Health Services Safety Investigations Body

Investigation report

Unintentional overdose of morphine sulfate oral solution

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Theme:
Medication

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A note of acknowledgement to families

We would like to thank the family of Len, whose experience is documented in this report. We would also like to thank the healthcare staff who engaged with the investigation for their openness and willingness to support improvements in this area of care.

About Len

Len was aged 89 years and was a retired electronic engineer. He had been married for 65 years, and he and his Wife lived independently in their own home. Len's son and daughter, and their families, were very important to him and they played an active role in each other's lives. In earlier years Len was physically active enjoying swimming, cycling, walking and being a lifeguard. He kept busy doing DIY throughout his life.

About this report

This aim of this report is to help improve patient safety in relation to the use of oral morphine sulfate solution (a strong pain-relieving medication taken by mouth), and to demonstrate how a systems-based approach to investigation can be applied. It is intended to increase knowledge about how HSIB identifies patient safety risks for national investigations and to improve understanding of and engagement with HSIB investigations. For readers less familiar with this area of healthcare, medical terms are explained within the report.

Executive Summary

Background

The aim of this investigation report is to help improve patient safety in relation to the use of oral morphine sulfate solution (a strong pain-relieving medication taken by mouth). It also aims to demonstrate the systems-based approach that HSIB uses to identify matters for national investigation, via a scoping investigation into a patient safety incident (referred to here as the 'reference event').

The reference event concerned Len, who took an accidental overdose of morphine sulfate oral liquid. Len's family referred their concerns to HSIB to consider whether Len's care highlighted any national safety issues that could be addressed through an HSIB investigation.

The results of the scoping investigation did not meet the criteria for a national investigation. However, HSIB thought it would be beneficial to publish a shorter investigation report highlighting specific risks which may be associated with morphine sulfate oral liquid and to improve understanding of and engagement with HSIB investigations.

The reference event - December 2020

Len, who was 89 years old, fell at home and developed pain in the right side of his chest. Len had previously been diagnosed with Charcot-Marie-Tooth (CMT) disease, which is a progressive disease that affects the nervous system.

Len developed breathing problems so contacted his GP practice by telephone. The GP asked Len some questions about his symptoms and offered him a face-to-face appointment that afternoon. At that appointment, the GP ruled out a chest infection, prescribed additional ibuprofen and told Len to continue taking paracetamol.

Len's family later called an ambulance because Len was very breathless and in pain. Len was taken to the emergency department at his local hospital. He was assessed by medical staff who diagnosed a suspected rib fracture. He was given additional pain relief. However, after returning home Len found that the lidocaine pain relief patches he was given irritated his skin and he stopped using them.

Len's family noticed that over the next 2 weeks he became quieter and less active.

Len again contacted his GP with ongoing breathlessness and pain. The GP prescribed Len morphine sulfate oral solution, which has a concentration of 10mg in 5ml, at a dose of 1.25ml to 2.5ml (which equates to 2.5mg to 5mg per dose) to be taken up to every 4 hours when required. Len's Wife collected the morphine solution from the pharmacy for him and Len took three doses of 5ml (10mg) morphine (two to four times the suggested dose) over the course of the day. Len and his Wife thought that the 10mg in 5ml strength on the manufacturer's label on the morphine bottle showed the correct dose.

The next morning Len's Wife could not wake him and called an ambulance. Len was taken to the emergency department with breathing difficulties, thought to be caused by a suspected accidental overdose of morphine, pneumonia and worsening of his CMT. Len initially recovered after receiving treatment, but a short time later was found to be unresponsive and was pronounced dead.

After his death, Len's GP phoned the family to offer their condolences. It was only when the family asked why Len had been prescribed such a high dose of morphine that it became clear that Len and his Wife had not seen the dispensing label on the outer packaging advising Len to take 1.25ml to 2.5ml.

Findings

The key findings from the investigation include:

- The initial choice of paracetamol and ibuprofen to control Len's pain following his fall was in line with national guidance.
- Len's pain was not effectively controlled on paracetamol and ibuprofen, therefore required review by his GP to address this.
- The choice of a morphine liquid was in line with national guidance and a reduced morphine dose was prescribed in line with recommendations for the older person and Len's degree of kidney dysfunction.
- Len's dose of morphine was displayed on the dispensing label attached to the outer box that the morphine was provided in. The label was not seen by Len or his Wife.
- Len and his Wife read the manufacturer's text on the morphine bottle, which showed the strength of the morphine liquid, and understood this to be the required dose.
- When Len was taken to hospital with difficulty with breathing, he was found to have taken an accidental dose of morphine, he had a chest infection and his CMT may have impacted on his breathing.

HSIB makes the following safety observations

The intention of this safety observation is to ensure that prescribed oral morphine solution can be consistently taken in line with the prescribers directions.

Safety observation O/2022/165:

It may be beneficial if manufacturers of morphine oral solution 10mg in 5ml ensure that any dose measurement aid, if supplied with the medication, is able to measure a full range of possible doses.

The intention of this safety observation is to ensure that professional bodies and regulators highlight the importance to their membership of participating in HSIB safety investigations to ensure that all relevant leaning can be obtained.

Safety observation O/2022/166:

It may be beneficial if professional bodies provided guidance and further support to their members to maximise the learning that can be achieved from safety investigations that may improve patient care.

1 Background

The aim of this investigation report is to help improve patient safety in relation to the use of oral morphine sulfate solution (a strong pain-relieving medication taken by mouth). It also aims to demonstrate the systems-based approach that HSIB uses to identify matters for national investigation. This section provides background and context relating to the aspects of healthcare discussed in the scoping investigation.

1.1 Acute pain

1.1.1 Acute pain is usually related to an obvious injury such as a bone fracture or operation. Acute pain can range from mild to severe and usually gets better in days or weeks. Usually, treatment only needs to be given for a short time while the person's injury starts to heal.

1.1.2 In the UK, the National Institute for Health and Care Excellence (NICE) has published a clinical knowledge summary for mild-to-moderate pain (National Institute for Health and Care Excellence, 2020). This aims to provide primary care practitioners such as GPs with an easy-to-access summary of the current evidence base and practical guidance on best practice. For adults and children aged over 16 years, it recommends a stepwise approach for managing mild-to-moderate pain (**see figure 1**).

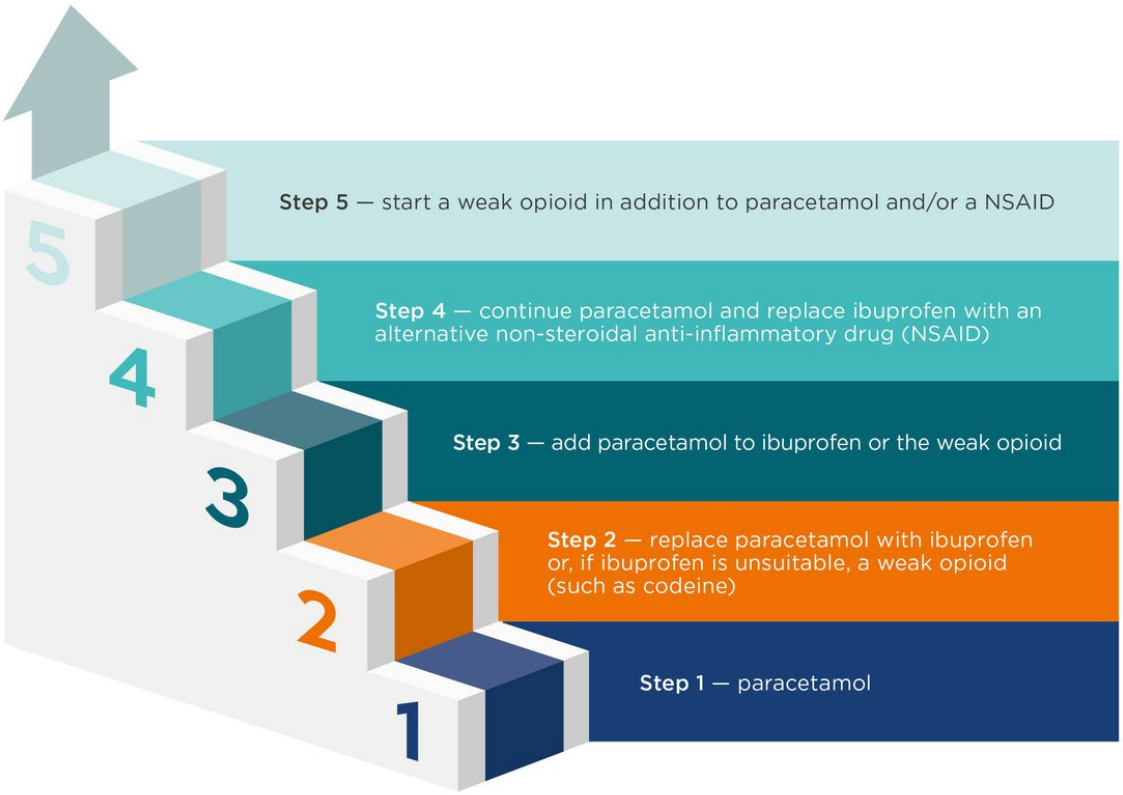

Figure 1 How to manage mild-to-moderate pain (National Institute for Health and Care Excellence, 2020)

1.2 Morphine

1.2.1 Morphine is a strong pain-relieving medication, one of a group of medications known as opioids. It is available only on prescription and comes in different forms, including a liquid. There are two different strengths of liquid morphine: a 10mg in 5ml oral (by mouth) solution and a 20mg in 1ml concentrate. If these two concentrations are mixed up there is a risk of a 10-times under or overdose. The prescribed dose of oral morphine varies from person to person. The dose will depend on how severe the person's pain is, how they have responded to previous pain-relieving medication and whether they are likely to have side effects. Usually, a person starts on a low dose of morphine and it is gradually increased until the pain is controlled (NHS, 2018).

