

Changes in intravenous fluid use patterns in Australia and New Zealand: evidence of research translating into practice

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Intravenous (IV) fluid administration is a nearly ubiquitous intervention in hospitalised patients. It is used to maintain euvolaemia in fasting patients, to replace physiological and pathophysiological fluid losses, to deliver medications and to manage haemodynamic instability.¹ The consumption of IV fluids is expected to increase, and the global market is expected to be worth an estimated \$7.2 billion by 2017.²

Crystalloid solutions such as 0.9% sodium chloride solution, balanced solutions such as compound sodium lactate solution, and acetated solutions such as PlasmaLyte are used in a variety of clinical situations.³ Artificial colloid solutions such as substituted hydroxyethyl starch (HES) (Voluven, Volulyte and StarQuin), succinylated gelatin (Gelifusine) preparations, and natural colloids such as various albumin solutions are typically used for fluid resuscitation.^{4,5} The type of fluid used appears to vary depending on clinician preference, cost, local guidelines and availability, and clinical requirements.⁴⁻⁶

Despite the importance of IV fluid therapy, it remains unclear whether and how fluid consumption varies in different regions and countries. It is also uncertain whether such differences in fluid consumption are of sufficient magnitude to warrant further investigation, or whether these differences are dependent on the type of fluid being investigated. Finally, there are no studies on how such changes have evolved over time. We aimed to describe the geographic and temporal differences in fluid consumption across Australia and New Zealand.

Methods

We conducted a retrospective ecological study examining current regional and temporal trends in fluid administration across Australia and New Zealand over the periods 2012–2013 and 2013–2014. The human research ethics committees of Monash University and the Austin Hospital approved the study (CF14/2949-2014001616 and LNR/14/Austin/408).

Data sources

Australian and New Zealand demographic data

National and state population data were accessed through the relevant government agency publications. For Australia, the state and territorial populations for 2012 and 2013 were taken from the Australian Bureau of Statistics December 2014 demographic statistics release.⁷ We used the 2013

ABSTRACT

Objectives: To describe changes in the use of intravenous (IV) fluid by quantity and type in different regions of Australia and New Zealand.

Design, setting and participants: We conducted a retrospective ecological study examining regional and temporal trends in IV fluid consumption across Australia and New Zealand over the periods 2012–2013 and 2013–2014, using national proprietary sales data as a surrogate for consumption, and demographic data from the public domain.

Results: More than 13.3 million litres of IV fluid were consumed in Australia and New Zealand in 2012–2013, and more than 13.9 million litres in 2013–2014, with colloid solutions accounting for < 2%. There was marked regional variation in consumption of fluids, by volumes and proportions used, when standardised to overall Australian and New Zealand values. There was no significant change in the overall volume of crystalloid solutions consumed but there was a significant decrease (9%; $P = 0.02$) in the ratio of unbalanced to balanced crystalloid solutions consumed. Consumption of all forms of colloid solutions decreased, with a 12% reduction overall ($P = 0.02$), primarily driven by a 67% reduction in the consumption of hydroxyethyl starch (HES) solutions.

Conclusions: The amount and type of IV fluid use, as determined by fluid sales, is highly variable across Australia and New Zealand. However, overall use of balanced crystalloid solutions is increasing and the use of HES has decreased dramatically.

Crit Care Resusc 2016; 18: 78–88

Population Estimates and Projections report from Statistics New Zealand to obtain data on the national population of New Zealand for 2012 and 2013.⁸

Australian and New Zealand fluid sales data

Data on sales of crystalloids and artificial colloids in New Zealand and Australia over the periods 1 June 2012 to 31 May 2013 and 1 June 2013 to 31 May 2014 were obtained from Baxter Healthcare (Sydney, NSW, Australia). These data were used as a surrogate for fluid consumption. The data were originally collected by IMS Health (Danbury, Conn, United States), a large information technology company

Table 1. Population demographics and gross intravenous fluid sales (L), by region and fluid type

