STANDARDISING INTRAVENOUS INFUSION CONCENTRATIONS FOR CHILDREN IN THE UK

A Proposal for a National Approach

From the Neonatal & Paediatric Pharmacists Group

STRATEGIC SUMMARY

The time for the NHS to standardise paediatric intravenous (IV) infusions is now. Policy and practice drivers are all in alignment, and the future of NHS procurement, technology and safety demand an urgent change from the standard weight-based approach to standard concentrations which are proven to be safer and more efficient for patient care.

The proposed framework is not complete, but offers the first list of published standard IV infusion concentrations in the UK. It will also support strategic efficiencies and support the development of “smart pump” drug libraries, the uptake and implementation of electronic prescribing, and the future development of licensed formulations.

The importance of pushing this forward now cannot be understated. A great deal of work has already been undertaken in this field but there is a risk that there will be duplication of effort by people distal to the frontline if we do not make our case today.

BACKGROUND

Intravenous medications for children and young people are primarily prescribed and administered on a bespoke weight-based basis using complex and highly variable approaches. A recent survey study in the UK identified over 150 discrete methods for preparation of infusions across multiple paediatric and neonatal care settings. (Oskarsdottir, Harris, Sutherland, Wignell, & Christiansen, 2018)

This variation adversely effects systems safety, and has been implicated in serious medication errors.(Keers, Williams, Cooke, & Ashcroft, 2013; National Patient Safety Agency, 2011) Furthermore it is inefficient, unreliable and complicated, leading to unseen patient safety risks. It has been demonstrated that bespoke weight-based preparation of infusions is unsafe with many infusions prepared incorrectly – in some cases with two-fold variations in concentration of prepared versus intended. (Aguado-Lorenzo et al., 2013; Parshuram et al., 2003; Wheeler et al., 2008) These deviations are regardless of the operator or amount of experience. Thus they are not amenable to person-centric interventions such as re-training as they are related to natural variation in perception and manipulation. (Parshuram et al., 2008)

The move to “standardised solutions” is one part of an approach to IV medication safety internationally, with demonstrable improvements in safety and service efficiency that comes with provision of ready-to-administer preparations. (Howlett, Breatnach, Brereton, & Cleary, 2020; Lehmann et al., 2006; Manrique-Rodríguez et al., 2013; Perkins, Aguado-Lorenzo, & Arenas-Lopez, 2016) By moving to pre-prepared solutions, nursing time used in IV preparation may be reduced by up to 60% releasing more time for care.(Sutherland et al., 2016)

These clear advantages in process efficiency have been taken fully on board by the Department of Health and Social Care with their plans for the reorganisation and transformation of NHS Aseptic Services in England.(Lord Carter of Coles, 2020) This plans to increase capacity and re-orientate NHS manufacturing capacity towards high-resource, high risk practices in order to make patients safer and improve care efficiency by reducing the burden of preparation on nurses. Primarily this will involve the mass manufacture of intravenous medications for patients in licensed manufacturing facilities and later in collaboration with private sector capacity. Standardisation of products, processes and training is a keystone element of this policy, and a UK-wide approach is required, with similar capacity reviews completed or being planned in the other UK home countries.

Without a national approach to standardisation, there is a risk that there will be variation at local or regional levels in the concentrations being used. This was demonstrated in the UK in adult intensive care, where it was found that among 30 medications, there were an average of 6 concentrations for each.(Borthwick,

Keeling, Keeling, Scales, & Waldmann, 2009; Borthwick, Woods, Keeling, Keeling, & Waldmann, 2007) Similar emerging patterns have been identified in paediatric practice in both the USA and UK. (Oskarsdottir et al., 2018; Phillips, 2011)

Furthermore the use of wide variations in concentration has led to variation in the design and development of associated safety technology – notably drug error reduction software (DERS) enabled infusion devices ("smart" pumps) where drug libraries are highly localised. This variation has led to patient harm.(Lyons et al., 2018; Schnock et al., 2017)

Consequently, the Health Safety Investigation Board has directed that smart pumps must be configured using a national library. (Healthcare Safety Investigation Branch, 2020) This intervention cannot be implemented in the UK without a national consensus on standard concentrations for children and neonates. This approach is feasible and has been delivered successfully in the Republic of Ireland (Howlett et al. 2019), Queensland, Australia (Cree et al., 2017) and is being developed in the United States of America. However, there are noted difficulties in the development of these frameworks for use in neonatal practice. Frequent barriers such as fluid load, high concentration solutions and multiple pump interactions with dose changes are offered up as reasons NOT to standardise in neonatal units "...without additional research…",(Brannon, 2006) however in single-centre studies these concerns have been shown to be unfounded.(Chapman et al., 2012; Christie-Taylor et al., 2012; Larsen et al., 2005)

PROPOSAL

That the Joint RCPCH/NPPG Standing Committee on Medicines (JMC) approves a framework of standard concentrations for use in neonates and children as part of a national drug library.

