DETAILED FINDINGS ABOUT THE MANAGEMENT OF HYPONATRAEMIA

Location of admission

In general, the reviewers stated that the ward the patient was first admitted to from the emergency department (ED) was appropriate (247/262; 94.3%), although eight patients should have been admitted directly to a critical care area, rather than to a general ward. It is possible that the wide availability of critical care outreach teams supported the management of hyponatraemia in both the ED and after admission to general wards, meaning that subsequent admission to a critical care area was not required. In addition, patients with severe clinical or biochemical hyponatraemia may have had the appropriate initial treatment in the emergency department (56% of hypertonic saline was administered in the ED) and so may not have required an admission to a critical care area. Due to the potential for over-correction of blood sodium there is a need for close monitoring for the 24 to 48 hours after hypertonic saline is admitted; this level of monitoring may not be possible outside of critical care.

In total, 219/270 (81.1%) patients admitted as an emergency were admitted to an acute/general medicine/elderly care ward area and 31/270 (11.5%) were admitted to a critical care (level 2 or 3) area (T5.1). Three patients were admitted to an endocrinology ward, reflecting that endocrinology care is typically delivered as a specialist consultation service to patients admitted to other ward areas. The majority of hospitals do not have specialist endocrine inpatient beds.

Table 5.1 Ward patient was first admitted to from the emergency department	Number of patients	%
Acute medical unit	171	63.3
General medical	40	14.8
Critical care	31	11.5
Care of the elderly	8	3.0
Cardiology	4	1.5
Endocrinology	3	1.1
General surgical	2	<1
Neurology	2	<1
Oncology	1	<1
Renal	1	<1
Unknown	7	2.6
Total	**270**	

Reviewer assessment form data

Treatment of hyponatraemia

It was reported that most hospitals had clinical guidelines on the assessment and management of hyponatraemia 130/156 (83.3%), and 75/130 (57.7%) of these guidelines stated who should be responsible for the oversight and care of patients with severe hyponatraemia.

The treatments provided in both the emergency admission-related and postoperative hyponatraemia groups are shown in Table 5.2. The vaptans are selective vasopressin V2-receptor antagonists, which are licenced for use in patients with autosomal dominant polycystic kidney disease and associated rapidly progressing kidney disease. Additionally, tolvaptan is licenced in the UK for the management of hyponatremia secondary to the syndrome of inappropriate antidiuretic hormone secretion (SIADH), although typically this use is limited to specific groups of patients.

Table 5.2 Treatments received for hyponatraemia	Emergency admissions		Postoperative hyponatraemia	
	Number of patients	% of all patients (n=270)	Number of patients	% of all patients (n=84)
0.9% sodium chloride solution	166	61.5	41	48.8
Fluid restriction	107	39.6	27	32.1
Hypertonic saline	49	18.1	6	7.1
Medications stopped	38	14.1	5	6.0
Other intravenous fluids	25	9.3	8	9.5
Diuretics	18	6.7	4	4.8
Oral sodium	16	5.9	8	9.5
None	10	3.7	13	15.5
V2 receptor antagonists (vaptans)	8	3.0	0	0.0
Demeclocycline	3	1.1	1	1.2
Enteral urea	0	0.0	0	0.0

Reviewer assessment form data

There was very low use of vaptans; this reflect either low availability of these drugs in hospitals, a lack of awareness by non-specialist clinicians of their potential use in the management of hyponatraemia or a limitation on their use due to local medicines management. Overall, the choice of treatment was deemed to be inappropriate for a quarter of both emergency admission patients (63/256; 24.6%) and postoperative hyponatraemia (22/74; 29.7%) (T5.3).

Table 5.3 Appropriateness of treatment choices for hyponatraemia	Emergency admissions		Postoperative hyponatraemia	
	Number of patients	%	Number of patients	%
Yes	193	75.4	52	70.3
No	63	24.6	22	29.7
Subtotal	**256**		**74**	
Unknown	14		10	
Total	**270**		**84**	

Reviewer assessment form data

Eight patients with a blood sodium level of 100 mmol/L were administered IV fluids; this was 0.9% sodium chloride in five patients, hypertonic saline in two patients and a combination of hypertonic saline and 0.9% sodium chloride in one patient. None of the patients with a sodium of less than 100

mmol/L died, and therefore the decision to administer intravenous (IV) fluids and the choice of IV fluids was not associated with an adverse outcome.

