

Introduction and Objective

- The Lord Carter report on aseptic services, the Royal Pharmaceutical Society guidance on safe handling of medicines, and the NHS Specialist Pharmacy Service advice on ready-to-administer (RtA) intravenous (IV) products, are aligned in their encouragement of ready-to-administer noradrenaline.(1-3)
- Ready-to-administer IV products, which are pre-filled to standard concentrations, simplify near-patient tasking, are the least risk-associated option in the critical care setting, and represent the best use of pharmacy skills to support to clinical areas.(1-3)
- RtA noradrenaline has not been universally adopted across the UK NHS.
- The objective was to quantify and compare the resource and cost impact of alternative approaches to noradrenaline administration, focusing on ready-to-administer (RtA) and administration-from-concentrate (AfC) strategies at an English NHS level.
- Also to create a model with the flexibility to support local level variation in clinical factors and so support provider decision-making.

Methods

- A *de novo* budget impact model (decision tree, Microsoft® Excel®) was developed and parametised at a national health service level to simulate AfC and RtA strategies in 2019 (pre-COVID-19 epidemic), which differ in both noradrenaline formation and mode of pumping (Table 1). Health outcomes are assumed equivalent and are excluded.
 - Noradrenaline AfC* was preparation from concentrate by nurses at the bedside, double-pumped in 80% of cases, and a single or volumetrically pumped otherwise.
 - Noradrenaline RtA* was ready-to-administer preparation, overseen by nurses, and volumetrically pumped in all cases.
- Population: people requiring noradrenaline vasopressor support for hypotensive shock.
- Service size: Noradrenaline usage for septic and undifferentiated shock in ICUs in England was measured in Noradrenaline days, calculated from the annual number of critical care cases requiring such support, and the mean length of stay for septic shock.(4)
- Perspective and setting: Payor, NHS intensive care in England.
- Time horizon: One year, projected from resource use over 24 hours (discounting not applicable).
- Outcomes: Nurse time given to noradrenaline preparation for hypotensive shock per year; cost of nurse resource; episodes of noradrenaline preparation; volume of noradrenaline consumed but not infused (waste); number of units of noradrenaline and dextrose or saline product; cost of products; total incremental cost including human resource and drug acquisition – the net monetary benefit (NMB).
- Uncertainty was explored using both fixed variation univariate sensitivity analysis (parameter uncertainty), and alternative scenario analysis (structural uncertainty), to measure impact on NMB at ICU level.