Region	Population [†]	Crystalloid solutions*				Colloid solutions				Total fluids	
		Saline [‡]	CSL	Acetate [§]	Total crystalloids	20% albumin [¶]	4% albumin ^{**}	Gelofusine ^{††}	Starch ^{‡‡}		
2012–2013											
NZ	4 435 700	1 071 466	301 208	372 627	1 745 301	873	5 447	6 815	10 974	24 108	1 769 409
AUS	22 917 637	7 350 401	3 835 018	201 513	11 386 932	14 903	112 922	48 677	25 967	202 468	11 589 400
ACT, NSW	7 734 777	2 518 316	1 455 359	83 226	4 056 901	5 341	31 134	6 863	8 422	51 759	4 108 660
VIC	5 680 502	17 44 769	1 101 160	15 819	2 861 748	3 474	26 891	12 514	8 621	51 499	2 913 246
QLD	4 608 886	1 782 600	791 441	87 573	2 661 614	3 291	32 456	5 116	4 648	45 510	2 707 124
WA	2 479 506	645 643	506 603	6 633	1 158 879	1 111	6 862	15 636	3 614	27 223	1 186 102
SA	1 662 197	501 012	249 570	7 224	757 806	1 263	12 514	7 957	590	22 324	780 130
TAS	512 475	206 249	119 829	804	326 882	290	2 028	492	73	2 884	329 766
NT	239 294	112 889	19 683	7 080	139 652	132	1 037	100	0	1 269	140 921
AUS and NZ	27 353 337	8 421 867	4 136 226	574 140	13 132 232	15 776	118 369	55 491	36 941	226 577	13 358 809
2013–2014											
NZ	4 475 100	1 231 277	381 663	431 465	2 044 405	993	6 184	5 111	6 807	19 095	2 063 500
AUS	23 307 564	7 314 712	4 144 483	279 977	11 739 172	14 913	115 567	46 375	5 554	182 408	11 921 580
ACT, NSW	7 849 120	2 540 654	1 612 889	100 613	4 254 155	5 397	29 701	5 962	3 338	44 397	4 298 552
VIC	5 787 086	1 642 750	1 100 928	20 019	2 763 697	3 428	29 608	12 283	734	46 051	2 809 748
QLD	4 687 417	1 735 309	870 888	122 829	2 729 026	3 115	34 416	5 519	927	43 976	2 773 002
WA	2 549 145	650 281	556 551	11 184	1 218 016	1 105	6 930	15 416	422	23 873	1 241 888
SA	1 67 7062	581 263	281 815	10 740	873 818	1 360	11 941	6 498	127	19 926	893 744
TAS	513 927	202 718	128 363	996	332 077	357	2 105	627	7	3 095	335 172
NT	243 807	119 090	20 943	19 836	159 869	153	868	70	0	1 090	160 959
AUS and NZ	27 782 664	8 545 989	4 526 146	711 442	13 783 577	15 906	121 751	51 486	12 360	201 503	13 985 080

CSL = compound sodium lactate. NZ = New Zealand. AUS = Australia. ACT = Australian Capital Territory. NSW = New South Wales. VIC = Victoria. QLD = Queensland. WA = Western Australia. SA = South Australia. TAS = Tasmania. NT = Northern Territory. * Australian, NZ, and Australian + NZ crystalloid values adjusted to account for national sales to veterinary agencies. † From government data. ‡ 0.9% sodium chloride solution. § PlasmaLyte (proprietary acetated solution). ¶ 20% human albumin solution. ** 4% human albumin solution. †† 4% succinylated gelatin solution. ‡‡ 6% hydroxyethyl starch + 10% pentastarch.

that specialises in provision of detailed health care data from more than 100 000 suppliers in over 100 countries to commercial and health care services. These are likely to be the most comprehensive sales data available, covering the entire IV fluid sector. Baxter Healthcare paid for data from IMS to use for sales forecasting purposes and market share estimation, which is standard practice in the health care industry. No information was available on 5% dextrose, 4% dextrose/0.18% saline or hypertonic saline. Baxter Healthcare provided us with these data for the purposes of this research. Within Australia and New Zealand, Baxter Healthcare is the sole supplier of crystalloids but not of colloids. CSL is the sole supplier of albumin solutions, Fresenius-Kabi is the sole supplier of starch solutions, and B. Braun is the sole supplier of gelatin solutions.

