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Trauma Pain: Is there a better pathway?

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Market Access Manager

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Sir Allen McClay - Galen Founder

ALMAC

Partnering with Healthcare Professionals & Patients to Advance Human Health

VISION STATEMENT

"Galen will be a patient and customer-centric company delivering best-in-class services for the development and marketing of pharmaceuticals globally"

Galen's Story

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GALEN	ALMAC	MCCLAY FOUNDATION	ALMAC GROUP
Founded in 1968 by the late Sir Allen McClay, the revered philanthropist and entrepreneur	Founded the Almac Group in 2002	He later established the McClay Foundation as a charitable institution, donating more than £20 million to enhance the research capabilities at Queen's University Belfast	A proud member of the Almac Group, wholly owned by the McClay Foundation whose overarching aim is to make a meaningful improvement and advancement in human health

Offerings of Almac

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Galen:
global pharmaceutical sales
& marketing organisation

Almac Clinical Technologies:
clinical trial technology and
expert technology

Almac Discovery:
biotech organisation

ALMAC
Partnering to Advance Human Health

Almac Clinical Services:
manufacture, distribution &
management of clinical trials

Almac Diagnostic Services:
biomarker discovery &
development

Almac Pharma Services:
drug product development;
commercial manufacture &
packaging

Almac Sciences:
API development &
analytical services

ASSOCIATION OF AMBULANCE CHIEF EXECUTIVES

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Delayed Hospital Handovers: Impact Assessment of Patient Harm

The key finding of our clinical review which looked at samples of handover delays of over an hour that occurred across the country on 4th January 2021, is that the proportion of patients identified as potentially having experienced harm is significant. Over 8 out of 10 of those whose handover was delayed beyond 60 minutes were assessed as likely to have experienced some level of harm, with just under 1 in 10 being classified as potentially experiencing severe harm. The extensive presence of the possibility of harm identified within this sample is deeply concerning. The number of delays experienced on 4th January 21 is typical of most days,[1]

In view of the harm that delays in handover can cause to patients, we seek to emphasise that **there is *still* not enough being done to adequately address this risk.** We need tangible steps be taken at national, regional and ICS level, to implement *rapid* system improvement, particularly for those hospitals where delayed handovers are occurring consistently. By rapid we mean in addition to the current improvement initiatives underway and the routine monitoring of related action plans.[1]

The continuing pressure on the NHS

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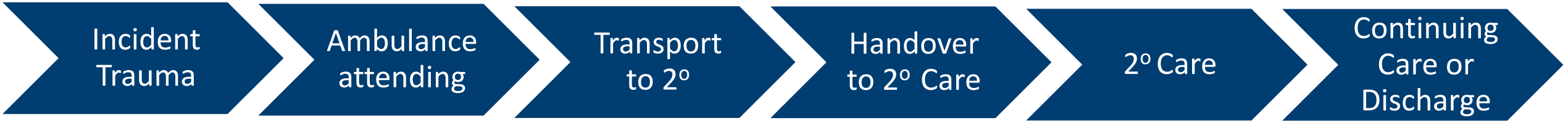
Trauma Patient Journey



The continuing pressure on the NHS

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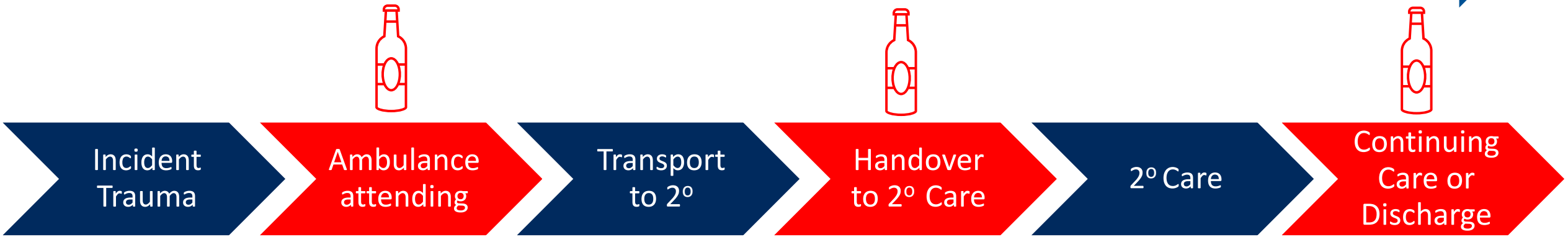
Trauma Patient Journey: The Bottlenecks