THE FRAMEWORK

The framework proposed (Appendix 1) has been developed using a multi-disciplinary approach in a single large tertiary children's centre. This has been thoroughly evaluated for safety and effectiveness in populations from 2kg and up, and has been found to be safer than weight based infusions.(Arenas-López et al., 2017; Rashed et al., 2015; Rashed et al., 2016) There is additional data supporting the longer term safety and effectiveness of the framework using "smart pump" data that is being prepared for publication.

This framework has been evaluated against a similar conceptual framework developed using inter-professional consensus methods by the Making it Safer Together (MiST) collaborative (Sutherland et al., 2017) and similarity extends to around 70%.

Given the time sensitive nature of the National Drug Library project, and the need to be "ahead of the curve" the leads for both frameworks have agreed that the proposed framework is suitable for all purposes and should form the basis of the National Drug Library for Children.

STRENGTHS

The proposed framework is:

- Reliably and robustly designed and validated using clinical simulation with clear acceptance thresholds of fluid load, in-use stability, and acceptable diluents

- In successful use in a large multi-speciality children's hospital for infants and children >2kg and rollout is in progress to areas outside of PICU at this site, and is being actively considered by other centres

- Peer reviewed for safety and effectiveness and published in respected journals

- Has great similarity to the MiST framework which JMC has previously endorsed. This framework has the added benefit of evidence of application and in-use data

CONSIDERATIONS

- Despite best efforts, this framework cannot generally be extrapolated into premature neonatal care, however has been used in infants down to 2kg.

- This framework is not exhaustive. There are many more infused medicines that are used throughout paediatric and neonatal practice. However, we are confident that this framework covers 90-95% of infused medicines used in the NHS in these populations.

- Standardised infusions are not a solution in themselves and may serve to present other opportunities for error elsewhere in the process.(Blandford et al., 2019). These errors include:
    - Selection errors (the wrong strength for a patient)
    - Calculation errors (as different calculations are required for administration)
    - Preparation errors (e.g. using the wrong diluent or volume)
    - Infusion device programming errors

- Rolling out standard concentrations is not straight forward and there is the need for supporting infrastructure and training to support delivery.

- It is believed that “smart pump” technology is the safest way to implement use of standard concentration infusions in paediatrics – not all centres currently have this technology
    - However, the strategy of pump manufacturers is currently to only offer DERS-enabled systems when infusion systems come up for replacement.

- This framework only covers continuous infusions and does not address the variation in bolus medications or intermittent infusions. However it provides a framework from which to start this process. This intervention may be viewed as a single measure to improve medication safety, but must be considered as part of a bundle of interventions (including “smart pumps,” bar code administration checks and pre-filled containers) to foster a systems-approach to IV medication safety.

- Any medication intervention carries risks associated with change. This requires careful consideration and consultation with stakeholders on the infrastructure and training requirements to safely implement them. For example:
    - There may be a perception that this represents a shift from “patient centred care” to “one size fits all”
    - The NHS needs to plan for how these ready-to-use solutions will be presented, and safely and securely stored

- The move to ready-to-administer infusions may be perceived to be a costly solution when ingredient drug costs are low, however this will offer far greater improvements in nursing efficiency and will release their time to nursing care. (Sutherland et al., 2016)

OPPORTUNITIES

- With appropriate support and infrastructure, there is the potential high uptake of these standard concentrations as seen in adult Intensive Care (Titiesari, Barton, Borthwick, Keeling, & Keeling, 2016) which in turn will drive development of ready-to-administer preparations

- A national drug library will offer efficiencies to the wider NHS in reducing the workload associated with development and implementation of smart pumps, electronic prescribing and patient records, and broader harmonisation initiatives across integrated care systems.

