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On the effectiveness and costs of inhaled methoxyflurane versus usual analgesia for prehospital injury and trauma

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Methoxyflurane

- Methoxyflurane (Penthrox®; Galen Ltd) is a volatile fluorinated hydrocarbon anaesthetic with analgesic properties in sub-anaesthetic doses
- Widely used as an inhalational analgesic in adults and children for over 40 years in Australia and New Zealand
- Easy to administer, with good safety profile
- UK licence is for emergency relief of moderate to severe pain in conscious adults with trauma pain
- Limited evidence of clinical and cost effectiveness in the prehospital setting

Aim

- To investigate benefits and economic costs of adding inhaled methoxyflurane to prehospital care for adults with moderate to severe pain from traumatic injury

Methods

- EMAS evaluated use of methoxyflurane added to usual analgesic practice (UAP) using volunteer ambulance staff from four stations trained to use it, Dec 2018 to Nov 2019

- Statistical modelling used to compare methoxyflurane to comparator analgesics used under UAP

EMAS data

- Methoxyflurane evaluation protocol (additional to UAP):
  - Establish indication for methoxyflurane
  - Obtain following verbal numerical pain scores (VNPS)
    - either prior to or at the time of administration
    - 5 minutes after administration
    - 30 minutes after administration
- Comparisons to analgesics
  - (i) Entonox®, (ii) Morphine IV, (iii) Paracetamol IV
  - Data sourced from UAP episodes requiring for eligibility that it satisfy the indication for methoxyflurane and have at least two VNPS recorded

Panel Ordered Probit Model

- Combined model of pain due to trauma, denoted Y^*, influenced by methoxyflurane d=1 or its comparator d=0

$$Y_{ij}^* = f(t_{ij}) + d_i \boldsymbol{\gamma}' \boldsymbol{x}_{ij} + (1 - d_i)\boldsymbol{\delta}' \boldsymbol{w}_{ij} + u_i + \varepsilon_{ij}$$

$$f(t) = \begin{cases} \beta_1 t + \beta_2 t^2 & d = 0 \\ (\beta_1 + \theta_1)t + (\beta_2 + \theta_2)t^2 & d = 1 \end{cases}$$

- Test that methoxyflurane relieves pain faster than comparator:

$$H_0\colon\ \theta_1 = 0 \ \text{ versus } \ H_1\colon\ \theta_1 < 0$$

- Time to least pain:

$$\text{Methoxyflurane: } -\frac{\beta_1 + \theta_1}{2(\beta_2 + \theta_2)} \qquad \text{Comparator: } -\frac{\beta_1}{2\beta_2}$$

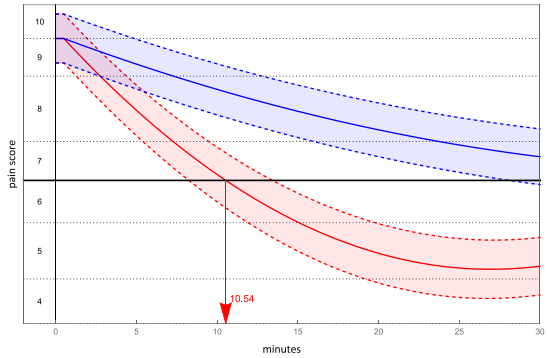
- Observation rules relate VNPS and Y^* complete the model:

$$\Pr\left(S_{ij} = s|\boldsymbol{X}\right) = \Pr\left(\alpha_s < Y_{ij}^* < \alpha_{s+1}|\boldsymbol{X}\right) \quad \text{where } -\infty < \alpha_1 < \cdots < \alpha_{10} < +\infty$$