The issues with the treatment(s) undertaken in both groups were broadly similar (T5.4). A total of 45 emergency admission-related hyponatraemia patients had both 0.9% sodium chloride and fluid restriction. This was inappropriate in only 10 patients; this reflects not only the challenge in the diagnosis of the cause of hyponatraemia, but also that on subsequent clinical assessment it may be appropriate to consider fluid restriction after a period of intravenous fluids or vice versa.

Table 5.4 Summary of issues identified with the treatments provided	Emergency admissions	Postoperative hyponatraemia
Hypertonic saline indicated	11	2
Fluids and restriction	10	3
Hypertonic saline NOT indicated	5	2
No indication for 0.9% Saline	3	N/A
No treatment given	2	5
Slower rate required	2	N/A
Fluid restriction not indicated	2	3
Not enough fluid given	2	N/A
Tolvaptan not indicated	2	N/A
Medications not reviewed/stopped	N/A	3
Further treatment required	N/A	1
Fluids not indicated	N/A	1

Reviewer assessment form data

Hyponatraemia in both the emergency admissions and postoperative groups had issues with use of hypertonic saline. There were 55 patients (49 emergency admissions, six postoperative) who received this as part of their treatment. The reviewers believed that hypertonic saline solution was not indicated for seven patients. In all seven this was because the severity of the hyponatraemia did not warrant the use of hypertonic saline solution, as the patient was asymptomatic or the reviewer's felt that there was no clinical evidence of hyponatraemic encephalopathy documented in the patient's notes.

A 2.7% sodium chloride solution was the most administered hypertonic saline (2.7% alone in 38 patients or combined 1.8% and 2.7% sodium chloride solution in 12 patients) (T5.5).

Table 5.5 Type of hypertonic saline solution administered	Number of patients
2.7 %	38
1.8 %	12
Both 2.7% and 1.8%	2
Subtotal	**52**
Unknown	3
Total	**55**

Reviewer assessment form data

International guidelines recommend the use of 3% hypertonic saline solution, although due to availability clinicians typically use 2.7% hypertonic saline.[26] The administration of 1.8% hypertonic saline will require larger volumes to deliver the same amount of sodium, this additional volume has a potential impact on baroregulated vasopressin secretion. It was more commonly administered by peripheral cannula rather than via central venous access.

Previous work has shown that administration of boluses of hypertonic saline is associated with better clinical outcomes.[27] Bolus administration occurred in 33 patients (bolus alone in 31, combined boluses and IV infusion in two) (T5.6). Typically, hypertonic saline was administered in a critical care area for 44 patients (ED resuscitation or level 2 or 3 critical care) (T5.7).

Table 5.6 Frequency of administration by IV bolus and/or IV infusion	Number of patients
IV boluses	**31**
IV infusion	**22**
IV boluses and infusion	**2**
Total	**55**

Reviewer assessment form data

Table 5.7 Location where hypertonic saline solution was administered	Number of patients
Emergency department resuscitation	28
Critical care (level 2 or level 3)	16
Endocrinology	2
General medicine	4
Subtotal	**50**
Unknown	5
Total	**55**

Reviewer assessment form data

Overall, where hypertonic saline was administered, in 17/55 patients there were issues with the decision to use, volume administered, rate of administration and/or duration of administration. While not captured in this study, the seniority and experience of the clinician involved in managing hyponatraemia is likely to impact on whether to treat with hypertonic saline, and where it is used, the appropriateness of how the hypertonic saline is prescribed and administered.

For 39/55 patients who were administered hypertonic saline outside of critical care, the grade of doctor who determined that hypertonic sodium could be identified in 22 sets of case notes. Ten were consultants, 11 were specialist trainees or speciality doctor and one was a foundation doctor. Of the six patients who were administered hypertonic saline where the reviewers felt it was not indicated, the decision was made by a consultant in two patients and by non-consultant doctors in four patients.

