



London Ambulance Service
NHS Trust

Private & Confidential

Ms Melanie Sarah Lee
His Majesty's Coroner
Inner North London

London Ambulance Service
Chief Executive Office
Headquarters
220 Waterloo Road
London
SE1 8SD

22 December 2023

www.londonambulance.nhs.uk

Your Reference: Ann Newbury (deceased) / Inquest date 10th November 2023

Dear Madam

Thank you for the Prevention of Future Deaths report issued on the 13th November 2023 to the London Ambulance Service NHS Trust in relation to our attendance to Frances Ann Newbury on the 20th May 2023. We note that the PFD report raises concern in relation to naloxone administration in cardiac arrest. I would like to firstly like to extend my deepest sympathies on behalf of London Ambulance Service NHS Trust to Ms Newbury's family and friends on their tragic loss.

I am aware that London Ambulance Service NHS Trust received a query raised in relation to the administration of naloxone on the 8th November 2023 (two days prior to the listed Inquest date). I would like to apologise that we were not able to provide a response ahead of the inquest and we recognise that this may have assisted your investigation and provided an overview of expected practice.

In order to inform this response, we have undertaken a detailed clinical review of the care provided. This has involved a Learning from Death review which identified that, whilst it is recognised that Ms Newbury had a history of drug abuse, the attending clinicians were advised that Ms Newbury had taken [REDACTED] at around 2100 the previous evening. There was no overt direct indication that Ms Newbury had taken opioids immediately preceding her death.

Whilst it is recognised that Ms Newbury had a long term history of opioid use, naloxone was not considered at the time of the cardiac arrest as there was no immediate history of opioid use and a clinically feasible cause of the arrest was identified, which was a current infection. The resuscitation attempt focused on high quality chest compressions and effective ventilation. It was recognised by the clinicians that naloxone would not have reversed the effects of [REDACTED]. The information reported to the clinicians at the time of attendance was that Ms Newbury had taken [REDACTED] the previous evening.

Where a patient takes an 'overdose' of opioids the mode of cardiac arrest is one where there is depression of the central respiratory drive, leading to reduced respirations (breathing) which results in cerebral hypoxia (decreased oxygen within the brain tissue). Opioids exert their analgesic effects predominately through agonist binding at μ receptors in the brain and spinal cord. This produces the analgesic and euphoric effects often seen in patients who have taken an opioid. Where opioids have been taken in excessive amount, the result can cause respiratory depression and impair sensitivity to hypoxaemia (low oxygen in blood)

/hypercarbia (increased levels of carbon dioxide) through mechanisms involving μ and GABA-A (γ -aminobutyric acid A) receptors.

Asphyxia (deprivation of oxygen), through the respiratory depression (reduction in an individual's breathing), develops and this leads to further cerebral hypoxia. Ultimately it is the hypoxia/hypercarbia which cause a diminishing cardiac output and may finally sadly result in a patient's cardiac arrest. Where a patient is in cardiac arrest, there is immediate and ongoing artificial ventilation in an attempt to correct any ventilatory failure. Naloxone is a competitive antagonist (receptor site blocker) for the opioid and its administration aims to diminish the effects of the opioid, however, once a patient is in cardiac arrest (as opposed to respiratory arrest) the focus should be on high quality standard life support including artificial ventilation, chest compressions and adrenaline administration.

Where a patient presents in cardiac arrest, the key aim is to attempt to restart the heart through artificial ventilation and chest compressions. Whilst it is recognised that naloxone has formed part of the resuscitation process for a number of years where opioid use is suspected, there are no randomised studies looking at the efficacy of naloxone in opioid-induced cardiac arrests nor evidence that naloxone will reverse cardiac arrest. It is highlighted that there are some reasonable concerns that by using naloxone this may detract clinicians from ensuring the most effective chest compressions are delivered. In essence it is the hypoxic/hypercarbic insult which has caused the cardiac arrest and naloxone will not facilitate the heart restarting.

The 2015 American Heart Association Guidance details:

- It may be reasonable to administer intramuscular or intranasal naloxone based on the possibility that the patient is not in cardiac arrest.
- Standard resuscitative measures should take priority over naloxone administration, with a focus on high-quality Cardio Pulmonary Resuscitation (CPR chest compressions plus ventilation).
- We can make no recommendation regarding the administration of naloxone in confirmed opioid-associated cardiac arrest. Patients with opioid-associated cardiac arrest are managed in accordance with standard Advanced Cardiovascular Life Support (ACLS) practices.