- A national framework once adopted will offer improvements in:
    - Nursing capacity as time to prepare medication doses is reduced substantially
    - Demand and capacity planning for drug shortages and requirements
    - Uptake of medication safety interventions including barcode medication administration, electronic prescribing, information presentation
    - Training efficiency with reduced resource required to induct practitioners into local practice as these infusion practices will be transferrable.

- A national framework will provide a basis for the strategic development of licensed formulations of IV medications specifically for neonates and children which continues to be an enormous gap in our needs.

FUTURE WORK

The implementation of standard concentrations offers a great deal to the NHS, however much of this has not been evaluated. Nor would it be appropriate to delay implementation to facilitate “more research” – infusion systems are being replaced, DERS systems are being updated and EPR systems are being selected and implemented today.

In line with the NHS Strategy for Patient Safety, there is an imperative to ensure that evaluation and measurement is embedded in this intervention to demonstrate ongoing benefits. Furthermore, while we present this framework “as is”, there must be space for pragmatic adaptation and adjustment with time, that can be

implemented centrally with appropriate adjustments throughout the system. Thus we recommend a national approach, with co-ordination through Medusa or other suitable group, and collaboration with educational institutions and industry to ensure adaptations are made swiftly and safely.

REFERENCES

Aguado-Lorenzo, V., Weeks, K., Tunstell, P., Turnock, K., Watts, T., & Arenas-Lopez, S. (2013). Accuracy of the concentration of morphine infusions prepared for patients in a neonatal intensive care unit. *Archives of Disease in Childhood*, *98*(12), 975–979. https://doi.org/10.1136/archdischild-2013-304522

Arenas-López, S., Stanley, I. M., Tunstell, P., Aguado-Lorenzo, V., Philip, J., Perkins, J., … Tibby, S. M. (2017). Safe implementation of standard concentration infusions in paediatric intensive care. *Journal of Pharmacy and Pharmacology*, *69*(5), 529–536. https://doi.org/10.1111/jphp.12580

Blandford, A., Dykes, P. C., Franklin, B. D., Furniss, D., Galal-Edeen, G. H., Schnock, K. O., & Bates, D. W. (2019). Intravenous Infusion Administration: A Comparative Study of Practices and Errors Between the United States and England and Their Implications for Patient Safety. *Drug Safety*, 1–9. https://doi.org/10.1007/s40264-019-00841-2

Borthwick, M., Keeling, S., Keeling, P., Scales, K., & Waldmann, C. (2009). Towards standardisation of drug infusion concentrations in UK critical care units. *Journal of the Intensive Care Society*, *10*(3), 197–200. https://doi.org/10.1177/175114370901000309

Borthwick, M., Woods, J., Keeling, S., Keeling, P., & Waldmann, C. (2007). A survey to inform standardisation of intravenous medication concentrations in critical care. *Journal of the Intensive Care Society*, *8*(1).

Brannon, T. S. (2006). Ad hoc versus standardized admixtures for continuous infusion drugs in neonatal intensive care: cognitive task analysis of safety at the bedside. *AMIA ... Annual Symposium Proceedings / AMIA Symposium. AMIA Symposium*, *33*(3), 862. Retrieved from http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=1839298&tool=pmcentrez&rendertype=abstract

Chapman, A. K., Lehmann, C. U., Donohue, P. K., & Aucott, S. W. (2012). Implementation of computerized provider order entry in a neonatal intensive care unit: Impact on admission workflow. *International Journal of Medical Informatics*, *81*(5), 291–295. https://doi.org/https://dx.doi.org/10.1016/j.ijmedinf.2011.12.006

Christie-Taylor A., S., & Tait A., P. (2012). Implementation of standard concentration medication infusions for preterm infants. *Infant*, *8*(5), 155–159. Retrieved from https://login.proxy.bib.uottawa.ca/login?url=http://search.ebscohost.com/login.aspx?direct=true&db=cin20&AN=2011694634&site=ehost-live

Cree, M. L., Stocker, C. F., Tu, Q. M., & Scaini, L. F. (2017). Adherence to standard medication infusion concentrations and its impact on paediatric intensive care patient outcomes. *Australian Critical Care*, (November 2014), 3–7. https://doi.org/10.1016/j.aucc.2017.07.003

Healthcare Safety Investigation Branch. (2020). *Procurement, usability and adoption of "smart" infusion pumps*. Retrieved from www.hsib.org.uk/tell-us-what-you-think