Ambulance Quality Indicators February 2022

Ambulance Service	All incidents	Incidents with transport to ED	Incidents with transport not to ED	Face to face incidents with no transporting	Incidents with face to face response	See & Treat	Convey to ED
	A7	A53	A54	A55	A56	A55 / A7	A53 / A7
England	644,006	339,067	32,168	200,576	571,811	31.1%	52.6%
London	93,099	49,238	3,353	29,084	81,675	31.2%	52.9%

81,000 Ambulance attendances each month in London
More than 49,000 conveyed to ED each month

2. NHS. Ambulance Quality Indicators. [Assessed May 2022]. https://www.england.nhs.uk/statistics/statistical-work-areas/ambulance-quality-indicators/

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Ambulance Quality Indicators February 2022

Code	Ambulance Service	Count of incidents	Resources allocated	Mean resources allocated	Resources arriving	Mean resources arriving
C1		A8	A39	A39 / A8	A40	A40 / A8
	England	67,539	138,321	2.05	103,434	1.53
RRU	London	8,983	23,267	2.59	17,738	1.97
C1T		A9	A41	A41 / A9	A42	A42 / A9
	England	44,193	89,622	2.03	68,214	1.54
RRU	London	6,257	16,037	2.56	12,461	1.99

2 ambulances attending each call
160,000 ambulances committed every month

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2. NHS. Ambulance Quality Indicators. [Assessed May 2022]. https://www.england.nhs.uk/statistics/statistical-work-areas/ambulance-quality-indicators/

Secondary Care ED Activity: The 4 STPs in London

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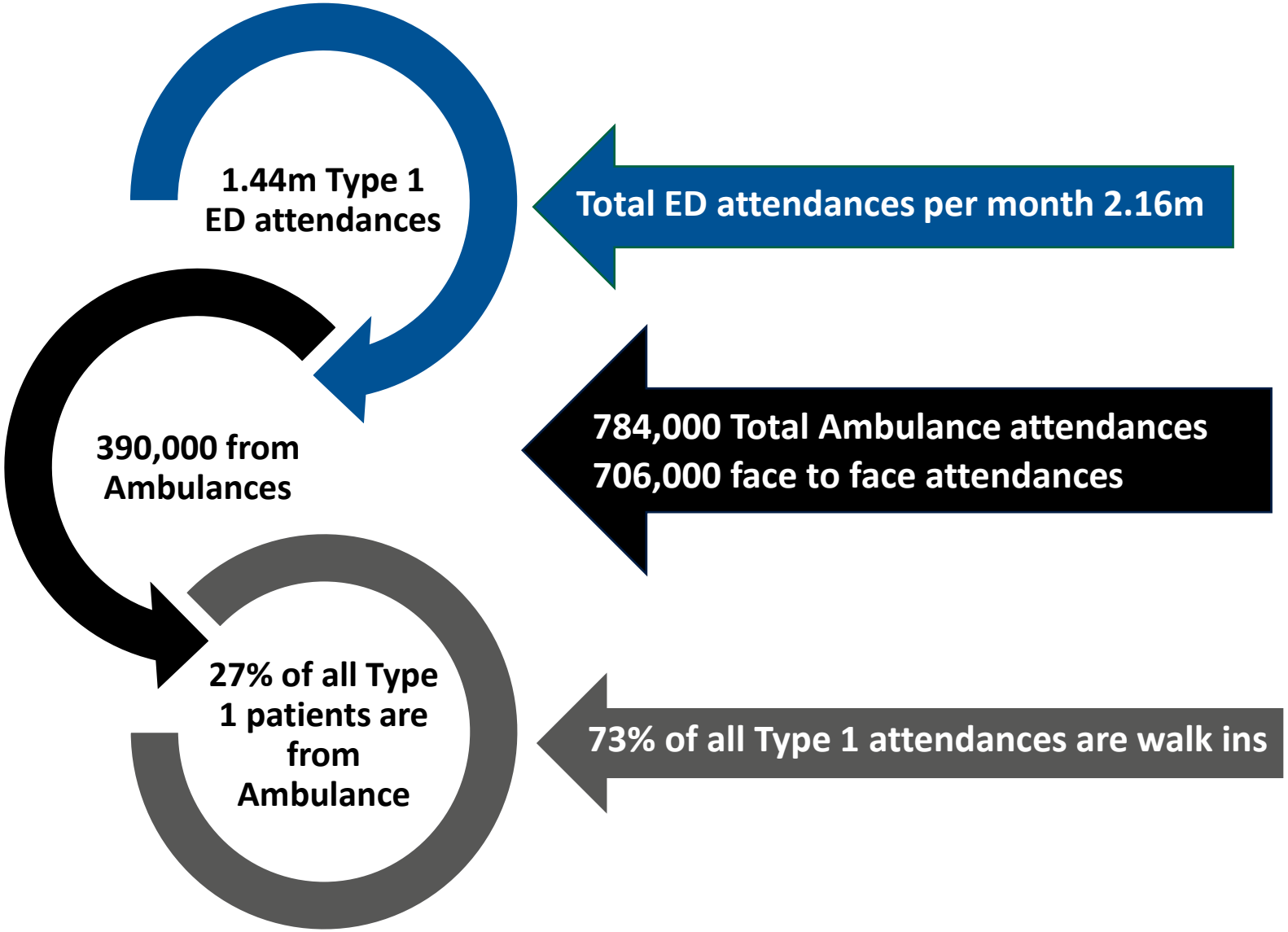
STP	A&E attendances				A&E attendances > 4 hours from arrival to admission, transfer or discharge				Emergency Admissions	
	Type 1 Departments - Major A&E	Type 2 Departments - Single Special	Type 3 Departments - Other A&E	Total attendances	Type 1 Departments	Type 2 Departments	Type 3 Departments	Total Attendances > 4 hours	>4 hours from decision to admit to admission	>12 hours from decision to admit to admission
-	1,419,896	41,910	711,947	2,173,753	514,034	1,157	34,477	549,668	136,297	22,506
East London Health & Care Partnership (STP)	49,018	3,137	34,599	86,754	21,185	315	3,542	25,042	5,522	1,155
North London Partners In Health & Care (STP)	55,649	5,995	12,397	74,041	20,523	12	1,178	21,713	4,231	1,144
North West London Health & Care Partnership (STP)	51,097	3,770	49,450	104,317	8,780	0	3,087	11,867	4,914	232
South West London Health & Care Partnership (STP)	45,333	284	11,834	57,451	12,646	0	10	12,656	2,880	665