Baxter Healthcare, using proprietary predictive modelling, imputed the artificial colloid sales data for New Zealand over the 2013–2014 period. As the same regional administration and sales team provides service in the Australian Capital

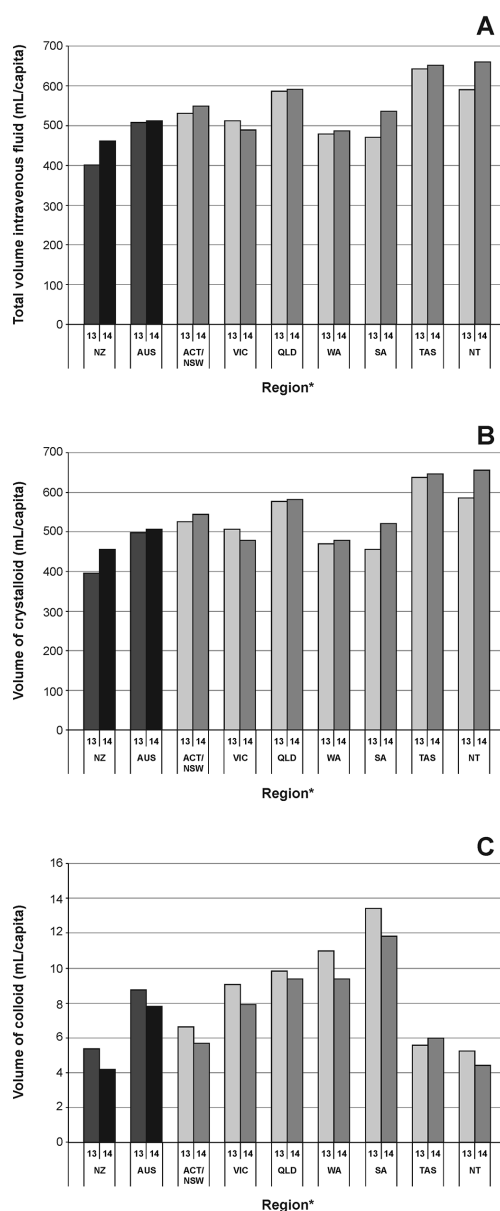
Territory and New South Wales, Baxter Healthcare amalgamated the data for these two regions. Regional data for New Zealand were unavailable and it was treated as a single administrative area. Data were corrected for veterinary sales where possible; these were only available at a national level, and only for crystalloid solutions.

In Australia, naturally derived colloid solutions of 4% and 20% human albumin are freely available from the Australian Red Cross Blood Service as a by-product of blood product manufacture. We obtained data on their delivery from the Red Cross, the National Blood Authority and CSL.

Data handling

The total volume of crystalloids and colloids purchased in both Australia and New Zealand was calculated by multiplying the volume per unit by the number of units sold. This was repeated for New Zealand alone and the individual states and territories, and for each individual type of fluid. The volume purchased per capita was also calculated.

Figure 1. Intravenous fluid consumption per capita, by region, 2012–2013 and 2013–2014



* NZ = New Zealand. AUS = Australia. ACT = Australian Capital Territory. NSW = New South Wales. QLD = Queensland. WA = Western Australia. SA = South Australia. TAS = Tasmania. NT = Northern Territory. 13 = 2012–2013. 14 = 2013–2014.

A. Total volume of crystalloid and colloid solutions. **B.** Total volume of acetated solutions, lactated salt solutions and 0.9% sodium chloride solutions. **C.** Total volume of 20% albumin solutions, 4% albumin solutions, 6% hydroxyethyl starch solutions, 10% pentastarch and 4% succinylated gelatin solutions.

For the purposes of comparison, total fluid sales across the whole of Australia and New Zealand were treated as the index population. Sales of Hartmann's solution and compound sodium lactate solution were combined under the heading of compound sodium lactate, and Voluven,

Volulyte and StarQuin 6% solution sales, as well as sales of a very small quantity of pentastarch in New Zealand in 2012–2013, were combined under the heading of starch.