Howlett, M. M., Breatnach, C. V., Brereton, E., & Cleary, B. J. (2020). Direct observational study of interfaced smart-pumps in pediatric intensive care. *Applied Clinical Informatics*, *11*(4), 659–670. https://doi.org/10.1055/s-0040-1716527

Keers, R. N., Williams, S. D., Cooke, J., & Ashcroft, D. M. (2013). Prevalence and Nature of Medication Administration Errors in Health Care Settings: A Systematic Review of Direct Observational Evidence. *Annals of Pharmacotherapy*, *47*(2), 237–256. https://doi.org/10.1345/aph.1R147

Larsen, G. Y., Parker, H. B., Cash, J., O'Connell, M., & Grant, M. C. (2005). Standard drug concentrations and smart-pump technology reduce continuous-medication-infusion errors in pediatric patients. *Pediatrics*, *116*(1), e21-5. https://doi.org/10.1542/peds.2004-2452

Lehmann, C. U., Kim, G. R., Gujral, R., Veltri, M. a, Clark, J. S., & Miller, M. R. (2006). Decreasing errors in pediatric continuous intravenous infusions. *Pediatric Critical Care Medicine*, *7*(3), 225–230. https://doi.org/10.1097/01.PCC.0000216415.12120.FF

Lord Carter of Coles. (2020). *Transforming NHS Pharmacy Aseptic Services in England*. London.

Lyons, I., Furniss, D., Blandford, A., Chumbley, G., Iacovides, I., Wei, L., … Franklin, B. D. (2018). Errors and discrepancies in the administration of intravenous infusions: a mixed methods multihospital observational study. *BMJ Quality & Safety*, (7 April 2018), bmjqs-2017-007476. https://doi.org/10.1136/bmjqs-2017-007476

Manrique-Rodríguez, S., Sánchez-Galindo, A. C., López-Herce, J., Calleja-Hernández, M. Á., Martínez-Martínez, F., Iglesias-Peinado, I., … Fernández-Llamazares, C. M. (2013). Impact of implementing smart infusion pumps in a pediatric intensive care unit. *American Journal of Health-System Pharmacy*, *70*(21), 1897–1906. https://doi.org/10.2146/ajhp120767

National Patient Safety Agency. (2011). Intravenous morphine administration in neonatal units - Signal. Retrieved May 13, 2014, from http://www.nrls.npsa.nhs.uk/resources/?entryid45=130181

Oskarsdottir, T., Harris, D., Sutherland, A., Wignell, A., & Christiansen, N. (2018). A national scoping survey of standard infusions in paediatric and neonatal intensive care units in the United Kingdom. *Journal of Pharmacy and Pharmacology*, *70*(10), 1324–1331. https://doi.org/10.1111/jphp.12992

Parshuram, C. S., Ng, G. Y. T., Ho, T. K. L., Klein, J., Moore, A. M., Bohn, D., & Koren, G. (2003). Discrepancies between ordered and delivered concentrations of opiate infusions in critical care. *Critical Care Medicine*, *31*(10), 2483–2487. https://doi.org/10.1097/01.CCM.0000089638.83803.B2

Parshuram, C. S., To, T., Seto, W., Trope, A., Koren, G., & Laupacis, A. (2008). Systematic evaluation of errors occurring during the preparation of intravenous medication. *Canadian Medical Association Journal*, *178*(1), 42–48.

Perkins, J., Aguado-Lorenzo, V., & Arenas-Lopez, S. (2016). Standard concentration infusions in paediatric intensive care: the clinical approach. *Journal of Pharmacy*

and Pharmacology. https://doi.org/10.1111/jphp.12604

Phillips, M. S. (2011). Standardizing i.v. infusion concentrations: National survey results. *American Journal of Health-System Pharmacy*, *68*(22), 2176–2182. https://doi.org/10.2146/ajhp110001

Rashed, A.N., & Tomlin, S. (2015). Are we delivering safe intravneous opioid infusions in paediatric patient? Evaluation of the current practice in a UK paediatric hospital. *Drug Safety*, *38*(10), 1021. https://doi.org/10.1007/s40264-015-0346-0

Rashed, Asia N., Tomlin, S., Aguado, V., Forbes, B., & Whittlesea, C. (2016). Sources and magnitude of error in preparing morphine infusions for nurse-patient controlled analgesia in a UK paediatric hospital. *International Journal of Clinical Pharmacy*, *38*(5), 1069–1074. https://doi.org/10.1007/s11096-016-0369-3