In the case of Ms Newbury, the ambulance clinicians were absolutely confident that she was in established cardiac arrest and that her cardiac arrest was unwitnessed. No clear timeframe of the arrest was able to be established and she was promptly identified to be in asystolic (absence of heart beat and electrical activity) arrest.

The International Liaison Committee on Resuscitation (ILCOR) advised

“We did not identify any studies reporting any critical or important outcomes of adults or children with suspected opioid-associated cardio / respiratory arrest in any setting, comparing bystander naloxone administration (intramuscular or intranasal) plus conventional CPR, to conventional CPR only.”

A recent extensive review conducted on behalf of the American Heart Association published in 2021 concluded¹

“If the patient is definitely pulseless and receiving standard resuscitation, including assisted ventilation, naloxone is unlikely to be beneficial. Because there is a theoretical basis for harm, standard resuscitation alone is indicated. Opioid antagonism to prevent Opioid Associated (OA) -Out of Hospital Cardiac Arrest in patients with OA central nervous system and respiratory depression is always reasonable and should be delivered along with CPR when it is uncertain whether the patient is pulseless.”

Overall the evidence base suggests that where cardiac arrest is established and confirmed from opioid use, naloxone has limited efficacy in reversing the cardiac arrest. The Joint Royal Colleges Ambulance Liaison Committee (JRCALC) Clinical Practice Guidance advise the use of naloxone in cardiac arrest, noting that this has been unchanged and more recently the empirical reviews of the clinical evidence have been undertaken. I have asked that our Consultant Paramedics and Associate Clinical Directors who both are members of the JRCALC resuscitation group, request that a review is undertaken of JRCALC current guidance in light of the emerging clinical evidence, in respect of opioids.

We do recognise that there may be some ‘novel’ synthetic opioids where the opioid in itself may cause a more marked direct myocardial depression than heroin and in these cases there may be an increased clinical need to consider naloxone in such arrest, although these agents are not usually drugs of recreational use or abuse and are very uncommon. In this area there is limited evidence upon which to base any recommendation.

We would not be critical of a decision to administer naloxone in cardiac arrest as long as this does not distract from the essential, evidence based, aspects of life support which includes high quality chest compressions and artificial ventilation. Equally where an informed clinical decision is made that the patient is in established cardiac arrest we would not be critical of a decision to focus on effective resuscitation. In this case there was no clear indication of opioid use immediately prior to the collapse, and Ms Newbury was in established cardiac arrest. On balance, we are not of the view that naloxone was mandated and believe this would not have changed the outcome.

That said, the LAS is absolutely of the view that naloxone should be administered where a patient presents with respiratory depression and/or is peri (near) arrest, in this instance it is recognised to be lifesaving and we absolutely support its administration. In March 2022, the London Ambulance Service initiated the availability of high concentration naloxone on specialist resources utilised by the Trust. This was in recognition of the potential for highly potent synthetic opioids where stronger doses of naloxone may be required. We are also highly supportive of naloxone in community programs, for those where there is a high risk of overdose.

Whilst we recognise that this did not prevent the sad outcome in this case, we hope this assists in providing assurance that as a Trust we have taken a robust review of naloxone administration in this case and the wider use of naloxone in established cardiac arrest.

We would be very happy to discuss and present the work the LAS is doing to improve cardiac arrest survival in London. This includes a London wide programme to increase early bystander life support as well as

¹ Dezfulian C, Orkin AM, Maron BA, et al. Opioid-Associated Out-of-Hospital Cardiac Arrest: Distinctive Clinical Features and Implications for Health Care and Public Responses: A Scientific Statement from the American Heart Association. *Circulation*. 2021;143(16):e836-e870. doi:10.1161/CIR.0000000000000958

increasing the accessibility to public access defibrillators and trained responders and we are working with our agencies who have regular contact with opioid users around utility of naloxone to be available to others.

If you would like to take up this offer please contact [REDACTED] Consultant Paramedic, who leads for the Trust on resuscitation [REDACTED]

Yours faithfully

[REDACTED]

[REDACTED]

Chief Executive Officer