1.2.2 The usual starting dose of morphine sulfate oral liquid for an adult with acute pain is 10mg, with the starting dose being 5mg for an older adult (Joint Formulary Committee, 2021). It is recommended that a lower dose of morphine is used:

- To start with in older adults as they are more at risk of opioid adverse effects. The dose can be slowly increased if needed.
- In people with reduced kidney function, because the opioid stays longer in the person's body as the kidney does not clear it as effectively and it can build up, causing unwanted effects.

1.2.3 Taking too much morphine can be dangerous. The amount of morphine that can lead to an overdose varies from person to person. Overdose can cause coma, respiratory depression (breathing difficulty or short, shallow breathing), and pinpoint (very small) pupils. This can be treated by giving the antidote, naloxone, and by supporting the person's breathing with artificial ventilation (Joint Formulary Committee, 2021). In serious cases the person may need emergency treatment in hospital (NHS, 2018).

1.2.4 Oral morphine sulfate liquid has been directly linked to the cause of death in 13 'prevention of future death reports' issued by coroners since 2013, the majority of which related to its use for treating chronic (long-term) pain. There are a variety of reasons given for this including people 'swigging' from the bottle rather than measuring the dose, people being supplied large quantities over a long period of time, illicit use, self-harm, interactions between the morphine and other prescribed and illicit medication, and a lack of documentation of who collected the supply (Wickaware, 2021; NHS South Region South West, 2016).

1.3 Charcot-Marie-Tooth disease (CMT)

1.3.1 CMT is the most common inherited neurological condition in the world. It is estimated to affect 1 in 2,500 people (Saporta and Shy, 2013). It is a progressive disease that affects the nerves controlling the muscles that move a person's arms and legs, such as the muscles of the feet, hands and forearms. It can also cause numbness or loss of feeling. Rarely, a person's diaphragm can also become affected, leading to breathing difficulties (Muscular Dystrophy UK, 2015).

1.3.2 There is currently no specific treatment for CMT. Measures that can help people to manage living with CMT include physiotherapy, occupational therapy, orthotics (shoe or heel inserts), mobility aids, orthopaedic surgery, and pain management (Muscular Dystrophy UK, 2015).

1.4 Medicines packaging and labelling

1.4.3 The safe use of any medication relies on users reading the labelling and packaging carefully and accurately and being able to assimilate and act on the information provided (Medicines and Healthcare products Regulatory Agency, 2014).

1.4.4 The Human Medicines Regulations 2012 set out the legislative requirements for the packaging and labelling of medication (The Human Medicines Regulations 2012). These requirements are regulated by the Medicines and Healthcare products Regulatory Agency (MHRA) in the UK. Post-Brexit, the Human Medicines Regulations 2012 are being updated to specifically address the needs of the UK public.

1.4.5 Guidance is available to support medication manufacturers to ensure that the product labelling and package leaflet is accessible to, and understood by, the user (Medicines and Healthcare products Regulatory Agency, 2020; European Commission, 2009).

1.5 Labelling of dispensed medication

1.5.1 Dispensing is the process of preparing and issuing medication to a named person in response to a prescription. This involves the correct interpretation of the wishes of the prescriber and the accurate preparation and labelling of medication for use by the person.

1.5.2 People may come to harm if they cannot easily identify their medication, how to use it safely and effectively, or are not aware of any special precautions needed. Legislation sets out the information that must be included on a label applied to dispensed medication. Professional guidance recommends additional information that should be included on the label (Royal Pharmaceutical Society, 2021; National Institute for Health and Care Excellence, n.d.).

1.5.3 The National Patient Safety Agency has produced guidance on better design that healthcare professionals could apply to the dispensing process in order to improve patient safety. It provides detailed information to improve the readability of labels and positioning of the dispensing label, and aids to help people access their medication more easily (National Patient Safety Agency, 2007).

2 The reference event

The scoping investigation explored a patient safety incident, known as the ‘reference event’, which was referred to HSIB by Len’s family. The incident related to the care Len received from his general practitioner (GP), community pharmacy and an acute hospital Trust following a fall at home. Len was prescribed morphine sulfate oral solution for his pain and went on to take an accidental overdose of this medication.

2.1 Len's medical background

2.1.1 Len was 89 years old. Prior to a fall, Len was able to walk indoors with the help of a walking stick and could manage the stairs at home. He was independent with all activities of daily living, including driving his car and going for walks outside with his Wife's support.

2.1.2 Len had been diagnosed with Charcot-Marie-Tooth disease (CMT) in 2007. Len's family reported that his CMT had always affected his feet, causing ankle instability and issues with his balance and gait, which got worse as he got older. In 2010, Len had been referred to the respiratory service as he was short of breath and was found to have mild problems with his diaphragm.

2.2 Len's care

2.2.1 A summary timeline of Len's care leading up to the reference event is set out in figure 2.

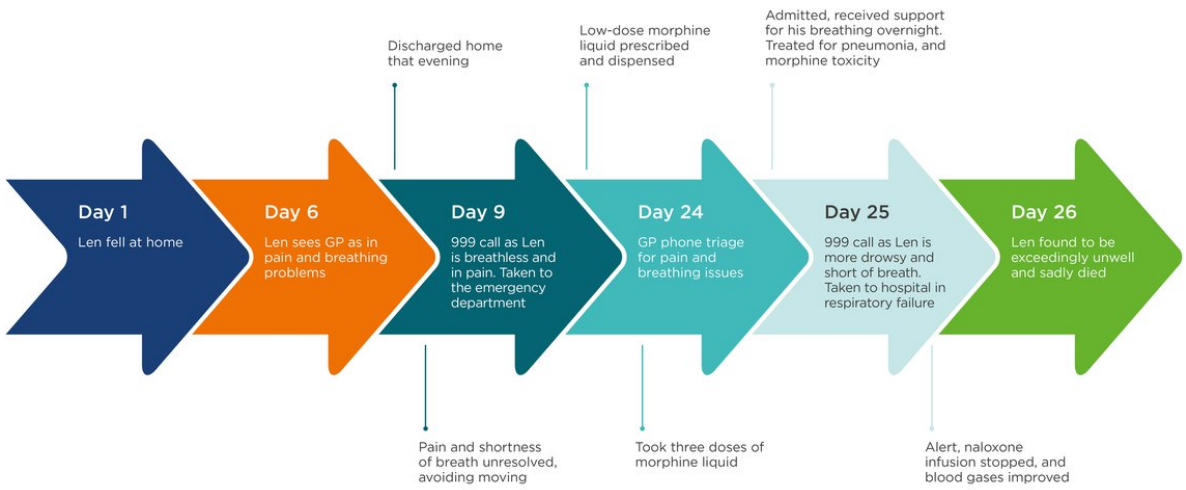

Figure 2 Summary timeline of Len's care in 2021

2.2.2 On day 1, while at home Len got up suddenly and fell forward onto his arm and sustained injuries to his chest and his face. Following this fall, Len developed pain in the right side of his chest which radiated towards the left side of his chest.

2.2.3 On day 6, in the morning Len called his GP practice and spoke with his GP about his ongoing pain and breathing problems. The GP carried out a telephone triage and assessed that Len needed an 'in person' review and made an appointment to see him that afternoon.

2.2.4 The GP's notes from his consultation that afternoon state that Len was tender on the front of the left side of his chest, and he had slightly shallow breathing (that is, he was only breathing with the top part of his lungs). On examination, Len's chest was clear, and his temperature was within the expected range at 36.5C. This indicated to the GP that Len did not have any infection causing his breathing problems.

2.2.5 The GP documented that he discussed pain relief with Len and noted that Len had an intolerance to some forms of pain relief: tramadol and codeine. The GP prescribed ibuprofen by mouth 400mg three times a day for 2 weeks and omeprazole while taking the ibuprofen. Omeprazole helps to protect a person's stomach from complications while they are taking ibuprofen. The GP advised Len:

- to take paracetamol and ibuprofen
- to call back if the pain got worse or he became short of breath
- to practise deep breathing every few minutes, to help prevent him getting a chest infection.

2.2.6 On day 9, Len was breathless and his family described that 'he was unable to get more than 3 words out in a sentence'. He spoke with his daughter-in-law on the telephone. She dialled 999 and paramedics arrived at Len's house 10 minutes after the 999 call was made. They found him in pain, short of breath at rest and having difficulty breathing. He was taken by ambulance to the emergency department (ED) at his local hospital.