Statistical analysis

We performed statistical analyses using Stata, version 13 (StataCorp) and calculated simple proportions and percentages. The Wilcoxon signed-rank test was used to identify significant differences in the sales of each fluid type between the two periods across all regions. A two-sided *P* value of 0.05 was considered to be statistically significant.

Results

Demographics and gross fluid sales data

The gross national and regional fluid sales and population data are shown in Table 1. More than 13.3 million litres of IV fluid were sold (and probably consumed) in Australia and New Zealand in the 2012–2013 period, and more than 13.9 million litres in 2013–2014. Crystalloid sales dwarfed colloid sales, with only 227 000 L of colloid fluids being consumed in 2012–2013 and 201 000 L in 2013–2014 (Table 1, Figure 1).

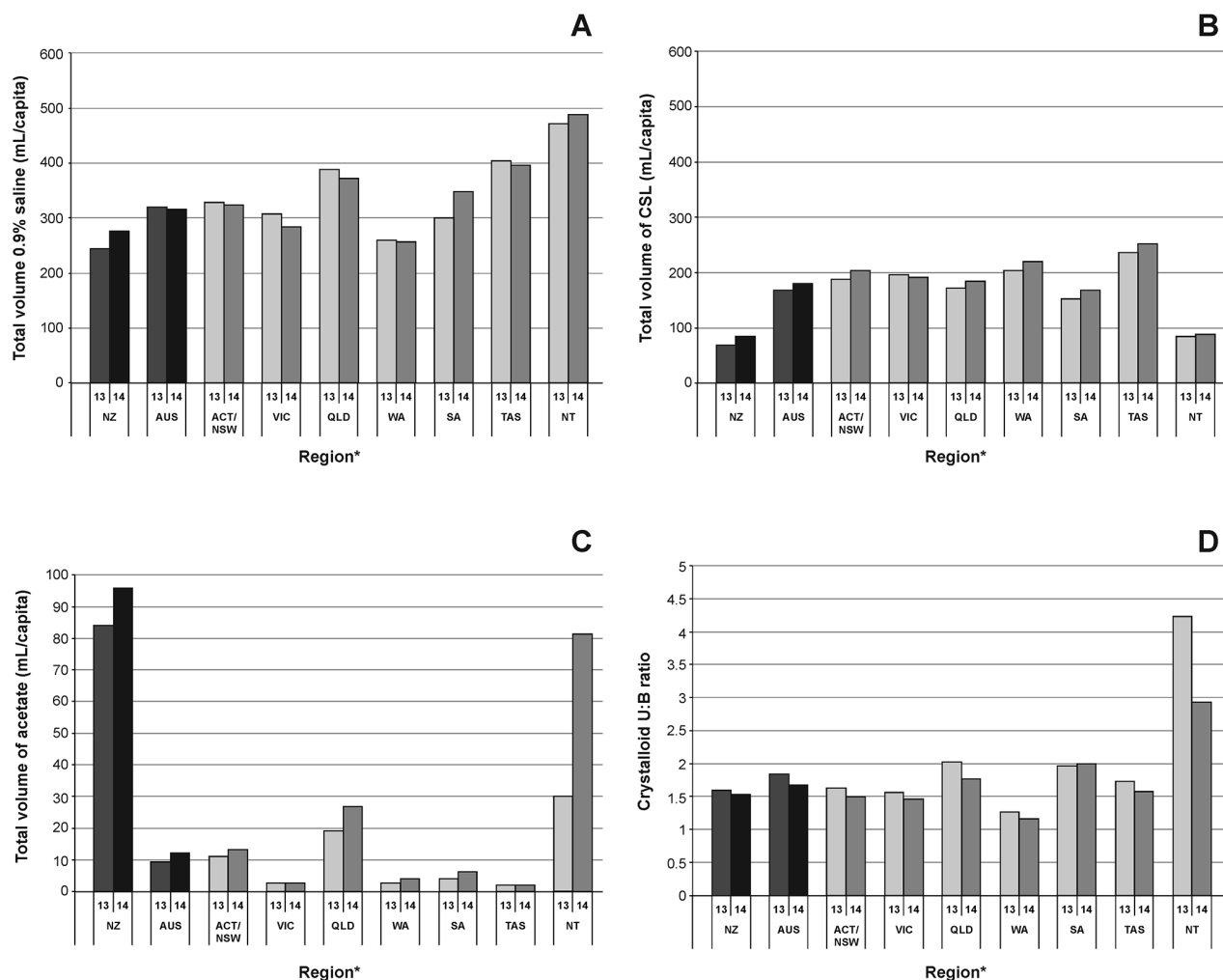
Regional differences in overall fluid consumption