Figure 1. Simplified decision tree

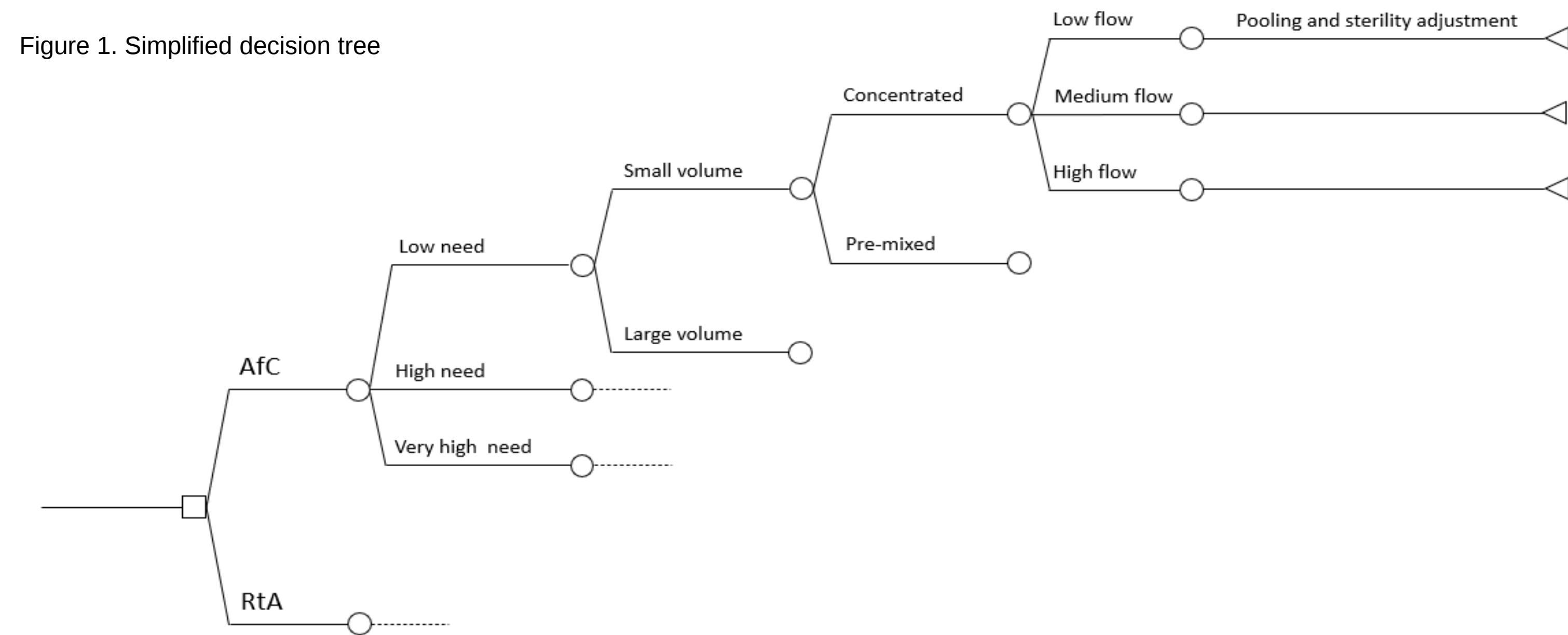


Table 1. Model parameters and settings

Service and population size		
ICU and HDU beds in England	4,123	(15)
Critical care cases of shock with noradrenaline support in England per year	30,396	(4)
Mean durations of noradrenaline support per admission (days)	7.6	(4)
Total noradrenaline support per year (patient days)	231,011	
Preparation of solution for infusion		
Proportion concentrated noradrenaline prepared at bedside	100%	
Proportion of concentrated noradrenaline prepared aseptically	0%	
Proportion of preparation and pump set-up by band 5 nurse	50%	
Proportion of preparation and pump set-up by band 6 nurse	50%	
Noradrenaline waste, single or volumetric pump changeover (mls)	0	
Noradrenaline waste, double pump changeover (mls)	10	
Maximum preparation sterility period (hrs)	24	
Staff time on preparation tasks (minutes)		
Prepare syringe/infusion bag from ampoule(s), check and label	11.5	
Preparing syringe/infusion bag from pre-mixed vial, check and label	2	
Second nurse check of an ampoule drawn preparation	3	
Second nurse check of a pre-mixed preparation	1	
Set-up/changeover of single or volumetric pump syringe/bag	1	
Set-up/changeover of double pump syringe	10	
Unit costs of consumables and resources		
4mg in 4ml noradrenaline ampoule	£1.06	(8)
8mg in 8ml noradrenaline ampoule	£3.20	(8)
4mg in 50ml vial ready-to-administer noradrenaline (Sinora®)	£7.90	(12)
8mg in 50ml vial ready-to-administer noradrenaline (Sinora®)	£7.37	(13)
5% dextrose or 0.9% saline, 100ml	£1.47	(9)
Nurse band 5 per working hour	£38.49	(7)
Nurse band 6 per working hour	£47.61	(7)
Clinical preferences for formulation and administration		
	RtA	AfC, if dif.
Formulation: concentrated	100%	0%
Formulation: ready-to-administer	0%	100%
Requirement low. 0.1 mcg/kg/min noradrenaline	10%	
Requirement high. 0.2 mcg/kg/min noradrenaline	80%	
Requirement very high. 0.4 mcg/kg/min noradrenaline	10%	
Flow rate low. 2.8ml/hr	0%	
Flow rate medium. 5.6ml/hr	100%	
Flow rate high. 11.3ml/hr	0%	
Pooling of 4mg ampoules to 8mg solution	80%	n/a
Pooling of 4mg ampoules to 16mg or 32mg solution	50%	n/a
Proportion double pumped	80%	0%
Proportion single or volumetrically pumped	20%	100%
Preparation volume small. 50ml	80%	100%
Preparation volume medium. 100ml	20%	n/a