2.2.7 In the ED, blood tests were carried out and a chest X-ray performed. There was no sign of infection or a rib fracture on Len's chest X-ray. The treatment plan was to optimise Len's pain relief. He was started on a lidocaine patch (a type of local anaesthetic plaster that works by causing a temporary loss of feeling in the area where the patch is applied) to be applied for 12 hours each day to manage his pain. He was advised to take ibuprofen regularly and given breathing exercises to do each day.

2.2.8 A discharge letter that was sent to Len's GP stated that his diagnosis was a suspected right-side rib facture and Len was advised to:

- take regular ibuprofen and paracetamol
- do breathing exercises
- use lidocaine patches to manage the pain
- make a GP appointment as a follow-up.

2.2.9 That evening Len's pain and breathing problems continued. When he spoke with his family on the telephone, he was still struggling to get his words out. The lidocaine patch was irritating Len's skin, so he stopped using them. Over the next 2 weeks Len remained at home but was not his 'usual self'. He avoided moving and spent a lot of time sitting and falling asleep. He was uncomfortable and had intermittent problems with his breathing.

2.2.10 On day 24, Len's family told the investigation that he reported still feeling out of breath. He had a telephone triage consultation with his GP who documented that Len was 'finding deep inspiration [taking a breath] still very painful'.

2.2.11 The GP documented that Len was to try a low dose of oral (taken by mouth) morphine solution to control his pain. Len was prescribed morphine sulfate 10mg in 5ml oral solution at a dose of 1.25ml to 2.5ml (2.5mg to 5mg) to be taken up to every 4 hours when required.

2.2.12 Len's Wife collected his morphine sulfate oral solution from the community pharmacy. The morphine was supplied in a 300ml glass bottle with a child-resistant lid. The bottle came in an outer cardboard box, as shown in figures 3 and 4. The box also contained a 5ml oral syringe.

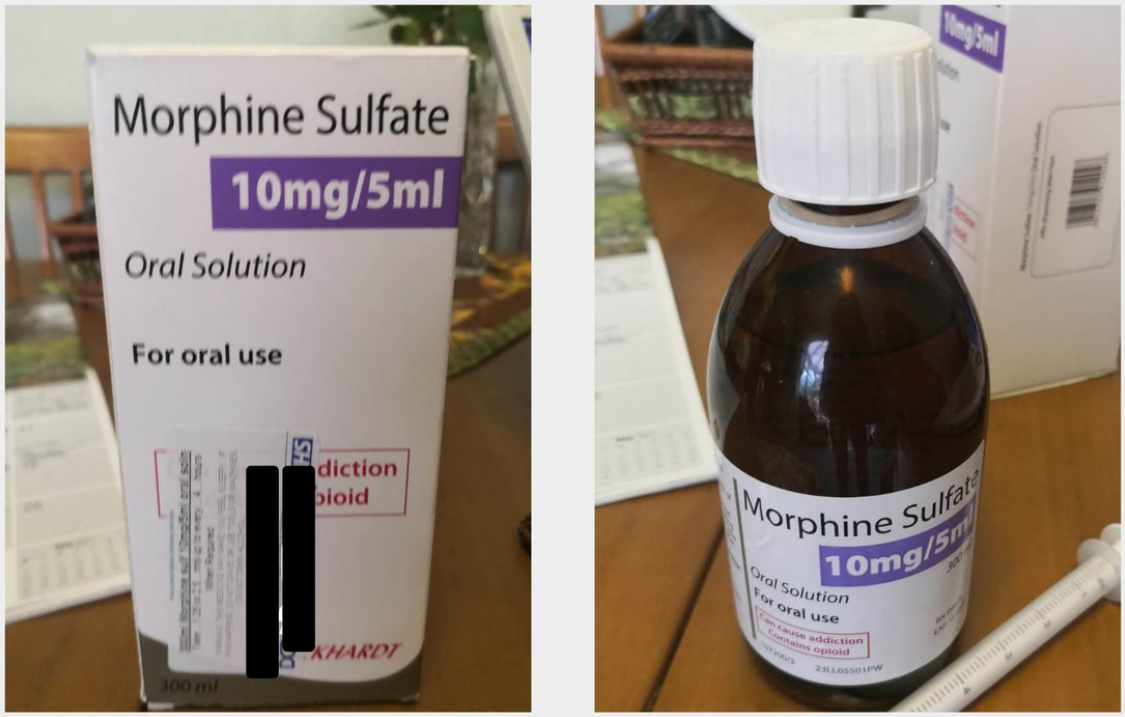

Figure 3 Morphine sulfate liquid bottle packaging and labelling

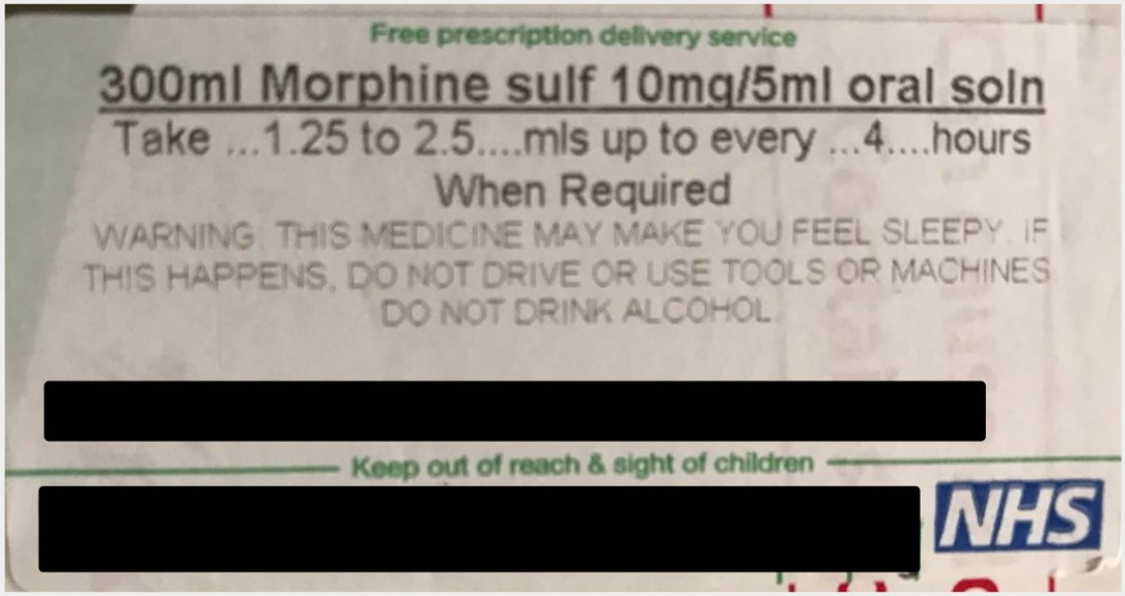

Figure 4 Close-up of dispensing label on the outer box

2.2.13 When Len's Wife got home, she and Len read the patient information leaflet provided with the morphine liquid together. Len took a 5ml (10mg) dose at 14:00 hours and another at 18:00 hours. This was between two and four times the dose he had been prescribed.

2.2.14 Len's son telephoned that evening to check on him. When they heard that he had been prescribed morphine, his daughter-in-law was concerned and advised Len not to take any more. His daughter-in-law was an advanced nurse practitioner and was concerned that the morphine could further impact on Len's breathing or cause a further reaction, due to his extreme sensitivity to codeine. She was not aware of the dose he had taken or the dose prescribed. Len decided to take one more dose at 22:00 hours and was going to follow up with the GP the next day.

2.2.15 On day 25, Len's Wife woke up and said good morning to Len, but he did not answer. She thought Len was in a deep sleep and left him in bed while she went to the kitchen. She returned to check on him when he did not appear for breakfast and realised that he had not moved. She tried to speak to Len but was unable to wake him. She was not sure what to do, so sought advice from a neighbour and they called 999. An ambulance was dispatched and arrived 9 minutes later.

2.2.16 The paramedics recorded that Len looked tired, was drowsy and mildly confused, but was ‘still able to interact and answer questions’. Len was severely short of breath; he was given treatment to help him breathe and was started on oxygen.

2.2.17 Len was taken to his local hospital’s ED. He was triaged and an electrocardiogram (ECG – to check his heart rhythm), chest X-ray, monitoring (including temperature, respiratory rate, heart rate, blood pressure, oxygen saturation (the level of oxygen in a patient’s blood)) and blood tests were all completed.

2.2.18 Len’s blood test results showed that he was not able to take in enough oxygen to breathe. When this happens, a patient is described as being in respiratory failure. The ED doctors discussed Len’s care with a specialty respiratory doctor, who also sought advice from a more senior respiratory consultant. They identified several possible causes for Len’s deterioration; these included:

- the morphine liquid taken the day before
- his chest wall injury (suspected rib fracture)
- chest infection
- worsening of problems with Len’s breathing potentially associated with his CMT
- a combination of these.

2.2.19 Len received a range of treatment for these potential issues, including:

- support with his breathing via a special face mask
- antibiotics for possible pneumonia (swelling inflammation of the tissue in one or both lungs, usually caused by a bacterial infection)
- naloxone to block the effects of the morphine liquid Len had taken
- intravenous fluids to ensure that he was hydrated and to keep his kidneys working.

