of clinical evidence (guidelines, clinical protocols, etc.) and best-practice development and adoption
- Supporting clinical decision-making through relevant policy-making

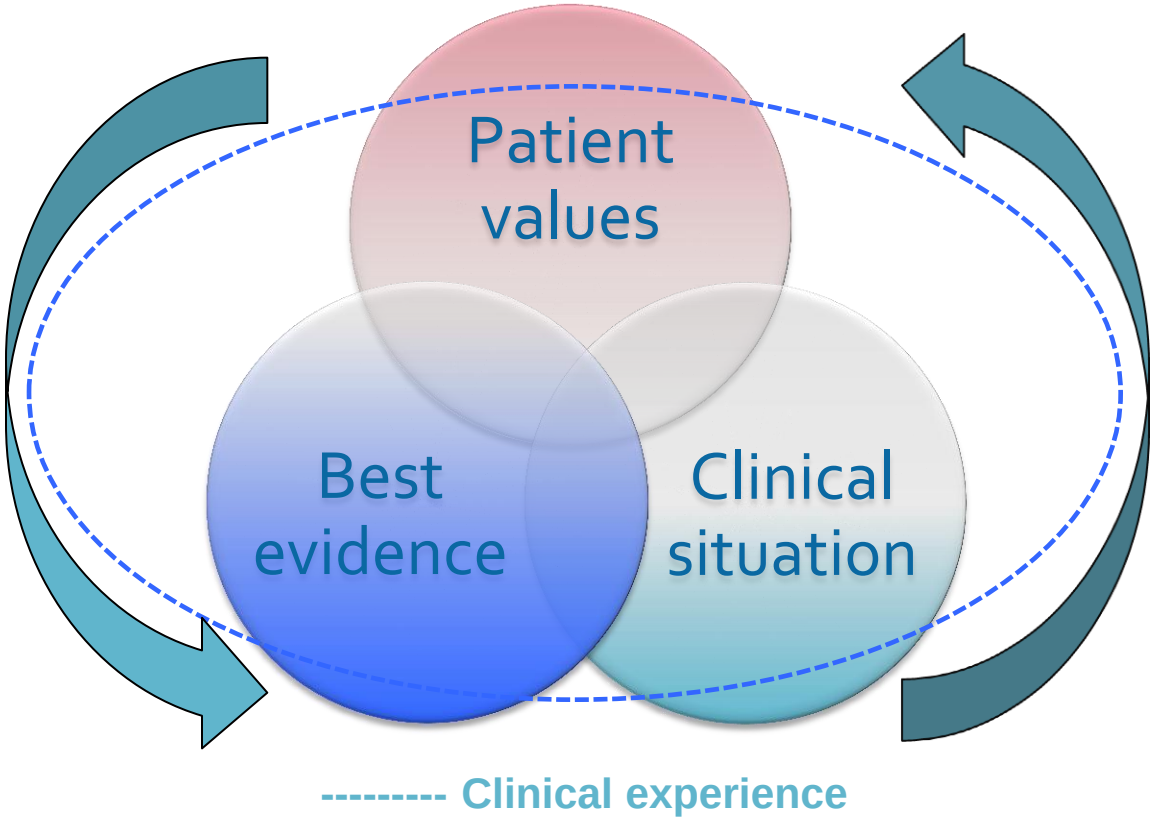


Figure modified from: Evidence-Based Medicine: How to Practice and Teach It (SE Straus, P Glasziou, WS Richardson). 2010. Elsevier Health Sciences.

Key messages

- Inter- and intra-agency heterogeneity (methodology, evidence-grading classification, data used, evidence base and decision-making)
- PRO evidence is particularly relevant for SCS and SNM therapies as certain outcomes are only known to the patients themselves; need for tools that allow to validate and appraise such evidence in a standardized fashion
- EBM principles and methods, such as the application of the PICO approach, could help address heterogeneity in terms of methodological issues (i.e., clinically relevant subpopulations, comparator selection, appropriate outcomes) and contribute to the creation of a more sustainable evidence base

➢ Certain degree of methodological convergence on effectiveness (PICO in EUNetHTA's Core Model, NICE Guidelines Manual, MSAC assessment)

Questions?