The consumption of fluid varied in quantity and composition for the 2012–2013 and 2013–2014 periods according to region. The relative proportions of the individual fluid types consumed in each region over these periods are shown graphically in Figures 1 and 2. In 2012–2013, 523 mL of IV fluid were consumed per capita among the whole Australian and New Zealand population, and in 2013–2014, 488 mL were consumed per capita. The variation in consumption between regions when standardised to overall Australian and New Zealand values was marked, with New Zealand consuming 18% less IV fluid, and Tasmania consuming 32% more during the same period. Similarly variable results were obtained from 2013–2014 data (Tables 2 and 3).

Regional differences in crystalloid consumption

The volume and composition of crystalloid solutions varied between regions in both periods. The regional standardised volume of crystalloids consumed per capita varied between 82% and 133% of overall Australian and New Zealand consumption in 2012–2013, and between 92% and 133% in 2013–2014 (Tables 2 and 3, Figure 2). The proportional use of crystalloid fluid types varied markedly between regions in both periods. The consumption of acetated solutions in New Zealand was 400% greater than their overall consumption across Australia and New Zealand in 2012–2013, but was 90% less in Tasmania, with a similar variation seen in 2013–2014. The ratio of unbalanced to

Figure 2. Regional consumption of crystalloid solutions in Australia and New Zealand, by fluid type (estimated by sales per capita), 2012–2013 and 2013–2014



* NZ = New Zealand. AUS = Australia. ACT = Australian Capital Territory. NSW = New South Wales. QLD = Queensland. WA = Western Australia. SA = South Australia. TAS = Tasmania. NT = Northern Territory. 13 = 2012–2013. 14 = 2013–2014.

A. Saline = 0.9% sodium chloride solution. **B.** CSL = compound sodium lactate. **C.** Acetate = PlasmaLyte (proprietary acetated solution). **D.** U:B = ratio of unbalanced to balanced crystalloid solutions.

balanced crystalloid solutions consumed varied from 87% to 236% of the overall Australian and New Zealand values in 2012–2013, and from 71% to 179% of these values in 2013–2014.

Regional differences in colloid consumption

The volume and composition of colloid solutions varied markedly between regions in both periods. The regional standardised volume of colloids consumed per capita varied from 64% to 162% of overall Australian and New Zealand consumption in 2012–2013, with similar variations in 2013–2014 (Tables 2 and 3, Figure 3). The proportional use of differing colloid types varied markedly between

regions over the two time periods. The consumption of starch solutions in New Zealand was 183% that of Australia and New Zealand overall in 2012–2013, and 345% that of Australia and New Zealand overall in 2013–2014. The ratio of natural colloid solutions (albumin) to synthetic colloid solutions (gelatins and starches) used varied from 25% to 806% of the standardised Australian and New Zealand values in 2012–2013, and from 28% to 675% of the 2013–2014 Australian and New Zealand values. Artificial colloid use was dominant in New Zealand, but albumin solutions appeared to be more popular across Australia. No starch was used in the Northern Territory in either period (Tables 2 and 3).