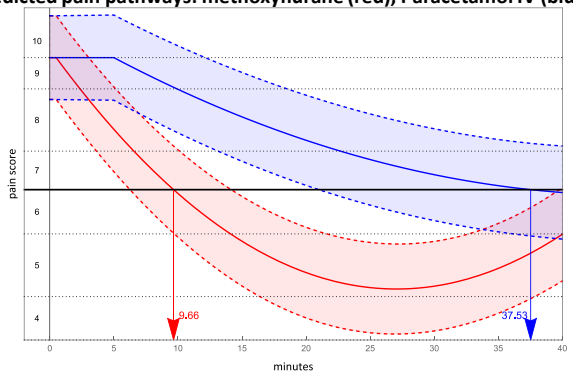
Results snapshot

	Methoxy	Entonox®	Methoxy	Morphine IV	Methoxy	Paracetamol IV
ESTIMATION SAMPLE						
Patient numbers	406	753	406	802	406	278
Observations	2856		3160		1883	
TIME PATHWAYS						
β_1	-0.071**		-0.108**		-0.081**	
β_2	0.001**		0.001**		0.001**	
θ_1	-0.136**		-0.088**		-0.128**	
θ_2	0.003**		0.002**		0.003**	
Time to least pain	26.44	44.46	26.50	41.77	26.57	40.77
SCENARIO						
Duration severe pain	10.54	Not predicted to exit	10.47	20.09	9.66	37.53

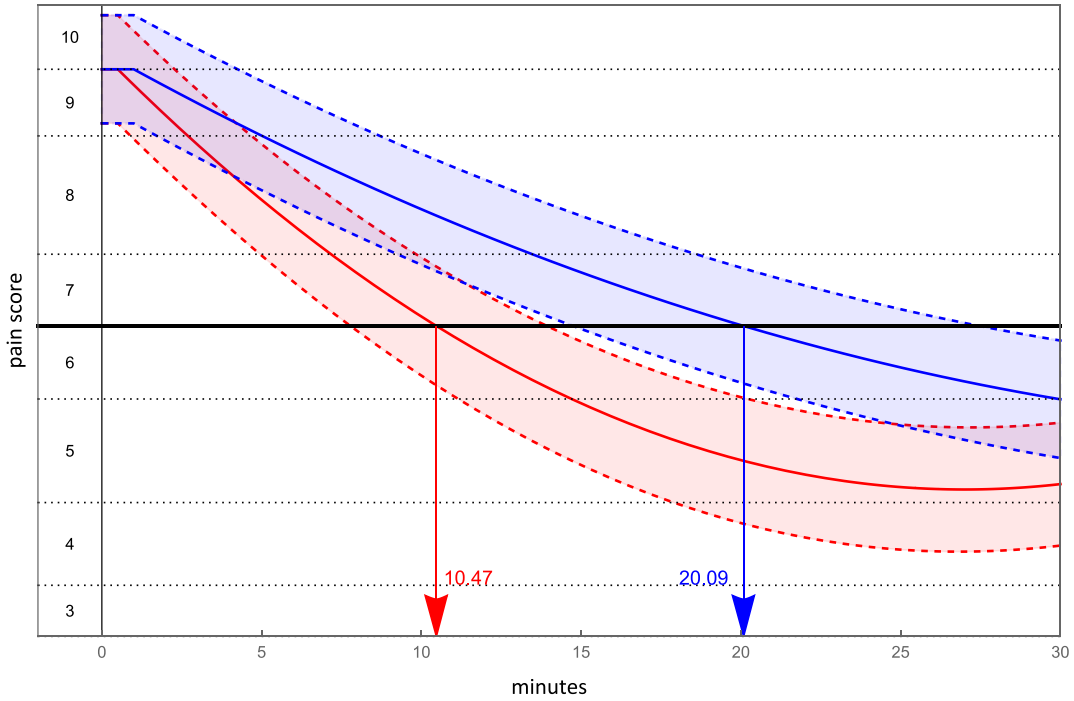
Predicted pain pathways: methoxyflurane (red), Entonox® (blue)



Predicted pain pathways: methoxyflurane (red), Paracetamol IV (blue)



Predicted pain pathways: methoxyflurane (red), morphine IV (blue)



Cost

- Methoxyflurane versus Entonox®
  - The benefits of methoxyflurane over Entonox® are obtained for the additional cost per treated patient of £12.30
    - Assumption: zero net difference in all other costs due to pain management
    - Costs and benefits arising beyond patient handover not included
    - Not included is the patient benefit due to reduced morbidity arising from speed of pain relief

- Methoxyflurane versus Potency 3 IV
  - The benefits of methoxyflurane over Potency 3 IV are obtained for the additional cost per treated patient of £10.24
    - Assumption: zero net difference in all other costs due to pain management
    - Costs and benefits arising beyond patient handover not included
    - Not included is the patient benefit due to reduced morbidity arising from speed of pain relief

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