2.2.20 A planned computerised tomography (CT) scan was undertaken to help understand why Len was having difficulty breathing. He was noted to be less alert so was given more naloxone to reverse any effects that morphine was having on his level of consciousness. This was reported in Len’s medical notes as having ‘no real effect’.

2.2.21 Len was then reviewed by the specialty respiratory doctor. Len’s CT report showed evidence of pneumonia and the doctor confirmed that Len had been prescribed and received antibiotics The plan was to continue to support Len’s breathing, start a naloxone infusion and transfer him to a specialist respiratory ward.

2.2.22 That evening, Len was transferred to the respiratory ward. The doctors noted that he was ‘deeply asleep but stable’. He continued to be closely observed with regular bloods tests taken and reviewed by a senior doctor.

2.2.23 Overnight, Len was reported to be ‘more alert, comfortable [and] not in pain’. He was confused but able to drink tea and water, and had passed urine. Staff were able to reduce the support for Len’s breathing.

2.2.24 On day 26, Len was alert, eating and drinking. The naloxone infusion was stopped, and his respiratory support was further reduced.

2.2.25 That morning Len was reviewed by the medical team. He reported feeling better than he had overnight but could not recall how he ended up in hospital. Antibiotics were continued for his pneumonia and Len remained on intravenous fluids. Plans were made to start getting Len ‘up and about’ and to plan for his discharge.

2.2.26 At 18:00 hours Len was noted to be alert, comfortable and pain free.

2.2.27 Later that evening, a central monitor on the ward alarmed to signal that Len had a low heart rate. A nurse responded and found Len unconscious. They put out a call to ask the emergency resuscitation response team to attend the ward immediately. When Len was assessed by the emergency team, he showed no signs of life. Len was given further naloxone, but this did not have any effect. Sadly, Len was pronounced dead. The main causes given on Len’s death certificate were respiratory failure, pneumonia and CMT.

2.2.28 On day 27, the GP telephoned the family to offer his condolences. It was only when the family asked the GP why Len was prescribed such a high dose of morphine sulfate liquid that Len’s Wife noticed the dispensing label on the outer morphine box with Len’s prescribed dose printed on it.

3 Investigation process and methodology

This section outlines the timeline of the referral of Len’s care to HSIB and the scoping investigation. It includes the methods and evidence used in the investigation process to determine whether factors identified in Len’s care met the criteria for an HSIB national investigation. It also describes the criteria HSIB used to decide whether to go ahead with the investigation.

3.1 Notification of the reference event

3.1.1 Len's family notified HSIB of their concerns in June 2021 using HSIB's online form 'submitting a patient safety concern'. The scoping investigation was completed between September 2021 and January 2022.

3.1.2 A summary timeline of the HSIB referral and scoping investigation process is set out in figure 5.

Figure 5 Summary timeline of how HSIB processed Len's referral

3.2 The scoping investigation

3.2.1 The referral from Len's family was discussed at an HSIB internal governance meeting in September 2021 and a decision was made to go ahead with a scoping investigation.

3.2.2 Based on the information available to HSIB at that time, it was considered that the referral may highlight a patient safety risk concerning the safety measures in place to prevent death from unintentional overdose following the prescribing, dispensing and self-administration of oral morphine liquid in the community. The start of the investigation was delayed because of the ongoing effect of the COVID-19 pandemic on NHS services and HSIB processes.

3.2.3 The scoping investigation set out to collect and analyse evidence relating to potential lines of enquiry identified from Len's family's online referral form letter to HSIB and initial information collected by HSIB. The lines of enquiry are shown in table 1.

Table 1 Issues to be explored by the scoping investigation

Potential lines of enquiry
Prescribing morphine liquid to Len
Risks associated with remote GP consultation
Prescribing morphine liquid without a face-to-face appointment
The size of the writing on the prescription label
Packaging and labelling related to dosage and warning instructions provided
Large font displaying the strength of the oral morphine solution on the bottle
Supplying 300mls of oral morphine liquid to Len
Inability to open the child-resistant lid
Safety-netting advice (advice given to patients) around morphine toxicity, signs and symptoms of concern
Whether the naloxone infusion was stopped too soon to treat morphine liquid overdose
Implication of oral morphine solution 10mg in 5ml being a Schedule 5 controlled drug, rather than the tighter controls of a Schedule 2 for other forms of morphine

Controlled drugs are those medications that are subject to higher levels of regulation as a result of government decisions that they are harmful when misused. The Misuse of Drugs Regulations 2001 sets out who can supply and possess controlled drugs and the activities needed to prevent their misuse. The regulations divide controlled drugs into five ‘Schedules’, with Schedule 1 being the most harmful and Schedule 5 the least harmful (The Misuse of Drugs Regulations 2001).

3.2.4 The investigation team collated and reviewed evidence from Len’s family, information from the Trust and GP involved in Len’s care, and conversations with clinical staff. This included:

- Len’s GP and hospital medical records
- interviews with Len’s Wife, son, daughter, and daughter-in-law
- an interview with the respiratory consultant who cared for Len during his admission to hospital with respiratory failure
- an interview with the Trust’s chief pharmacist.

3.2.5 The investigation contacted Len’s GP practice. The practice informed HSIB that because of the pressures it was facing due to COVID-19, it was unable to engage with the scoping investigation at that time. HSIB did receive detailed documentation of the GP’s interactions with Len.

3.2.6 The community pharmacy declined to participate in the scoping investigation. The investigation tried to engage with the pharmacy on a number of occasions by email, telephone, and recorded post. The investigation also spoke with local commissioners and NHS England and NHS Improvement national pharmacy teams to identify whether any further support could be offered to assist in engaging with the pharmacy. Despite this, the investigation was unable to obtain engagement from the pharmacy and so was unable to complete investigation work that may have assisted in fully considering the patient safety risks presented in Len's care.

3.2.7 The investigation engaged with a GP subject matter advisor to gain an insight into morphine liquid prescribing in primary care.

3.2.8 The investigation gathered and reviewed local and national guidance on acute pain management, rib fracture, the packaging and labelling of dispensed medication, opioid prescribing, and opioid toxicity (the symptoms of too much morphine).

3.2.9 The findings from the scoping investigation were assessed against the lines of enquiry (see 4.4.1) and were found not to meet the criteria for a HSIB national investigation:

Outcome impact – what was, or is, the impact of the safety issue on people and services across the healthcare system?

Len's case highlights a range of complex local factors that do not represent national safety risks. In the context of Len's other health concerns, the investigation cannot determine whether or to what extent an accidental overdose of morphine liquid contributed to Len's death. The scoping investigation did not identify any evidence to suggest that the use of oral liquid morphine for acute pain had been identified to have a negative impact on patients across the healthcare system.

Systemic risk – how widespread and how common a safety issue is this across the healthcare system?

The scoping investigation found no evidence that the circumstances of Len's care were replicated at a national level. Key concerns highlighted by coroners' reports and engagement with NHS staff about oral liquid morphine related to its use in chronic pain and its illegal use, not the acute pain experienced by Len.

Learning potential – what is the potential for an HSIB investigation to lead to positive changes and improvements to patient safety across the healthcare system?

The investigation did not identify national factors that could lead to significant learning from Len's care surrounding oral morphine liquid prescribing. Issues surrounding chronic opioid use is one of the national medicines safety improvement workstreams being run by NHS England and NHS Improvement (NHS, n.d.). The potential for improvements in medicines packaging, design and labelling were limited in the context of the specific circumstances of Len's care.

3.3 Investigation method

3.3.1 HSIB adopts a no-blame approach to all investigations and aims to understand the healthcare system in its entirety, for example the equipment, physical space, tasks, human capabilities and organisational culture, to establish the factors most likely to have contributed to adverse outcomes in patient care. This section outlines how this current investigation was undertaken.

3.3.2 The investigation adopted the Systems Engineering Initiative for Patient Safety (SEIPS) to understand the system-wide factors and interactions involved in Len's care. SEIPS was first described by Carayon and colleagues (2006) as a framework for understanding the structures, processes and outcomes in healthcare and the relationships between them. It is a systems engineering approach with human factors principles embedded within it. Figure 6 provides a representation of SEIPS (Holden et al, 2013).

3.3.3 SEIPS describes how components of the work system produce work processes that result in different outcomes. Work system factors are described below (Holden et al, 2013; Carayon et al, 2006):

- People: the people working in the particular system, the patient and their family.
- Tasks: undertaken by people, and which can vary in complexity or variety.
- Equipment: used to undertake the tasks, and which can vary in usability and functionality.
- Internal environment: the physical space around people (for example, layout, noise and temperature).
- Organisation: conditions external to people to support the organisation of, for example, resources and activity.
- External environment: factors outside of the healthcare institution, such as policy, societal or economic factors.