201,000 Type 1 ED attendances per month in London

63,000 Type 1 ED attendances > 4hrs

3. NHS. Attendance and Emergency Admission Monthly Statistics, NHS and Independent Sector Organisations in England. https://www.england.nhs.uk/statistics/statistical-work-areas/ae-waiting-times-and-activity/

NHS England: ED and Hospital Activity per Month



3. NHS. Attendance and Emergency Admission Monthly Statistics, NHS and Independent Sector Organisations in England. https://www.england.nhs.uk/statistics/statistical-work-areas/ae-waiting-times-and-activity/

Waiting Times

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< 4 hour waiting times

2011/12 Q1: 95.5%
2019/20 Q3: 71.4%

# of Type 1 attendees

2011/12 Q1: 3,586,381
2019/20 Q3: 4,116,384

4. Nuffieldtrust. A&E Waiting Times. [Accessed May 2022]. https://www.nuffieldtrust.org.uk/resource/a-e-waiting-times

The continuing pressure on the NHS

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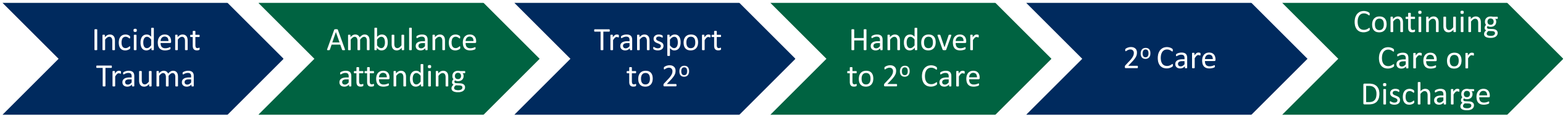
Trauma Patient Journey: What to Focus On?