Due to the risk of over-correction patients who are administered hypertonic saline outside of critical care should be admitted to critical care for at least 24-48 hours of monitoring (including regular blood sodium measurements).[22,28,29] Of the 28 patients administered with hypertonic saline in an emergency department, only 11 were admitted to a critical care unit. The reviewers felt that five other patients were inappropriately admitted to a general ward area rather than critical care.

Monitoring

Blood sodium levels were monitored appropriately in 185/234 (79.1%) patients admitted as an emergency and 61/75 (81.3%) patients with postoperative hyponatraemia (T5.8). When hypertonic saline was administered, blood sodium levels were not monitored appropriately in 9/44 (20.5%) patients (T5.9).

The issues with monitoring were due to blood sodium levels not being rechecked soon enough and/or inappropriate frequency of monitoring after administration of hypertonic saline solution. The use of indwelling venous lines (for example midline catheters) or arterial lines may assist with the increased frequency of blood tests required in patients with severe hyponatraemia and especially following the administration of hypertonic saline.

Table 5.8 Appropriateness of blood sodium monitoring for emergency admission and postoperative hyponatraemia	Emergency admissions		Postoperative hyponatraemia	
	Number of patients	%	Number of patients	%
Yes	185	79.1	61	81.3
No	49	20.9	14	18.7
Subtotal	**234**		**75**	
Unknown	36		9	
Total	**270**		**84**	

Reviewer assessment form data

Table 5.9 Appropriateness of blood sodium monitoring when hypertonic saline administered	Number of patients
Yes	35
No	9
Subtotal	**44**
Unknown	11
Total	**55**

Reviewer assessment form data

When monitoring blood sodium levels, particularly after the administration of hypertonic saline, it is important that the same analytical method (either point-of-care or laboratory) is used to prevent differences in results between the analytical methodology impacting on the 'reported' rise in blood sodium levels. Therefore, it is essential that if the repeat testing is done using point-of-care analyses, the results are integrated into the laboratory electronic reporting systems, or they are accurately documented in the patient's medical notes, so that the trends in blood sodium levels are easily visible to anyone involved in the patient's care.

Over-correction of blood sodium levels, such as too-rapid increase in blood sodium concentrations, occurred in 22 patients and this was thought to have been avoidable in nine patients. The reviewers considered that more frequent sodium checks (four patients), excessive hypertonic saline solution (two patients) and failure to recognise a rapid rise in sodium (two patients) made the over-correction avoidable. In 12 patients, an attempt was made to re-lower the sodium with 5% dextrose

in ten patients and desmopressin in two. There was no harm reported in relation to those patients who had over-correction of the hyponatraemia.

As illustrated in the case below, rapid recognition of hyponatraemia in the emergency department and use of a local hyponatraemia management proforma can ensure appropriate administration and monitoring of hypertonic saline solution and recognition of the risk of blood sodium over-correction.

CASE STUDY

A 35-year-old patient with bulimia, alcohol excess, vomiting and history of a GI bleed presented to hospital and had a seizure in ED. Their sodium level was 115 mmol/L having been normal three days earlier. The initial seizure due to hyponatremia was recognised, and the patient received IV hypertonic saline in the ED. There was clear documentation of use of the local guideline, which included a completed 'hyponatraemia proforma' that gave clear instructions about the sodium levels over the first 48 hours, plus advice about the rate of correction/what to do in case of over-correction.

The reviewers considered that this demonstrated a good assessment in the ED with rapid appropriate treatment of clinically and biochemically severe hyponatraemia. The completion of the hyponatraemia proforma showed a clear treatment/investigation plan had been put in place for the patient.

The range of blood sodium concentrations on discharge for patients admitted with hyponatraemia is shown in Figure 5.1. The median (inter-quartile range)) blood sodium for emergency admission-related hyponatraemia had increased from the lowest blood sodium of 120 (116 to 123) mmol/L to 131 (128 to 134) mmol/L on discharge (F5.2). Similarly, for postoperative hyponatraemia it had increased from 125 (122 to 128.5) mmol/L to 132 (129 to 134) mmol/L on discharge (F5.3).