Processes can be physical, cognitive or behavioural, and lead to outcomes for patients, professionals or healthcare institutions. Interactions between the various components of the work system leads to different outcomes, both positive and negative. The framework includes feedback loops, which represent the adjustments systems make over time

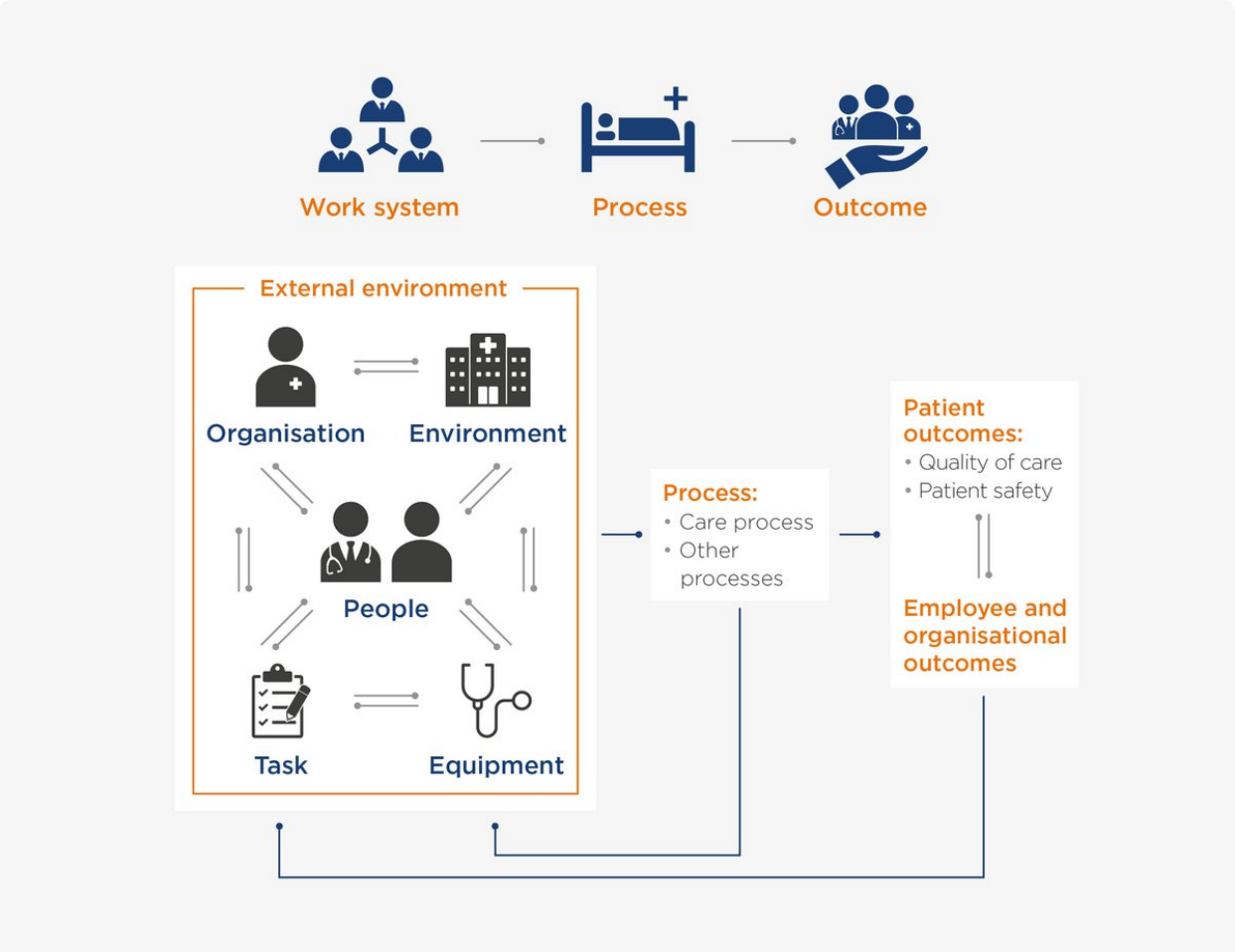

Figure 6 A representation of the SEIPS framework

3.3.4 The scoping investigation adopted an iterative approach; as further information was gained additional interviews or data sources were identified. Data was then coded using the themes in the SEIPS framework to understand the interactions within the work system and factors that contributed to Len's care.

4 Analysis and findings from the scoping investigation

Len had a number of contacts with the healthcare system during his treatment following his fall. The investigation focuses on the prescribing, dispensing and self-administration of morphine liquid for acute pain management in the community setting, and the treatment of morphine toxicity (the symptoms of too much morphine) arising from this. The different work systems (see 3.3.3) are described in turn, specifically the:

- GP consultation
- dispensing and self-administration of morphine liquid

- treatment of morphine toxicity.

4.1 GP consultation

4.1.1 The scoping investigation explored the interactions between Len and the GP on the day that the morphine oral solution was prescribed. It also accounted for the context of these interactions following Len's earlier GP appointment and emergency department (ED) attendance. A summary of these interactions is set out in figure 7.

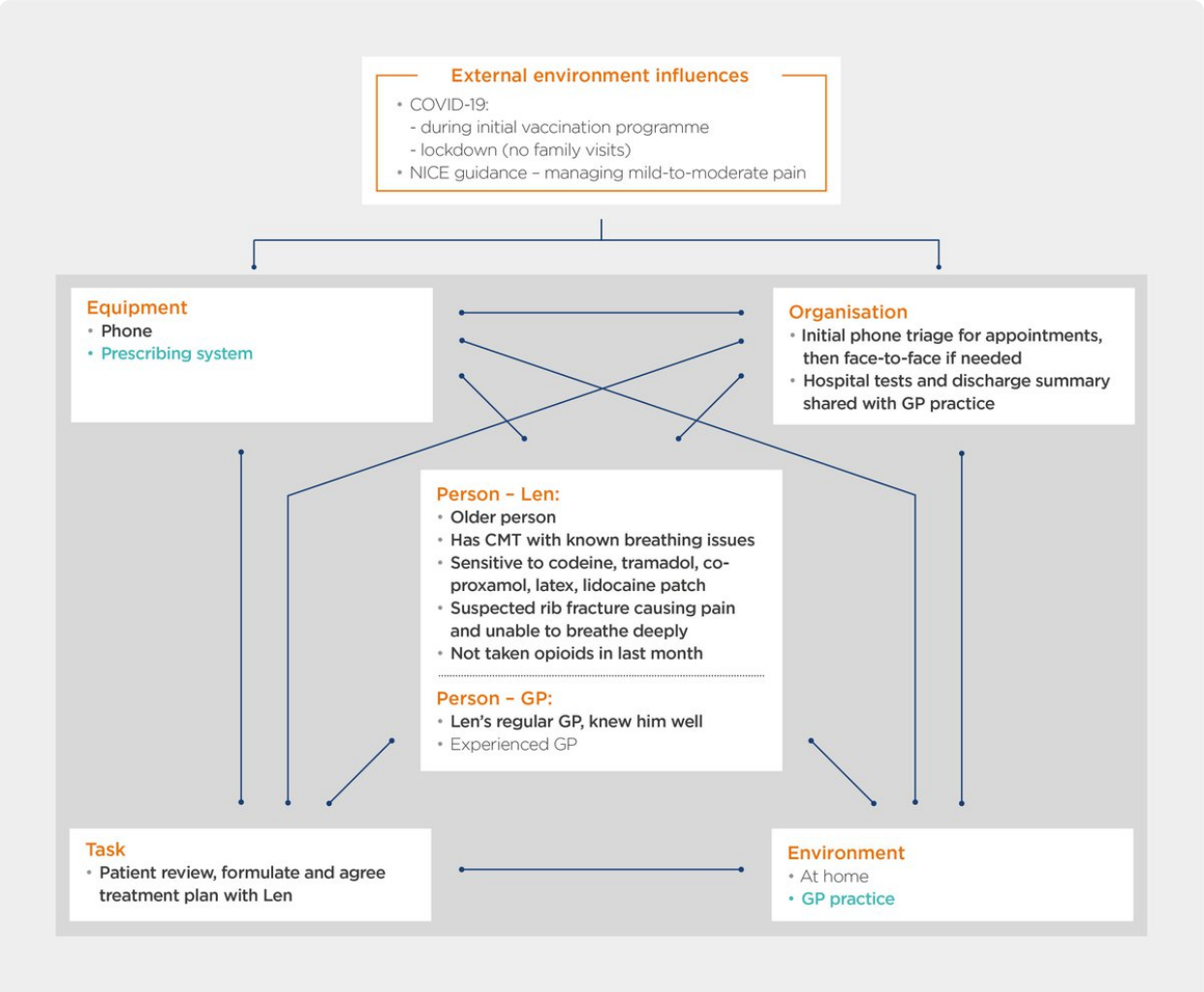

Figure 7 Management of primary care GP consultation: work system interactions (Key: bold dark grey is a key issue, bold light teal unable to explore)

4.1.2 Each time Len contacted the GP practice after his fall he spoke with his own GP, who knew Len well as he had treated him for many years.

4.1.3 Because of the COVID-19 pandemic the GP practice had moved to a system of telephone triage for patients requesting an appointment. The GP would then assess whether it was appropriate to talk to the patient on the telephone or see them face-to-face.

4.1.4 When Len spoke with the GP on day 26 the GP had seen Len in person 18 days earlier and had the clinical investigation findings and discharge summary from Len's ED visit 15 days earlier.