East Midlands Ambulance Service

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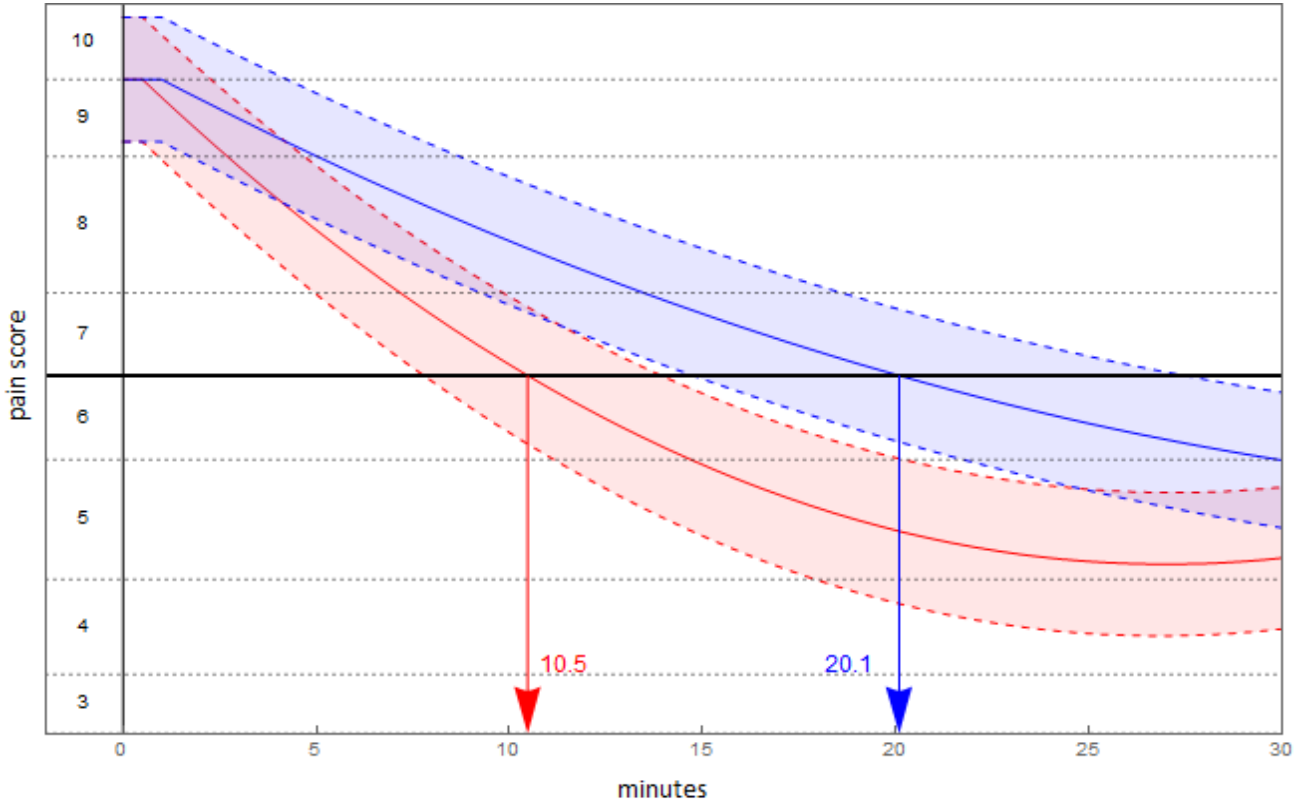
Predicted pain pathways: methoxyflurane (red) vs morphine IV (blue)

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

Murray D Smith, Elise Rowan, Robert Spaight, Niro Siriwardena.

CaHRU
Community and Health Research Unit

NHS
East Midlands Ambulance Service
NHS Trust



P<0.001
Penthrox n=406
IV Morphine n=802

5. Data on File. Galen Ltd.

Penthrox (Methoxyflurane) acts more than three times quicker than the most frequently used – and also inhaled – analgesic for trauma pain, Entonox, more than three times quicker than intravenous paracetamol and twice as quick as intravenous morphine to reduce trauma pain from severe to moderate pain levels.

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Impact of Penthrox on a Patients Journey through ED

Penthrox®
methoxyflurane
Just breathe

ST MARY'S SERVICE EVALUATION SUMMARY

Service evaluation of methoxyflurane versus standard care for overall management of adult patients with pain due to injury.[1] The aim was to assess the impact of Penthrox in adult patients with moderate to severe trauma pain in terms of patient length of stay in the Emergency Department (ED), compared to standard care*

71 MINUTES

Faster discharge

Penthrox patients **discharged** on average **71 minutes faster** than those treated with standard care*

HOW?