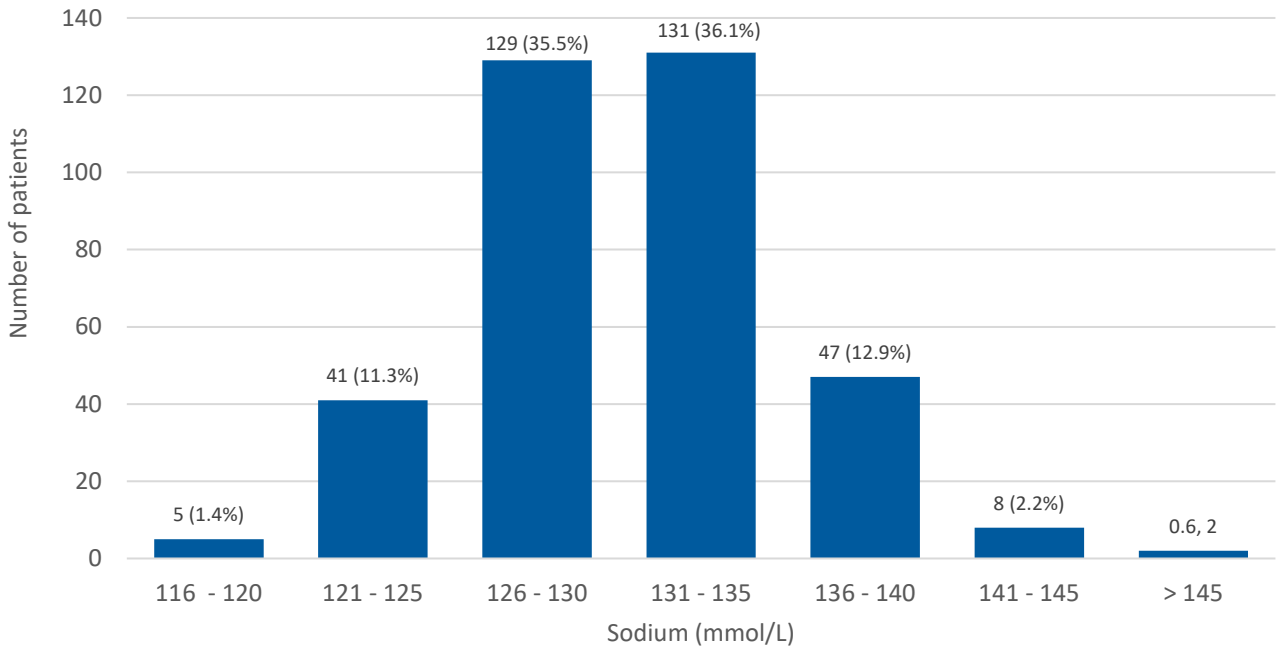

Figure 5.1 Post-discharge sodium concentrations

Clinician questionnaire data (n=363, unknown for 29)