4.1.5 Len had been at home since he was discharged from hospital on day 9. At that time the country was in a COVID-19 lockdown. Therefore, there was a need to avoid any unnecessary contact with vulnerable people such as Len. The GP had to balance the risks associated with COVID-19 against the appropriateness of carrying out the consultation over the telephone.

4.1.6 The medical notes show that the GP documented that Len had no fever, cough, or productive sputum (he was not coughing up mucus). When combined with the 'normal' chest X-ray from the ED, the records show that the GP ruled out a chest infection as the cause of Len's symptoms. As the investigation was unable to engage with Len's GP, it instead engaged with a GP subject matter advisor to understand this decision-making process and seek their opinion based on the care Len received. The GP subject matter advisor explained that, given the context, the telephone consultation and exclusion of a chest infection appeared reasonable.

4.1.7 The records demonstrated that the GP understood Len may still be in pain from his suspected rib fracture. He noted that Len was taking paracetamol and ibuprofen but was allergic to the lidocaine patch that had been started after his visit to the ED. In adults, codeine, dihydrocodeine, or tramadol (different types of opioid medication) are recommended for treating mild-to-moderate pain where paracetamol alone or combined with a non-steroidal anti-inflammatory drug (NSAID) (such as ibuprofen) has failed (National Institute for Health and Care Excellence, 2020).

4.1.8 It was important to adequately manage Len's pain so that he could breathe deeply and do the breathing exercises that he had been advised after his suspected rib fracture diagnosis. This is because shallow breathing can increase a person's chance of developing a chest infection. When Len spoke with the GP on day 24, he was still in pain, not breathing deeply and avoiding movement.

4.1.9 The records showed that the GP documented the nature of Len's intolerance to codeine and tramadol. They decided to try a low dose of morphine oral liquid as an alternative, noting that if Len were to experience side effects from the morphine 'then [this] should wash out relatively quickly'. This was in line with NICE guidance (see 1.1.2) and the stepped approach to pain management.

4.1.10 The GP was also aware of Len's Charcot-Marie-Tooth (CMT) disease, having documented it in the records for this consultation.

4.1.11 Len was not known to have any airway disease that meant morphine should be avoided and Len was prescribed a dose of 1.25ml to 2.5ml (2.5mg to 5mg) in line with the suggested individualised prescribing, factoring in Len's age, pain, reduced kidney function and that he had not taken any opioids in the last month. The GP subject matter advisor confirmed to the investigation that this appeared to be a reasonable approach to take.

4.1.12 The GP prescription required Len to receive 300ml of oral liquid morphine, prescribed at a dose of 1.25ml to 2.5ml up to every 4 hours as required. This volume would last Len between 20 and 40 days. The investigation was told that an opioid may be needed to treat the pain from a rib fracture for a period of weeks. If Len were to need to take the morphine every 4 hours at the doses prescribed, then 300ml was an appropriate volume to ensure Len could continue to take morphine without having to visit his GP again while his suspected rib fracture healed.

4.1.13 As the investigation was not able to interview the GP, the only information available about the consultation was the detail recorded in Len's medical notes. It is not known what advice Len was given about how to take the morphine, what to do if he experienced side effects and whether he was warned about the signs of taking too high a dose. However, the investigation did find that Len and his Wife were able to read the information leaflet contained within the dispensed morphine oral solution which also contains information about potential side effects and overdose (see 1.2.3). This was confirmed by Len's Wife who explained that she had handwritten the times that Len could take a dose of morphine on the information leaflet.

4.2 Dispensing and administration of morphine liquid

4.2.1 The section explores the interaction between Len, his family members and the community pharmacy. As noted in section 3 the investigation was not able to engage with the community pharmacy. Those aspects of the community pharmacy work system that it was possible to explore are described here, and summarised in figure 8.

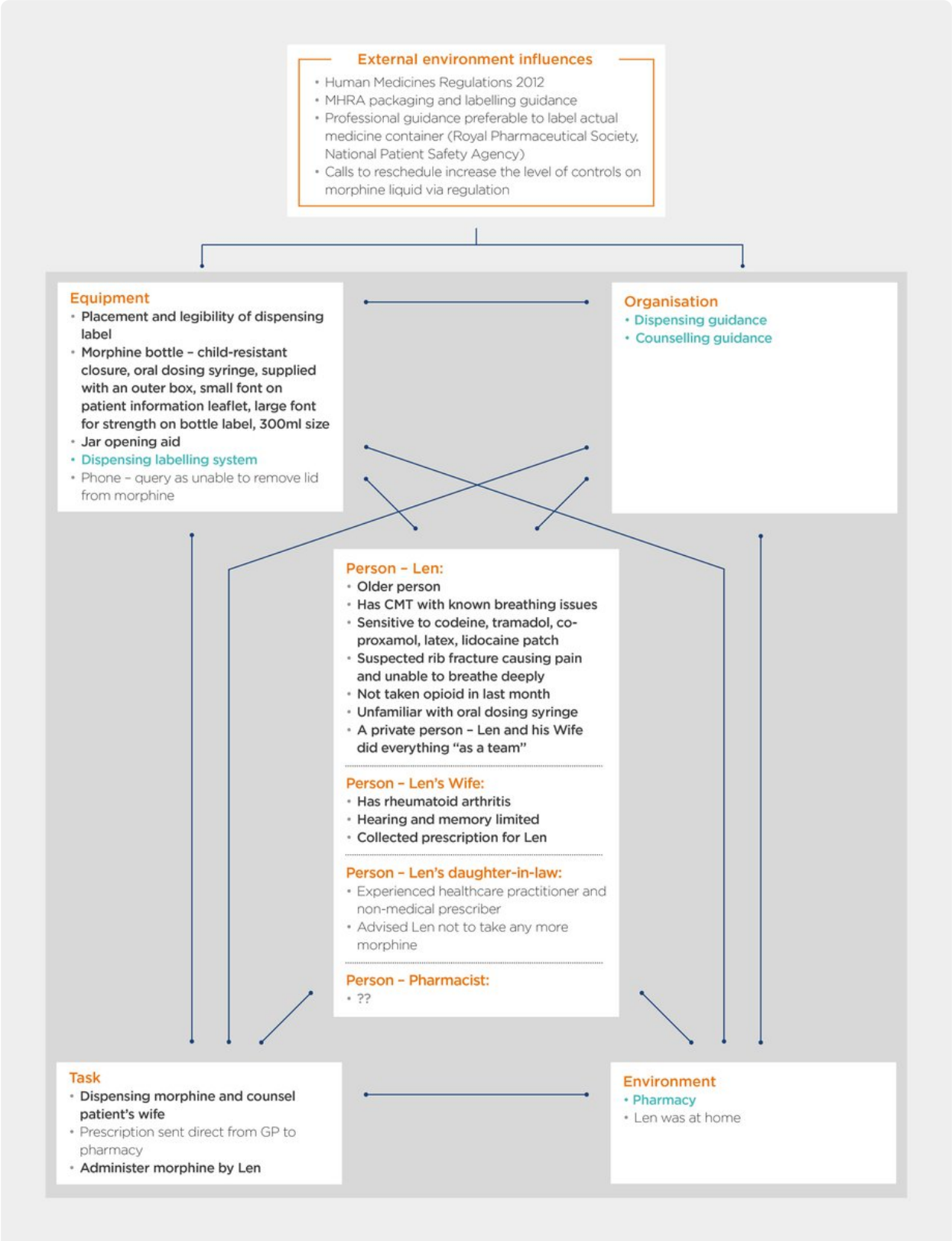

Figure 8 Management of dispensing and administration: work system interactions (Key: bold dark grey is a key issue, bold light teal unable to explore)

4.2.2 The investigation has been unable to speak with the community pharmacy. It is therefore not known whether the staff involved would have remembered this specific event. Handing out prescriptions is a frequent and routine activity, and the event occurred some months before the investigation began. However, it would have been possible to learn how this task is usually done which could have given further insight into how Len's prescription may have been issued. The intention of this safety observation is to ensure that professional bodies and regulators highlight the importance to their membership of participating in HSIB safety investigations to ensure that all relevant leaning can be obtained.

HSIB makes the following safety observations

Safety observation O/2022/166:

It may be beneficial if professional bodies provided guidance and further support to their members to maximise the learning that can be achieved from safety investigations that may improve patient care.

4.2.3 Len's Wife collected the morphine from the community pharmacy for him. The investigation is aware of factors that may have affected whether any advice given could be heard or recalled by Len's Wife when she collected the morphine. Len's Wife was recovering from surgery on her ears for an existing hearing problem and had some known memory problems. When taken together with the passage of time since she collected the prescription, the investigation cannot be certain whether any advice given could have been heard, and if it was heard, whether Len's Wife now remembers it.

4.2.4 The morphine liquid was dispensed and labelled by the community pharmacy in line with the GP prescription. The dispensing label was placed vertically on the outer box that contained the morphine bottle (see figure 3). There was no dispensing label on the morphine bottle itself. Inside the box was a patient information leaflet and a graduated 5ml oral syringe (see figure 9); these are provided by the medication manufacturer.