- May negate the need for procedural sedation
- May negate the need for a resus bed
- No opioid-related post-treatment monitoring is required
- May reduce the number of staff required

Penthrox may **save up to 50%** on the cost of treatment per patient depending on the type of trauma injury

PENTHROX has shown it can **reduce** the average **length of stay per patient** in the department:

- for **shoulder dislocations** over **3 hours**
- for **upper limb** injuries: over **1 hour**†
- for **pelvic, hip & femoral** injuries: over **1 hour**†

Authors concluded that **early use of Penthrox** can **positively impact length of stay** within the ED and **provide effective pain relief** for patients.

71 MINUTES

Faster discharge

Penthrox patients **discharged** on average **71 minutes faster** than those treated with standard care*

6. Young L et al. Adv Ther. 2020 May;37(5):2520-2527.

ASSOCIATION OF AMBULANCE CHIEF EXECUTIVES

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Delayed Hospital Handovers: Impact Assessment of Patient Harm

When very sick patients arrive at hospital and then have to wait an excessive time for handover to ED clinicians, to receive assessment and definitive care, it is entirely predictable and almost inevitable that some level of harm will arise. This may take the form of a deteriorating medical or physical condition, or distress and anxiety, potentially affecting the outcome for patients and definitely creating a poor patient experience. Any assumption that for the patient to wait on the ambulance, being cared for by ambulance clinicians, is acceptable because they are in a 'safe setting' is neither appropriate nor safe. Ambulance clinicians are not trained to care for patients for lengthy periods of time; the ambulance environment and available equipment are not designed for extended periods of patient care; and the ambulance and crew are needed to respond to other patients who have called 999.[1]

Working Together: Next Steps

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We believe that part of the solution is to **change one very small piece of the treatment pathway**, that is the choice of the first-line analgesic for the emergency relief of moderate to severe trauma pain.

How do we work with you to improve patient care across the emergency care environment through this simple change in analgesia?

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One company
One culture
One goal

ONE GALEN

50+
Years of experience

76
Current products

25
Locations worldwide

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References

1. Association of Ambulance Chief Executives. Delayed Hospital Handovers: Impact assessment of patient harm. [Accessed May 2022]. www.aace.org.uk

2. NHS. Ambulance Quality Indicators. [Assessed May 2022]. https://www.england.nhs.uk/statistics/statistical-work-areas/ambulance-quality-indicators/

3. NHS. Attendance and Emergency Admission Monthly Statistics, NHS and Independent Sector Organisations in England. https://www.england.nhs.uk/statistics/statistical-work-areas/ae-waiting-times-and-activity/

4. Nuffieldtrust. A&E Waiting Times. [Accessed May 2022]. https://www.nuffieldtrust.org.uk/resource/a-e-waiting-times

5. Data on File. Galen Ltd.

6. Young L et al. Adv Ther. 2020 May;37(5):2520-2527.

PENTHROX 99.9%, 3 ml inhalation vapour, liquid: Please refer to the Summary of Product Characteristics (SmPC) before prescribing. Abbreviated Prescribing Information.