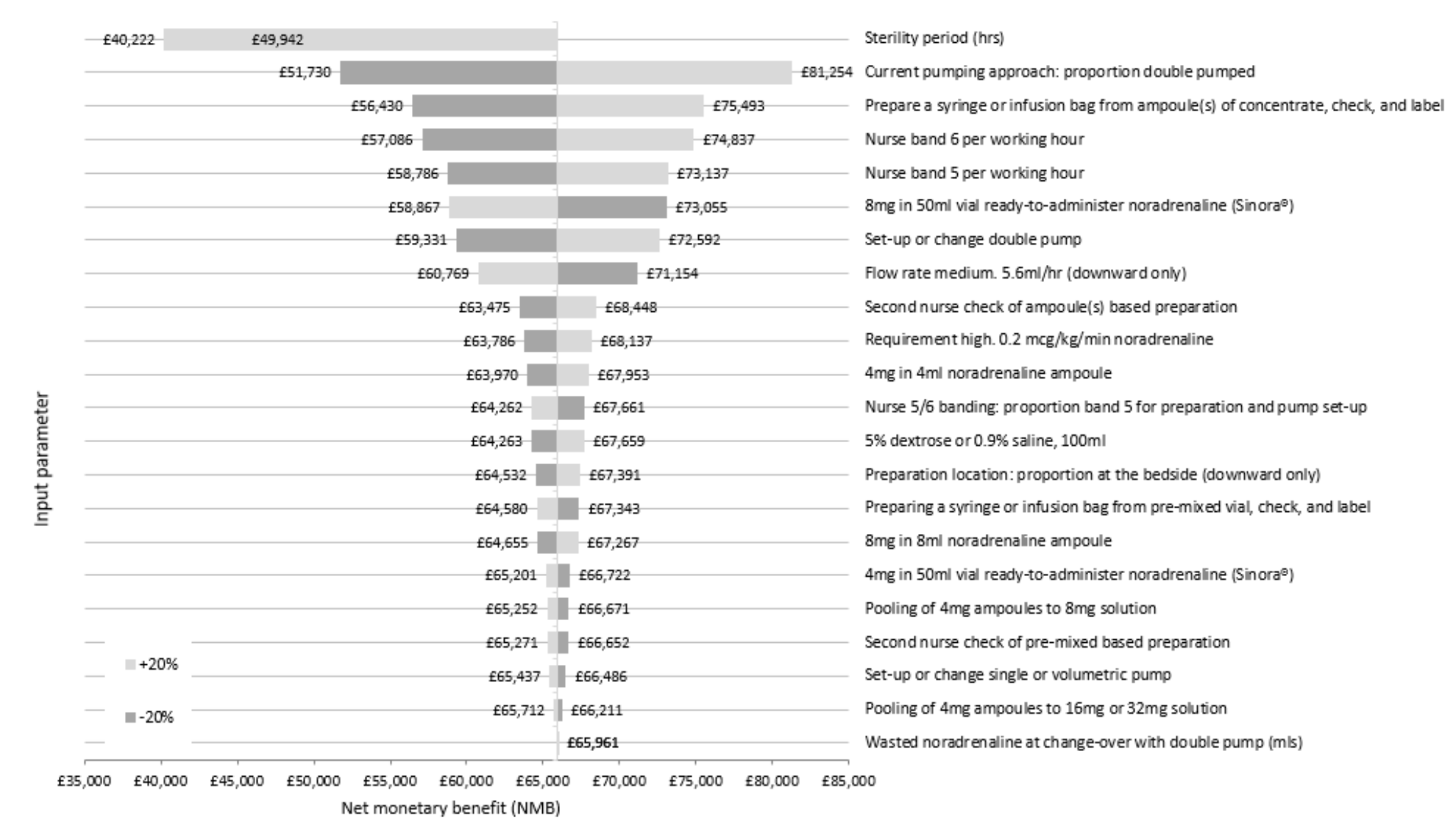
Table 2. Cumulative task time spent by ICU nurses preparing and delivering noradrenaline (7.5hr w/days)