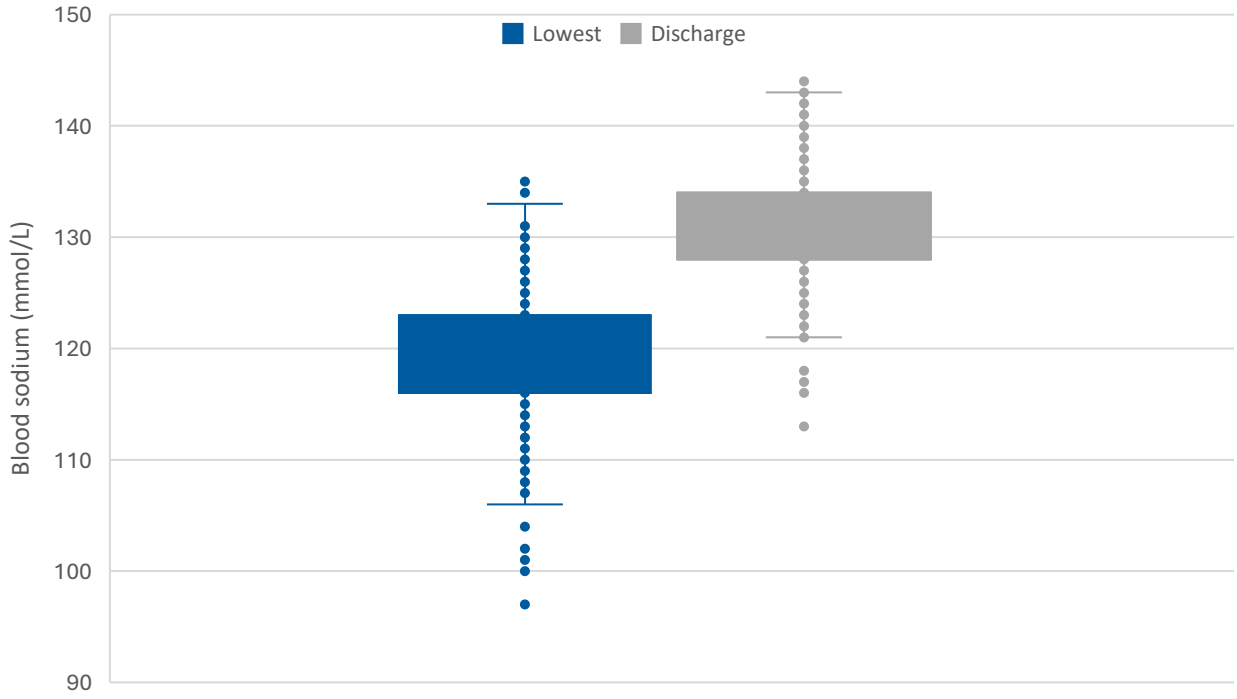

Figure 5.2 Comparison of change from lowest blood sodium levels to discharge blood sodium levels in patients with emergency admission-related hyponatraemia

Clinician questionnaire data (n=362; unknown for 30)