Presentation: Each bottle of PENTHROX contains 3 ml of methoxyflurane 99.9%, a clear, almost colourless, volatile liquid, with a characteristic fruity odour. Each PENTHROX combination pack consists of one bottle of 3 ml PENTHROX, one PENTHROX Inhaler and one Activated Carbon (AC) chamber. **Indications:** Emergency relief of moderate to severe pain in conscious adult patients with trauma and associated pain. **Dosage and administration:** PENTHROX should be self-administered under supervision of a person trained in its administration, using the hand held PENTHROX Inhaler. It is inhaled through the custom-built PENTHROX inhaler. **Adults:** One bottle of 3 ml PENTHROX as a single dose, administered using the device provided. A second bottle should only be used where needed. The frequency at which PENTHROX can be safely used is not established. The following administration schedule is recommended: no more than 6 ml in a single day, administration on consecutive days is not recommended and the total dose to a patient in a week should not exceed 15 ml. Onset of pain relief is rapid and occurs after 6-10 inhalations. Patients are able to titrate the amount of PENTHROX inhaled and should be instructed to inhale intermittently to achieve adequate analgesia. Continuous inhalation of a bottle containing 3 ml provides analgesic relief for up to 25-30 minutes; intermittent inhalation may provide longer analgesic relief. Patients should be advised to use the lowest possible dose to achieve pain relief. *Renal impairment:* Methoxyflurane may cause renal failure if the recommended dose is exceeded. Caution should be exercised for patients diagnosed with clinical conditions that would pre-dispose to renal injury. *Hepatic impairment:* Cautious clinical judgement should be exercised when PENTHROX is to be used more frequently than on one occasion every 3 months. **Paediatric population:** PENTHROX should not be used in children and adolescents under 18 years. For detailed information on the method of administration refer to the SmPC. **Contraindications:** Use as an anaesthetic agent. Hypersensitivity to methoxyflurane, any fluorinated anaesthetic or to any of the excipients. Patients who are known to be or genetically susceptible to malignant hyperthermia. Patients or patients with a known family history of severe adverse reactions after being administered with inhaled anaesthetics. Patients who have a history of showing signs of liver damage after previous methoxyflurane use or halogenated hydrocarbon anaesthesia. Clinically significant renal impairment. Altered level of consciousness due to any cause including head injury, drugs or alcohol. Clinically evident cardiovascular instability. Clinically evident respiratory depression. **Warnings and Precautions:** To ensure the safe use of PENTHROX as an analgesic the lowest effective dose to control pain should be used and it should be used with caution in the elderly or other patients with known risk factors for renal disease, and in patients diagnosed with clinical conditions which may pre-dispose to renal injury. Methoxyflurane causes significant nephrotoxicity at high doses. Nephrotoxicity is thought to be associated with inorganic fluoride ions, a metabolic breakdown product. When administered as instructed for the analgesic indication, a single dose of 3 ml methoxyflurane produces serum levels of inorganic fluoride ions below 10 micromol/l. In the past when used as an anaesthetic agent, methoxyflurane at high doses caused significant nephrotoxicity, which was determined to occur at serum levels of inorganic fluoride ions greater than 40 micromol/l. Nephrotoxicity is also related to the rate of metabolism. Factors that increase the rate of metabolism such as drugs that induce hepatic enzymes can increase the risk of toxicity with methoxyflurane as well as sub-groups of people with genetic variations that may result in fast metaboliser status. Methoxyflurane is metabolised in the liver, therefore increased exposures in patients with hepatic impairment can cause toxicity. PENTHROX should be used with care in patients with underlying hepatic conditions or with risks for hepatic dysfunction. Previous exposure to halogenated hydrocarbon anaesthetics (including methoxyflurane when used as an anaesthetic agent), especially if the interval is less than 3 months, may increase the potential for hepatic injury. Potential effects on blood pressure and heart rate are known class-effects of high-dose methoxyflurane used in anaesthesia and other anaesthetics. Caution is required with use in the elderly due to possible reduction in blood pressure. Potential CNS effects such as sedation, euphoria, amnesia, ability to concentrate, altered sensorimotor co-ordination and change in mood are known class-effects. The possibility of CNS effects may be seen as a risk factor for potential abuse, however reports are very rare in post-marketing use. PENTHROX is not appropriate for providing relief of break-through pain/exacerbations in chronic pain conditions or for the relief of trauma related pain in closely repeated episodes for the same patient. PENTHROX contains the excipient, butylated hydroxytoluene (E321) which may cause local skin reactions (e.g. contact dermatitis), or irritation to the eyes and mucous membranes. To