Nurse task	AfC	RtA	Increment (change)
Drug preparation and checking (syringe/infusion bag)	26,797	4,620	-22,177 (83%)
Pump set-up and subsequent changeovers	15,154	1,540	-13,614 (90%)
Total	41,952	6,160	-35,791 (85%)
Total whole-time-equivalents (WTEs)	206.7	30.3	176.3

Table 3. Cost of noradrenaline treatment hypotensive shock in England

Nurse task	AfC	RtA	Increment (change)
Noradrenaline from concentrate	£2,374,281	£0	-£2,374,281
Ready-to-administer noradrenaline	£0	£5,655,161	£5,655,161
Dextrose or saline for dilution	£1,222,513	£0	-£1,222,513
Total cost of noradrenaline and dextrose	£8,652,692	£5,655,161	-£2,997,530
Nurses for drug preparation tasks	£8,652,692	£1,491,843	-£7,160,848
Nurses for pump preparation and reload tasks	£4,893,246	£497,281	-£4,395,965
Total cost of nursing time noradrenaline tasking	£13,545,938	£1,989,124	-£11,556,813
Net monetary benefit, England (per year)			£9,498,445
Net monetary benefit, per 29 bed ICU (per year)			£65,961
Net monetary benefit, per ICU bed (per year)			£2,304

Figure 2. Univariate sensitivity analysis of key parameters (fixed 20% +/- variation)



Results

- There are an estimated 30,396 adult admissions for shock requiring vasopressor support with noradrenaline in England. This equates to 231,011 days in 4,123 critical care beds.
- More nurse time is spent on drug preparation and pump management with the AfC strategy (Table 2).
- The basecase analysis predicted the AfC strategy required an average of 3.6 preparations per day and 33.6 ml of noradrenaline, versus 3.0 and 25.2 ml in the RtA strategy.
- Total drug acquisition cost was higher with an RtA strategy, but the nurse resource was lower. When differences in product acquisition and nurse resourcing were combined the net monetary benefit favoured an RtA strategy. (Table 3).
- Univariate sensitivity analysis: two parameters for demonstrated heightened sensitivity: the maximum sterility period (impacting the frequency of noradrenaline preparations being commenced near to the end of a sterility period), the proportion of noradrenaline double pumped (Figure 2).
- Scenario analysis: eradication of double pumping in the AfC strategy had the largest single impact of the six tests (75% reduction in ICU NMB).

Limitations and Conclusion

Limitations

- The number of noradrenaline support days for hypotensive and un-differentiated shock in critical care was necessarily approximated.
- National patterns of clinical preference for noradrenaline concentration, flowrate, vial pooling, sterility, and pumping method were not empirically derived; neither could be the estimated mean duration of nurse tasks.
- Conservatively, the analysis did not include any improved safety associated with reducing near-patient preparation.(3)
- Outcomes are not easily generalisable to the local level given known variation, or other healthcare systems (but model inputs may be user-defined).

Conclusion

- Volumetrically pumped ready-to-administer (RtA) noradrenaline can redirect significant nurse time from drug tasking to patient-facing care, so aligning protocol with the recommendations of Lord Carter's Report, the Royal Pharmaceutical Society and the NHS Specialist Pharmacy Service.

References

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