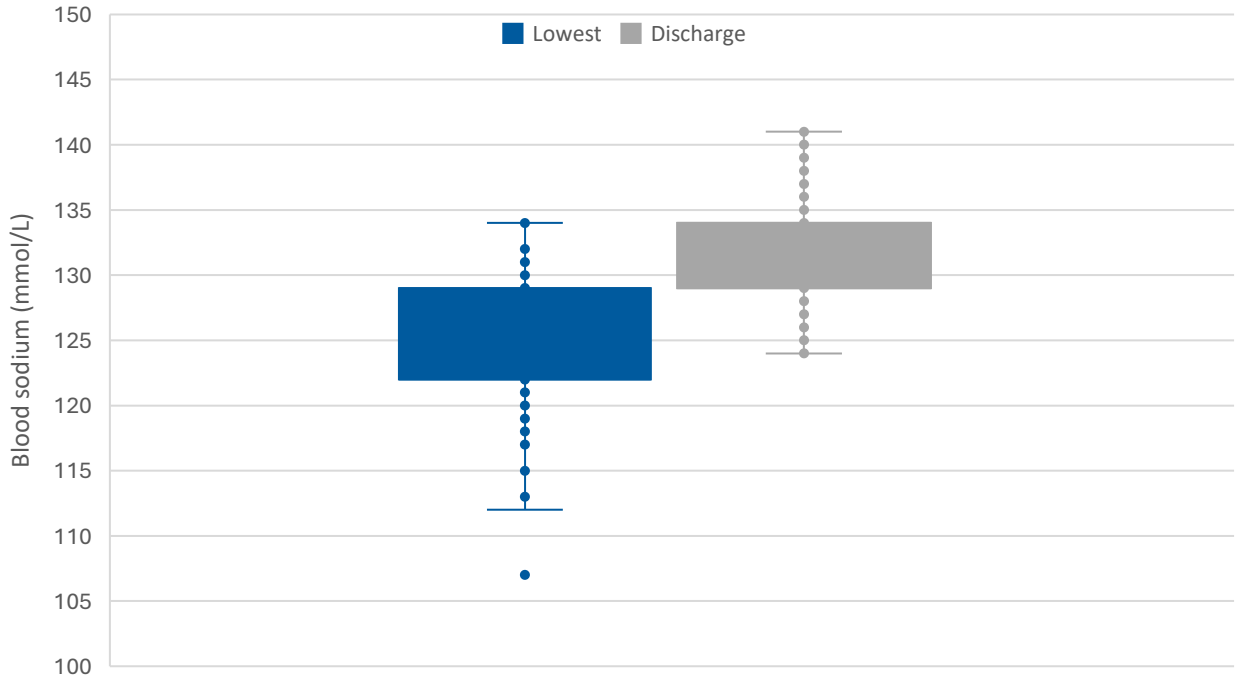

Figure 5.3 Comparison of change from lowest blood sodium to discharge blood sodium in patients with postoperative hyponatraemia.

Clinician questionnaire data (n=106)

There were 46/362 (12.7%) patients who were discharged with a sodium of 125 mmol/L or less. While this may be appropriate in some patients with known chronic hyponatraemia, others would require appropriate specialist follow-up rather than being discharged to the GP to monitor the sodium and 'treat', and this has to happen in an appropriate timeframe.

Medication interactions

Most patients admitted on an emergency basis with hyponatraemia were taking one or more medications prior to admission that could have contributed to their hyponatraemia (225/270; 83.3%) (T5.10).

Table 5.10 Medicines potentially associated with hyponatraemia used prior to admission to hospital	Number of patients	%
Antihypertensive agents	109	40.5
Protein pump inhibitors	106	39.4
Diuretics	76	28.3
Antidepressants	75	27.9
Antiseizure medication	29	10.8
Antipsychotic drugs	23	8.6
Steroids – oral*	19	7.1
Opioid drugs	17	6.3
Other (specified)	17	6.3
Steroids – inhaled	9	3.3
Anticancer agents	8	3.0
Antibiotics	6	2.2
Non-steroidal anti-inflammatory drugs (NSAIDS)	3	1.1

Reviewer assessment form data. Answers may be multiple; n=269

**Failure to take oral steroids can lead to hyponatraemia if stopping use can lead to adrenal insufficiency*

Of the 76 patients taking diuretics, 27 used thiazides, 19 used loop diuretics, and in 30 patients the type of diuretic was not specified. The median admission blood sodium concentration was similar for patients taking thiazide diuretics (117.6 mmol/L) and those taking loop diuretics (117.4 mmol/L).

Our sampling methodology, which focused on patients with more severe hyponatraemia, may have prevented us from showing an association between thiazide diuretic use and lower blood sodium concentrations at admission. Often the initiation of a medicine and/or a change in its dose can precipitate the development of hyponatraemia. The case reviews did not provide information on the timing of starting any medicines or dose changes in relation to the presentation with hyponatraemia.

Given the potential relationship between certain medicines and the development of hyponatraemia 157/270 (58.1%) patients with emergency admission-related hyponatraemia had one or more changes to the medications they were taking on admission that may have contributed to the development of the condition. These changes may have occurred at the time of admission, at any point during the admission, or at the point of discharge.

It is important to undertake a risk-benefit assessment before stopping a medication. For example, if the evidence for the development of hyponatraemia related to an anticonvulsant is weak, the benefit of stopping in relation to the hyponatraemia maybe minimal, while the risk of developing seizures from stopping may be significant.

The most common changes made were discontinuation of a medication likely to cause hyponatraemia (141 patients) or dose adjustments to reduce risk of recurrence of the hyponatraemia (12). Of note, 17 patients had a change from use of a proton pump inhibitor to famotidine (a gastric acid suppressant which is not associated with hyponatraemia) during admission or on discharge.

In terms of other specific treatments related to hyponatraemia, ten patients had slow sodium commenced, four patients were started/had an increased dose of steroid treatment, two were started on tolvaptan and one had a change in their previous dose of desmopressin.