reduce occupational exposure to methoxyflurane, the PENTHROX Inhaler should always be used with the AC Chamber which adsorbs exhaled methoxyflurane. Multiple use of PENTHROX Inhaler without the AC Chamber creates additional risk. Elevation of liver enzymes, blood urea nitrogen and serum uric acid have been reported in exposed maternity ward staff when methoxyflurane was used in the past at the time of labour and delivery. **Interactions:** There are no reported drug interactions when used at the analgesic dosage (3 – 6 ml). Methoxyflurane is metabolised by the CYP 450 enzymes, particularly CYP 2E1, CYP 2B6 and to some extent CYP 2A6. It is possible that enzyme inducers (such as alcohol or isoniazid for CYP 2E1 and phenobarbital or rifampicin for CYP 2A6 and carbamazepine, efavirenz, rifampicin or nevirapine for CYP 2B6) which increase the rate of methoxyflurane metabolism might increase its potential toxicity and they should be avoided concomitantly with methoxyflurane. Concomitant use of methoxyflurane with medicines (e.g. contrast agents and some antibiotics) which are known to have a nephrotoxic effect should be avoided as there may be an additive effect on nephrotoxicity; tetracycline, gentamicin, colistin, polymyxin B and amphotericin B have known nephrotoxic potential. Sevoflurane anaesthesia should be avoided following methoxyflurane analgesia, as sevoflurane increases serum fluoride levels and methoxyflurane nephrotoxicity is associated with raised serum fluoride. Concomitant use of PENTHROX with CNS depressants, such as opioids, sedatives or hypnotics, general anaesthetics, phenothiazines, tranquillisers, skeletal muscle relaxants, sedating antihistamines and alcohol may produce additive depressant effects. If opioids are given concomitantly with PENTHROX, the patient should be observed closely. When methoxyflurane was used for anaesthesia at the higher doses of 40–60 ml, there were reports of drug interaction with hepatic enzyme inducers (e.g. barbiturates) increasing metabolism of methoxyflurane and resulting in a few reported cases of nephrotoxicity; reduction of renal blood flow and hence anticipated enhanced renal effect when used in combination with drugs (e.g. barbiturates) reducing cardiac output; and class effect on cardiac depression, which may be enhanced by other cardiac depressant drugs, e.g. intravenous practolol during cardiac surgery. **Fertility, pregnancy and lactation:** No clinical data on effects of methoxyflurane on fertility are available. Studies in animals have shown reproduction toxicity. As with all medicines care should be exercised when administered during pregnancy especially the first trimester. There is insufficient information on the excretion of methoxyflurane in human milk. Caution should be exercised when methoxyflurane is administered to a nursing mother**. Effects on ability to drive and use machines:** Methoxyflurane may have a minor influence on the ability to drive and use machines. Patients should be advised not to drive or operate machinery if they are feeling drowsy or dizzy. **Undesirable effects:** The common non-serious reactions are CNS type reactions such as dizziness and somnolence and are generally easily reversible. Serious dose-related nephrotoxicity has only been associated with methoxyflurane when used in large doses over prolonged periods during general anaesthesia. The following adverse drug reactions have either been observed in PENTHROX clinical trials in analgesia, with analgesic use of methoxyflurane following post-marketing experience or are linked to methoxyflurane use in analgesia found in post-marketing experience and in scientific literature (refer to the SmPC for further details): **Very common (≥1/10):** dizziness; **common (≥1/100 to <1/10):** headache, somnolence, dry mouth, nausea; **uncommon (≥1/1,000 to <1/100):** increased appetite, anxiety, depression, disturbance in attention, euphoric mood, inappropriate affect, verbigeration, amnesia, dysarthria, dysgeusia, paraesthesia, peripheral sensory neuropathy, diplopia, flushing, hypertension, hypotension, cough, oral discomfort, oral pruritis, salivary hypersecretion, vomiting, hyperhidrosis, fatigue, feeling abnormal, feeling drunk, chills, feeling of relaxation; **not known:** affect lability, agitation, confusional state, dissociation, restlessness, altered state of consciousness, nystagmus, vision blurred, choking, hypoxia, hepatic failure, hepatitis, jaundice, liver injury, renal failure, hepatic enzyme increased, blood urea increased, blood uric acid increased, blood creatinine increased. **Overdose:** Refer to SmPC. **Legal Category:** POM. **NHS Price:** £18.46. **Marketing Authorisation Holder:** Medical Developments UK Limited c/o Price Bailey LLP, Causeway House, 1 Dane Street, Bishop's Stortford, Herts, CM23 3BT, United Kingdom. **MA Number:** PL 42467/0001.Full prescribing information available from: Galen Limited, Seagoe Industrial Estate, Craigavon, BT63 5UA, United Kingdom. **Date of Preparation:** April 2022.

Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard. Adverse events should also be reported to Galen Limited on 028 3833 4974 and select the customer services option, or e-mail customer.services@galen-pharma.com. Medical information enquiries should also be directed to Galen Limited.