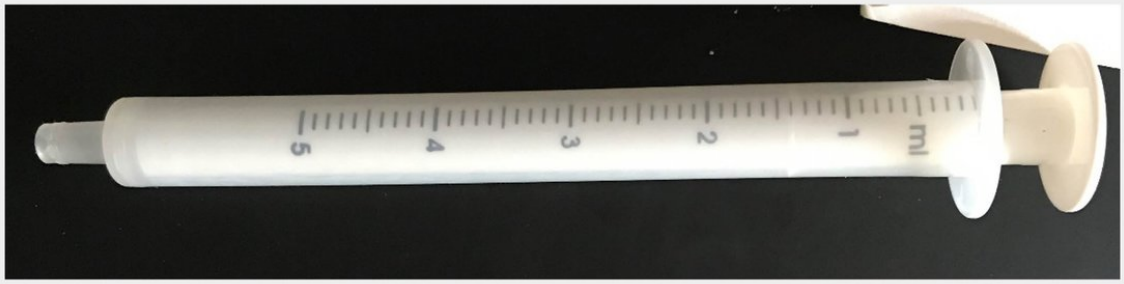

Figure 9 Graduated oral syringe supplied in the box with the morphine liquid by the manufacturer

4.2.5 Len and his Wife were unaware that the prescription label with the dose was on the box. They read the patient information leaflet provided and Len's Wife wrote down the times that Len could take a dose at the top of the leaflet.

4.2.6 The family told the investigation that Len and his Wife saw '10mg/5ml' in large bold font on the morphine bottle which they believed was the dose Len was supposed to take (see figure 10). They also saw the 5ml oral syringe which confirmed in their minds that the dose was 5ml. Len took this 5ml dose, which was two to four times higher than the prescribed dose of 1.25ml (2.5mg) to 2.5ml (5mg), on three occasions.

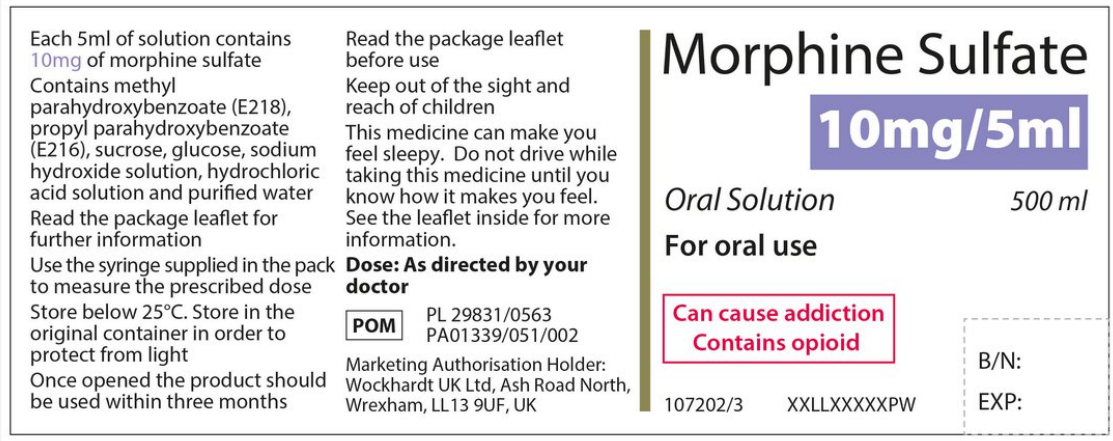

Figure 10 Manufacturer’s label on the morphine sulfate liquid bottle

4.2.7 The prescription Len received was for morphine 10mg in 5ml strength. The large bold font on the label of the morphine liquid bottle is intended to distinguish between the two different concentrations of morphine liquid available (see 1.2.1). This is in line with medication labelling legislation (The Human Medicines Regulations 2012), best-practice guidance (Medicines and Healthcare products Regulatory Agency, 2020) and the design for patient safety guidance on medication packaging and labelling (National Patient Safety Agency and Helen Hamlyn Research Centre, 2007).

The manufacturer’s label on the morphine bottle directs patients to ‘Use the syringe supplied in the pack to measure the prescribed dose’ (see figure 10). The oral syringe provided by the manufacturer in the box with the morphine sulfate was able to measure up to 5ml of liquid. The standard oral morphine solution starting dose is 10mg (5ml) for an adult, or 5mg (2.5ml) for an older person (Joint Formulary Committee, 2021). The syringe enables these doses to be measured. However, if a lower dose was required, for example, for an older person with mild kidney dysfunction as in Len’s case, the 1.25ml (2.5mg) dose could not be accurately measured. The syringe markings did indicate 1.2ml and 1.3ml measurements. The intention of this safety observation is to ensure that prescribed oral morphine solution can be consistently taken in line with the prescribers directions.

HSIB makes the following safety observation

Safety observation O/2022/165:

It may be beneficial if manufacturers of morphine oral solution 10mg in 5ml ensure that any dose measurement aid, if supplied with the medication, is able to measure a full range of possible doses.

4.2.8 Len and his Wife had limited manual dexterity and were unable to remove the child-resistant lid from the morphine bottle. The investigation heard that Len called the community pharmacy to ask how to open the bottle and was given instructions about to use the child resistant lid. However, they were still unable to open the bottle. The investigation was told that Len did manage to remove the lid with a kitchen jar opening aid. When the child-resistant lid was eventually removed, the plastic stopper fitted in the top of the medication bottle, also came out with the lid. This plastic stopper has a hole in the middle, to insert the syringe in, and allow you to invert the bottle to draw up the medication. Len and his Wife were left with an open bottle which they found difficult to place the syringe in and draw up the morphine.

Where medication is manufactured with a child-resistant lid, this can be changed to a non-child-resistant lid by the pharmacist, if the pharmacist is aware that this is a concern (Royal Pharmaceutical Society, 2021). The investigation noted that people with certain illnesses including arthritis and CMT, as well as many older adults, may struggle to open a child-resistant lid. Once Len had removed the lid, he was able to self-administer the morphine.

4.2.9 In Len's case, the prescription label, which had the dosing information on it, was placed on the outer box containing the bottle of morphine sulfate. This is in line with current legal requirements (Royal Pharmaceutical Society, 2021). However, the Royal Pharmaceutical Society notes that it may also be helpful to follow the National Patient Safety Agency (NPSA) labelling for dispensed medication recommendations (National Patient Safety Agency, 2007). These recommendations highlight the issue that if the outer container was to be discarded then the information on the label would also be lost. In the reference event, the dispensing label provided on the box, its vertical orientation and where it was applied also does not fully comply with the information in these recommendations.

4.2.10 The investigation found that it was difficult to find the NPSA recommendations online and they were no longer available on any NHS websites. The investigation noted that there had been significant changes to the healthcare landscape since publication of 'Design for patient safety: a guide to the design of dispensed medicines' (National Patient Safety Agency, 2007). These changes include the widespread use of tamper-evident seals on outer medication

packaging and the introduction of automated pharmacy dispensing which affects where the dispensing label can be placed. The investigation was unable to explore this further with the community pharmacy involved in the reference event.

4.2.11 The investigation also noted that neither Len nor his Wife noticed the dispensing label. This means that any issues relating to the readability of the label due to its design, font or size were not a contributory factor in Len's accidental overdose.

4.2.12 When Len's daughter-in-law heard that Len had been prescribed morphine, she was concerned about this decision. The family told the investigation that Len and his Wife "just didn't know what to do". Len's Wife told the investigation about the conflicting advice they faced and the difficult decision of whether to follow their daughter-in-law's advice, or that of Len's longstanding GP, whom Len "liked and trusted". Len decided to take one more dose of morphine and follow it up with the GP surgery the next day.

4.3 Management of morphine toxicity

4.3.1 This section explores the interactions between Len and the care provided by the ambulance service and acute hospital to manage his respiratory depression (problems with slow and ineffective breathing). A summary of these interactions is set out in figure 11.