Where medications were changed, most changes were communicated to the GP on discharge (140/151; 92.7%). Commonly the 'communication' to the GP that a medicine has been stopped is its absence from the patient's medication list at discharge. It can therefore be unclear whether this is an intentional discontinuation or an omission on discharge prescribing.

It is vital that there is clear documentation on discharge that the medicine has been actively discontinued and the underlying reasons for this decision should be included. Additionally, there should be guidance or details of who to contact about restarting the medication if that is needed.

CASE STUDY

A 36-year-old patient was referred to hospital by their GP with a low sodium and increased lethargy over the last few days. The patient had complex medical issues and was taking multiple medications. The patient received a timely medication review which included neurology input. The neurology review led to the stopping of the anti-seizure medication that could be associated with hyponatraemia, with an alternative started. This was clearly communicated to the GP and an outpatient neurology follow-up was booked for the patient.

The reviewers considered that this demonstrated very good communication between hospital clinical teams and with primary care in a complex medical case.

In those patients where no changes were made to medications during their hospital admission, reviewers identified that changes should have been made in 14/67 patients. These changes primarily involved stopping medicines associated with hyponatraemia (seven patients) and wider longer-term medication/disease management reviews (four patients). It was not possible to determine whether changes in medication were explained to the patient at the time of discharge. This is essential, as if patients are not aware of the changes, they might restart the stopped medicines using pre-dispensed supplies at home or contact the GP to request a repeat prescription.

Delays in treatment

Delays occurred in the investigation or management of hyponatraemia in 17/64 (26.6%) emergency presentations and 5/18 (27.8%) of postoperative hyponatraemia patients (T5.11). These delays were attributed to the impact of out-of-hours care where typically there was reduced medical, nursing and laboratory staff. Some of these delays could have been mitigated if clinicians had confidence to start treatment based on point-of-care testing (e.g. blood gas results) rather than waiting for laboratory results.

Table 5.11 Frequency of delays in investigation and/or management of hyponatraemia	Emergency admissions		Postoperative hyponatraemia	
	Number of patients	%	Number of patients	%
Yes	64	25.1	18	22.8
No	191	74.9	61	77.2
Subtotal	**255**		**79**	
Unknown	15		5	
Total	**270**		**84**	

Reviewer assessment form data

Reviewers identified issues with responsibility for the initial and then ongoing management of postoperative hyponatraemia. While the on-call general medicine team will provide advice on the management of hyponatraemia, they tend not to assume responsibility for the care of a postoperative surgical patient with hyponatraemia. This may be because the hyponatraemia could resolve quickly than the postoperative needs of the patient, which would be better managed by the surgical team.

In orthopaedic surgery, many hospitals have addressed this by providing proactive care for older patients undergoing surgery (POPS) teams. These teams support the orthopaedic surgeons and manage the hyponatraemia while the orthopaedic surgeons manage the orthopaedic issues in parallel,[29] Given the benefits that this model of care has delivered, there is increasing interest in it being delivered in other surgical specialties.[30]

Complications related to the hyponatraemia occurred in 30/270 (11.1%) of emergency admissions and 17/84 (20.2%) of postoperative hyponatraemia cases. Most commonly seizures which occurred in 20 patients and confusion in three. While there were no reported cases of cerebral vasospasm or acute cerebral oedema, it is possible that some of the seizures may have been related to these complications of hyponatraemia but were not detected by the treating clinical teams.

The development of postoperative hyponatraemia was more likely to lead to a longer length of stay than seen in those admitted with hyponatraemia (15/84; 17.9% vs 9/270; 3.3%).

There were 12 deaths in patients with hyponatraemia. Seven deaths were discussed at local morbidity and mortality (or similar) meetings; reviewers did not identify any remediable factors related to the hyponatraemia in any of the deaths.

Quality of care assessment and areas for improvement

According to the clinicians who treated the patients there were areas regarding the management of the patient's hyponatraemia that could have been improved in 121/392(30.9%) of emergency patients and 25/106 (23.6%) of postoperative cases.

