Are we Adequately Equipped to Assess Pain Therapies?

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Increasing Pressures in all Health-Care Systems

- Population demography
  - Aging population in almost all countries
  - Increasing obesity and physical inactivity
- Patient/Public expectation
  - More possibilities to intervene beneficially
  - “a pill for every ill!”
  - Lifestyle drugs/disease mongering
- Changing environment for new medicines
  - Mature market place

Pharmaceutical Market 2010

- Three decades of major advances
- Effective medicines for most common diseases
  - Often now ‘generic’ agents at low cost
  - Most needs met (at least to some extent)
- New medicines of two main types
  - Extend choice in existing crowded areas
  - New options in niche areas of unmet need
- Do the benefits justify the (opportunity) costs?

Health Technology Assessment

- Provides a logical framework for decisions
- Has to compare many options –
  - Different disease areas
  - Different interventions
  - Different patient groups
- Has to be as objective and dispassionate as possible
  - ...but still with a human face
- Inevitably produces ‘winners’ and ‘losers’

Pain Therapies and HTA

- Pain is a feared, even dreaded, symptom
- Clear clinical evidence of unmet need
- Many new drugs in the marketplace
- ...but many ‘failing’ in HTA processes
- Are new drugs for pain just not very good?
- ... is HTA methodology biased against therapies for pain?

Evidence-Base and Analysis

- Are the studies what is required?
  - Placebo v active control
  - Treatment-naïve v treatment-experienced
  - Responder-enriched v treatment-failure
  - Trial efficacy v real-world effectiveness
- Can health economics measure the benefits?
  - Generic v pain-specific
  - Absolute quality of life v sensitivity to change
  - Functional v psychological benefits
  - Healthcare v societal perspective

Clinical Studies in Pain Therapy - 1

- Busy therapeutic area (with generics++)
- Placebo-controlled studies show efficacy
  - ... but not comparative efficacy/effectiveness
  - ... not ‘place in therapy’
  - ... not ‘value to the payer’ (or the patient!)
- Active-comparator studies preferable
  - Actual comparator not crucial
  - A ‘standard’ therapy allows indirect comparison
  - Begins to show ‘value’ to all concerned

Clinical Studies in Pain Therapy – 2

- Treatment-naïve v treatment-experienced
- Responder-enriched v treatment failure
- Former overstate the likely efficacy
  - … and are unlikely to match clinical use
- Latter will reduce absolute efficacy
  - … but will match likely real-world use
  - … will show real clinical value
  - … will show real value to the payer

Clinical Studies in Pain Therapy – 3

- Trial efficacy v ‘real-world’ effectiveness
- A big issue in pain therapies
  - Drug treatment part of a ‘package’
  - Adherence/tolerability/persistence crucial
  - Complexity/titration tricky and poorly done
    - ..may actually falsely favour older therapies
- Post-marketing data important in pain
  - To demonstrate/prove real benefits
  - ...and underpin true value (clinical and €€€!!)

HTA and Pain Therapy

- Health-gain comprises 2 domains
  - Quantity of life (= survival benefit)
  - Quality of life
- Almost all pain therapies affect only QoL
  - Only possible to ‘score’ in one domain
- Survival usually easier to quantify than QoL
  - ...and change perhaps easier to demonstrate
- QoL measurement key in pain assessments

Quality of Life Assessment

- Generic measures
  - EQ-5D, SF-36, ...
- Pain-specific measures
  - WOMAC, RMQ, ...
- Preference-based measures
  - Time-trade-off
  - Standard gamble
- HTA prefers generic measures and preference-based measures

Generic Measures of QoL

- Well studied – large evidence base
- Familiarity in health economic circles
- Proven role across disease areas
- BUT
- May be poor in a single symptom (eg pain)
- May lack granularity to assess change
  - EQ-5D has 3 levels, SF-36 has 5 levels
- Often focus on function, not feelings
  - … may miss subtle psychological benefit (eg fear)

Pain-Specific Measures of QoL

- Numerous scales of varying quality/validity
- Often very disease-specific
  - Low back pain
  - Osteoarthritis
  - Cancer pain
- … may not generalise within the pain field
  - Pain as part of a disease v in isolation
- Little mapping to other QoL measures
  - … not possible to compare to other therapies
  - ‘double-counting’ of impacts of pain and therapy

Other QoL Assessment Methods

- Simple reporting methods
  - Visual analogue scale
  - Likert scale using descriptors
  - No ‘cost’ to low QoL values
- Preference-based methods
  - Time-trade-off
  - Standard gamble
  - Some penalty for low QoL values

Preference-Based QoL Assessments

- Most useful if collected within a clinical trial
  - ... often the least well recorded trial data
  - Less useful with ‘imaginary’ patients
- Can be very sensitive to change
  - ... important to define time-frame of assessment
- May still underestimate QoL change
  - ... subjects may gamble/exchange more for survival than for symptom relief
- Good normative data allows comparison across disease areas

HTA Time Horizon and Pain Therapy

- Chronic pain – trial data may underestimate true benefits
  - … needs HTA time horizon longer than trials
  - Requires assumptions about long-term benefits
  - Persistence with therapy often very uncertain
- Acute pain – may be hard to detect benefits
  - Migraine – severe symptoms but intermittent and very short-term
    - Impact may be lost over weeks-months horizon
    - May be a real ‘special case’!

HTA Perspective and Pain Therapy

- View from the healthcare system
  - Pain relief buys QoL (and may reduce burden on primary care, psychology, counselling...)
- View from wider society
  - As above PLUS return to the workplace, benefits for families, reduction in social benefit costs...
- How tangible/realisable are these benefits?
  - ... a real question in the current financial climate
- Issue of HTA perspective an active one

HTA Can Find Real Value!

- Anti-TNF drugs for rheumatic disease
  - Crowded therapeutic area
  - Expensive (and risky) therapies
  - Benefits largely in QoL terms
- Large QoL gain (and corresponding lowish cost-per-QALY) easily shown
- These are highly effective drugs
  - ... with a large incremental health gain
- ... ?? true of most drugs in the pain field

HTA and Pain Therapies

- Clinical studies need to be better
  - ...to focus on what everyone really wants to know
- Real-world effectiveness data needed too
- HTA methodologies imperfect
  - ... but can show benefits
  - ... could be developed to better capture QoL change and map this to other healthgain
- HTA bodies need to hear the specialist issues
  - ... and *vice versa!*
- We all need to see more effective therapies!!

Scottish Medicines Consortium

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