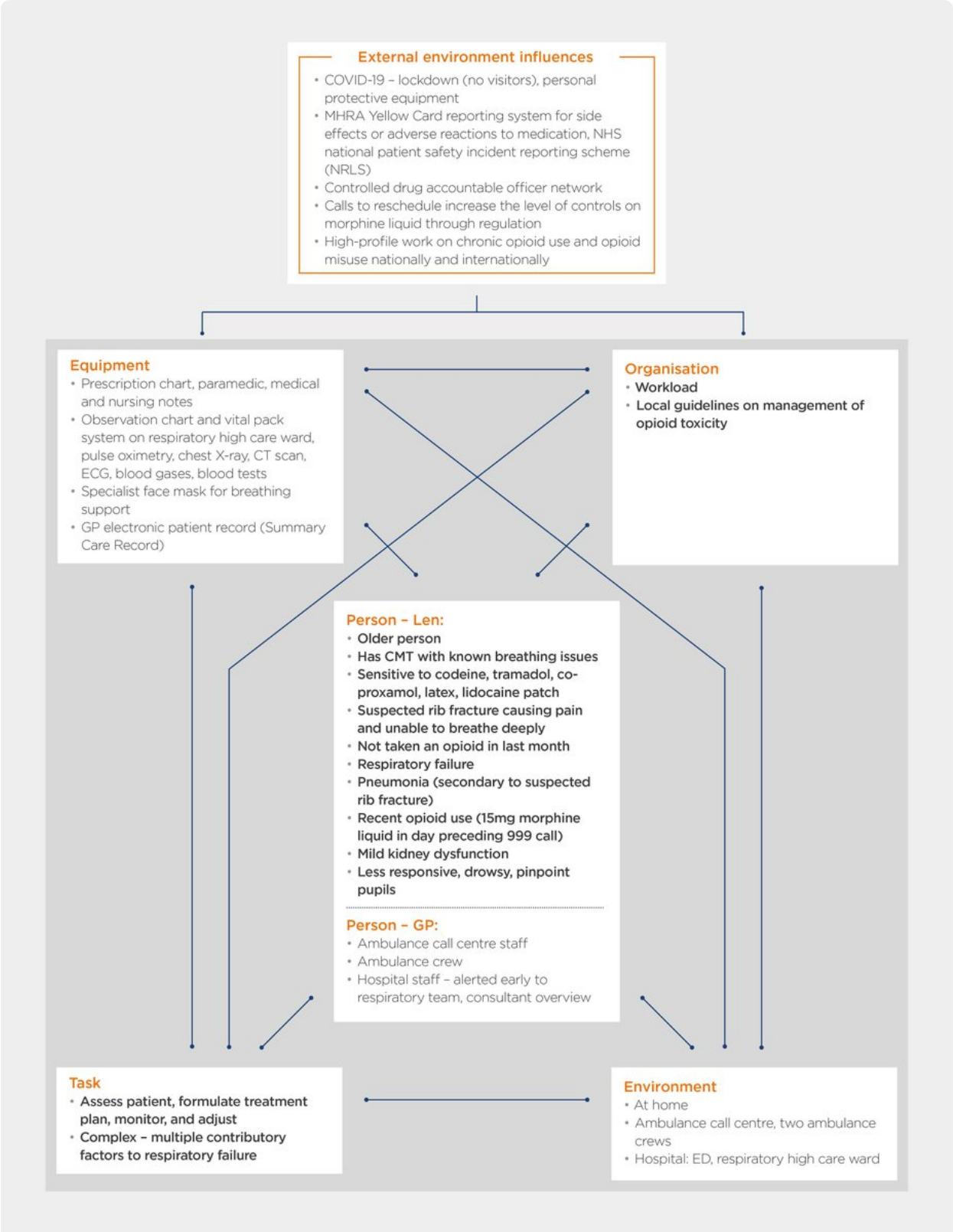

Figure 11 Management of morphine toxicity: work system interactions (Key: bold dark grey is a key issue)

4.3.2 Len was diagnosed with pneumonia when he was admitted to hospital. The investigation was told by staff that they understood Len had a suspected rib fracture and that the pneumonia may have occurred as a result.

4.3.3 When someone has a rib fracture, they may breathe shallowly and avoid coughing to avoid pain. The pain may prevent the person from breathing normally or clearing secretions from their lungs, leading to respiratory failure. Sufficient pain relief is needed not only to manage the pain but also to allow movement and coughing to clear respiratory secretions. Rib fracture increases the risk of pneumonia in all age groups, but older adults are at higher risk than younger adults (Quigley and Wheeler, 2021).

4.3.4 The investigation was unable to confirm whether Len was able to follow the advice he had been given about breathing exercises. However, the investigation heard that his mobility declined after his fall and especially just before his second admission to hospital.

4.3.5 The role that the morphine liquid played in Len's respiratory failure is not clear. On day 25 he had pinpoint (very small) pupils, was drowsy, had a reduced level of consciousness and breathing difficulties. These are known opioid side effects. However, when naloxone (the antidote to morphine) was given intravenously, it is documented that this produced a 'transient' (short-lived) improvement the first time it was given and 'no real improvement' when it was tried again later.

4.3.6 If Len's respiratory depression had been caused by the morphine liquid, the naloxone should have improved his respiration and level of consciousness. The Trust told the investigation that Len's respiratory failure was instead thought to be primarily due to issues arising from pneumonia and his CMT, but with the possibility that opioid toxicity could have contributed to his respiratory issues. Len's family told the investigation they did not believe CMT was a factor that contributed to Len's death.

4.3.7 The family reported being told by a doctor that Len had woken from his morphine-induced sleep and that he had been very unwell, due to his respiratory collapse as a result of the morphine.

4.3.8 Len also had mild kidney dysfunction which was slightly worse when he was admitted to hospital. As morphine is cleared from the body by the kidneys, and Len had mild kidney dysfunction, the morphine that he had taken earlier would remain in his body for longer. Naloxone has a short duration of effect, so to ensure that the morphine still in Len's body did not affect his breathing, it needed to be given by a continuous intravenous infusion (administered directly into his vein over a long time). This is in line with the Trust's guidelines on management of opioid toxicity. There was a delay between the decision to start the naloxone

infusion and when it was started. However, this did not affect Len's breathing as he was being supported with oxygen via a special face mask at this time and his oxygen saturation (the level of oxygen in his blood) was within the expected range.

4.3.9 The investigation explored whether it would have been appropriate to submit a 'Yellow Card' report. The Yellow Card scheme is a voluntary reporting scheme that is available for healthcare professionals, patients, carers, or members of the public (Medicines and Healthcare products Regulatory Agency, 2022). Through this scheme, anyone can report an adverse reaction to a medication, be it mild or severe. This includes suspected adverse drug reactions associated with an overdose of medication. It is always useful for the MHRA to obtain safety information about medication that has been in use for a long time and perceived to be 'well recognised', to ensure that patient information is kept up to date. The investigation was told by the Trust that a Yellow Card report should have been submitted in Len's case. However, it had not happened. The investigation was told that when staff were under great pressure Yellow Card reports did not always get submitted and that side effects related to respiratory issues from morphine sulfate were already recognised.

4.3.10 A previous HSIB investigation, 'Placement of nasogastric tubes' (Healthcare Safety Investigation Branch, 2020), explored how information on suspected medication safety concerns are collected and monitored.

4.4 Summary and conclusion

4.4.1 The scoping investigation considered the investigation's findings in light of the potential lines of enquiry identified from Len's family's online referral to HSIB and the initial information that was collected. The scoping investigation found that these potential lines of enquiry for a national investigation were not supported by factors identified during this episode of Len's care. This is set out below in table 2.

Table 2 Findings from the scoping investigation for the initial lines of enquiry

Potential lines of enquiry	Outcome from the scoping investigation
Prescribing morphine to Len	The prescription was appropriate accounting for Len's symptoms, medical history and known medication intolerance.
Risks associated with remote GP consultation	Len had been seen in person by his GP and in the ED prior to his remote consultation. All contact was with his regular GP.
Prescribing morphine without a face-to-face appointment	The GP excluded a chest infection and had previous clinical information from Len's prior GP and ED visit. Len was in pain and needed pain relief.
Writing size on the prescription label	The size of writing on the label was not a contributory factor in Len's care, as Len and his Wife did not notice the label before Len took his

Potential lines of enquiry	Outcome from the scoping investigation
	medication. The font size appeared to be in line with any relevant guidance.
Packaging and labelling related to dosage and warning instructions provided	Professional guidance is that it is preferable to label the actual medication rather than the packaging, but this is not a legal requirement. This guidance was drafted before widespread changes to dispensing practice and associated legal requirements. With no engagement from the community pharmacy to understand working practices the investigation was not able to pursue this line of enquiry further.
Large font displaying the strength of the oral morphine solution on the bottle	The large font is used to prevent confusion between the 10mg in 5ml oral solution and 20mg in 1ml concentrate. Manufacturers are recommended to differentiate between different strengths of the same medicine through typeface, type weight, colour and shape to avoid unintentional overdose.
Supplying 300ml of oral morphine to Len	Rib fractures may take 8 weeks or more to heal. The 300ml prescription was intended to last 30 days if the maximum prescribed dose of 2.5mg was taken regularly every 4 hours. This was not a contributory factor in Len's care as he only took three doses of medication.
Inability to open the child-resistant lid	This is not a contributory factor in Len's care as the family were able to open the bottle with assistance. With no engagement from the community pharmacy to understand working practices the investigation was not able to find out whether it could have changed the packaging to a non-child-resistant lid.
Safety-netting advice around morphine toxicity, and signs and symptoms of concern	The medication information, which sets out safety-netting advice, was available with the medication. With no engagement from the community pharmacy, an inability to engage with the GP practice, and Len's Wife's known hearing and memory problems, the investigation was not able to pursue this line of enquiry further.
Whether the naloxone infusion was stopped too soon to treat morphine overdose	The Trust guidelines were in line with national recommendations. These were followed and Len remained alert following the naloxone infusion being given.
Implication of oral morphine liquid 10mg in 5ml being a Schedule 5 controlled drug, rather than Schedule 2 controlled drug	These concerns relate to issues raised in coroners' prevention of future death notices primarily in relation to large quantities of oral morphine being provided for chronic use. This is not relevant to Len's care. The investigation was unable to engage with the community pharmacy to understand any impact this may have had on Len's care.

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