Schnock, K. O., Dykes, P. C., Albert, J., Ariosto, D., Call, R., Cameron, C., … Bates, D. W. (2017). The frequency of intravenous medication administration errors related to smart infusion pumps: A multihospital observational study. *BMJ Quality and Safety*, *26*(2), 131–140. https://doi.org/10.1136/bmjqs-2015-004465

Sutherland, A., Jemmett, L., & Barber, R. (2016). CHANGING INFUSION PRACTICE GENERATES SIGNIFICANT EFFICIENCIES IN NURSING TIME AND RESOURCE USAGE IN PAEDIATRIC INTENSIVE CARE. *Archives of Disease in Childhood*, *101*(9). https://doi.org/10.1136/archdischild-2016-311535.23

Sutherland, Adam, Christiansen, N., Wignell, A., & Harris, D. (2017). *FIXED CONCENTRATION INFUSIONS: A NATIONAL CONSENSUS FOR PAEDIATRIC AND NEONATAL CARE*. Retrieved from http://www.mist-collaborative.net/infusion-standardisation-project-results/

Titiesari, Y. D., Barton, G., Borthwick, M., Keeling, S., & Keeling, P. (2016). Infusion medication concentrations in UKs critical care areas: Are the Intensive Care Societys recommendations being used? *Journal of the Intensive Care Society*, *0*(0), 1–6. https://doi.org/10.1177/1751143716662664

Wheeler, D. W., Degnan, B. A., Sehmi, J. S., Burnstein, R. M., Menon, D. K., & Gupta, A. K. (2008). Variability in the concentrations of intravenous drug infusions prepared in a critical care unit. *Intensive Care Medicine*, *34*(8), 1441–1447. https://doi.org/10.1007/s00134-008-1113-9

APPENDIX 1

Framework of Concentrations

Drug	Weight band	Concentration	Volume
Morphine	2-5kg	0.05mg/ml	20ml
	5-20kg	0.2mg/ml	50ml
	>20kg	1mg/ml	50ml
Midazolam	2-5kg	0.5mg/ml	20ml
	5-20kg	1mg/ml	50ml
	>20kg	2mg/ml	50ml
Fentanyl	2-5kg	0.01mg/ml	20ml
	5-20kg	0.02mg/ml	50ml
	>20kg	0.05mg/ml	50ml
Clonidine	2-5kg	7.5microgram/ml	20ml
	5-20kg	15microgram/ml	50ml
	>20kg	40microgram/ml	50ml
Nordrenaline/ Adrenaline	2-5kg	0.02mg/ml	20ml
	5-20kg	0.04mg/ml	50ml
	>20kg	0.16mg/ml	50ml
Dopamine	2-5kg	2mg/ml	20ml
	5-20kg	4mg/ml	50ml
	>20kg	12mg/ml	50ml
Dobutamine	2-5kg	2mg/ml	20ml
	>5kg	5mg/ml	50ml
Furosemide	2-5kg	3mg/ml	20ml
	5-20kg	5mg/ml	50ml
	>20kg	10mg/ml	50ml
Labetalol	2-5kg	5mg/ml	20ml
	>5kg	5mg/ml	50ml
Milrinone	2-5kg	0.1mg/ml	20ml
	5-20kg	0.4mg/ml	50ml
	>20kg	1mg/ml	50ml
Vasopressin	Presents specific challenges with delivery systems that are unable to express infusion doses to four decimal places Currently no standard concentration is offered Some units use 20 or 50units in 50ml		
Amiodarone	2-5kg	2.5mg/ml	20ml
	5-20kg	12mg/ml	50ml
	>20kg	24mg/ml	50ml
Rocuronium	2-5kg	10mg/ml	20ml
	>5kg	10mg/ml	50ml

Vecuronium	2-5kg	1mg/ml	20ml
	>5kg	1mg/ml	50ml
Atracurium	2-5kg	2.5mg/ml	20ml
	5-20kg	5mg/ml	50ml
	>20kg	10mg/ml	50ml
Heparin	2-5kg	75 units/ml	20ml
	5-20kg	200 units/ml	50ml
	>20kg	1000units/ml	50ml
Insulin	2-5kg	1unit/ml	20ml
	>5kg	1unit/ml	50ml