Themes for improvement identified by the local clinicians mirrored those areas highlighted by the case reviewers and are summarised in Table 5.12. Further investigation was the biggest area for improvement for both emergency admissions and postoperative hyponatraemia.

Table 5.12 Themes of areas for improvement in the care provided	Emergency admissions	Postoperative hyponatraemia
	Number of patients	Number of patients
Further investigation	47	12
Sodium checks	22	7
Treatment choice	21	3
Specialist input	12	2
Fluid status	12	5
Medicines review	10	3

Clinician questionnaire data

The quality-of-care grading by the reviewers for emergency admission and postoperative hyponatraemia is shown in Figure 5.4. For both groups of patients, the main areas for improvement related to clinical issues rather than organisational issues (emergency admission: 133/265; 50.2% and postoperative: 51/83; 61.4%) (unknown for 5 and 1).

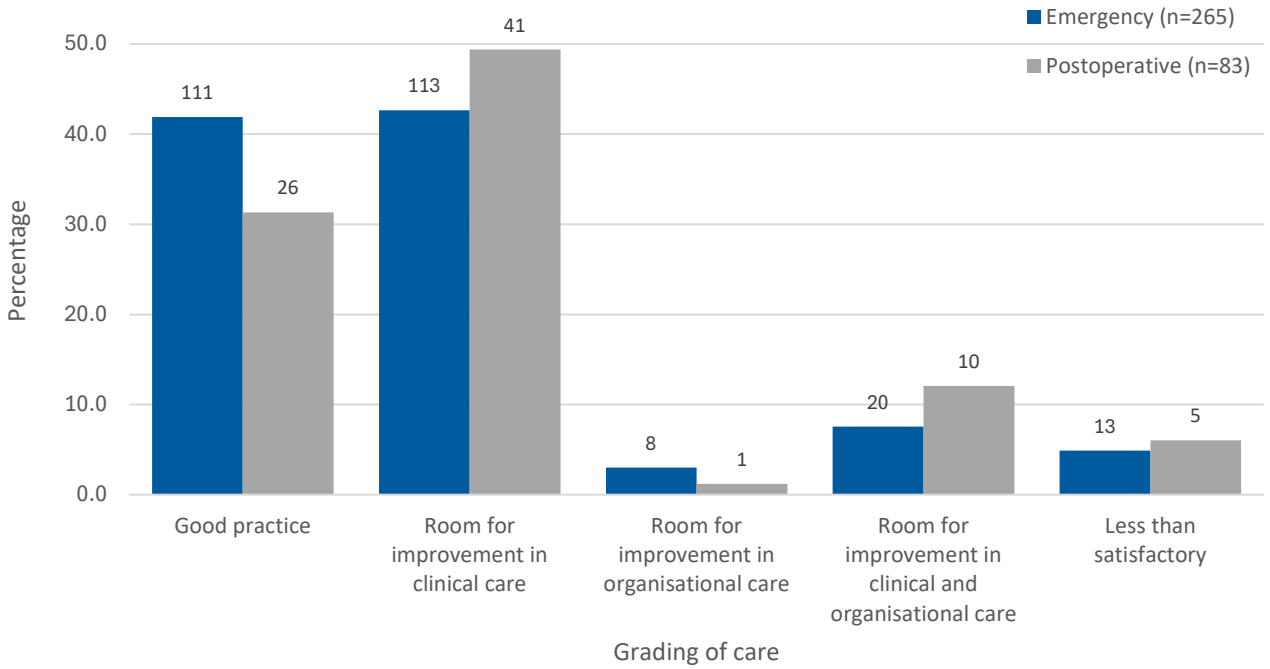

Figure 5.4 Assessment of overall quality of care for emergency admission and postoperative related hyponatraemia

Reviewer assessment form data

One area for improvement involves ensuring that follow-up on discharge is adequate and timely. In 35/270 (13.0) emergency admission-related hyponatraemia, the follow-up arranged on discharge was felt to be inappropriate. Themes identified included inadequate follow-up, inadequate instructions to the GP regarding repeat sodium measurements, and further investigation as outpatient required.