Table 2. Intravenous fluid consumption 2012–2013, volumes per capita and volumes standardised to Australian and New Zealand overall values

Region	Crystalloid solutions*				Colloid solutions						Total fluids	
	Saline [†]	CSL	Acetate [‡]	U:B [§]	Total crystalloids	20% albumin [¶]	4% albumin ^{**}	Gelofusine ^{††}	Starch ^{‡‡}	N:S ^{§§}		Total colloids
Fluid sold, mL/capita												
NZ	242	68	84	1.59	393	0.2	1.23	1.54	2.47	0.36	5.44	399
Australia	321	167	9	1.82	497	0.65	4.93	2.12	1.13	1.71	8.83	506
ACT/NSW	326	188	11	1.64	525	0.69	4.03	0.89	1.09	2.39	6.69	531
VIC	307	194	3	1.56	504	0.61	4.73	2.2	1.52	1.44	9.07	513
QLD	387	172	19	2.03	577	0.71	7.04	1.11	1.01	3.66	9.87	587
WA	260	204	3	1.26	467	0.45	2.77	6.31	1.46	0.41	10.98	478
SA	301	150	4	1.95	456	0.76	7.53	4.79	0.35	1.61	13.43	469
TAS	402	234	2	1.71	638	0.57	3.96	0.96	0.14	4.1	5.63	643
NT	472	82	30	4.22	584	0.55	4.33	0.42	0	11.69	5.3	589
Australia and NZ	308	151	21	1.79	480	0.58	4.33	2.03	1.35	1.45	8.28	488
Fluid totals (ratios, standardised to Australian and New Zealand volumes)												
NZ	0.79	0.45	4	0.89	0.82	0.34	0.28	0.76	1.83	0.25	0.66	0.82
Australia	1.04	1.11	0.43	1.02	1.04	1.12	1.14	1.04	0.84	1.18	1.07	1.04
ACT/NSW	1.06	1.25	0.52	0.92	1.09	1.19	0.93	0.44	0.81	1.65	0.81	1.09
VIC	1	1.28	0.14	0.87	1.05	1.05	1.09	1.08	1.13	0.99	1.1	1.05
QLD	1.26	1.14	0.9	1.13	1.2	1.22	1.63	0.55	0.75	2.52	1.19	1.2
WA	0.84	1.35	0.14	0.7	0.97	0.78	0.64	3.11	1.08	0.28	1.33	0.98
SA	0.98	0.99	0.19	1.09	0.95	1.31	1.74	2.36	0.26	1.11	1.62	0.96
TAS	1.31	1.55	0.1	0.96	1.33	0.98	0.91	0.47	0.1	2.83	0.68	1.32
NT	1.53	0.54	1.43	2.36	1.22	0.95	1	0.21	0	8.06	0.64	1.21
Australia and NZ	1	1	1	1	1	1	1	1	1	1	1	1

CSL = compound sodium lactate. NZ = New Zealand. ACT = Australian Capital Territory. NSW = New South Wales. VIC = Victoria. QLD = Queensland. WA = Western Australia. SA = South Australia. TAS = Tasmania. NT = Northern Territory. * Australian, NZ, and Australian + NZ crystalloid values adjusted to account for national sales to veterinary agencies. † 0.9% sodium chloride solution. ‡ PlasmaLyte (proprietary acetated solution). § Ratio of unbalanced to balanced crystalloid solution consumption. ¶ 20% human albumin solution. ** 4% human albumin solution. †† 4% succinylated gelatin solution. ‡‡ 6% hydroxyethyl starch + 10% pentastarch. §§ Ratio of natural (albumin) to synthetic (gelatin and starch) colloid consumption.

Temporal changes in overall fluid consumption

Across Australia and New Zealand between 2012–2013 and 2013–2014, there was an increase in IV fluid consumption of approximately 626 000 L, a gross increase of 5% but a statistically non-significant increase of only 3% in per-capita terms (Figure 4, Table 1, Table 4).

Temporal changes in crystalloid consumption

Although there was no statistically significant increase in the total volume of crystalloid sold per capita between the two periods, there was a significant increase in the consumption of lactated solutions (7%; $P = 0.02$) and acetated solutions (24%; $P = 0.02$) in Australia and New Zealand. This translated into a 9% decrease ($P = 0.02$) in the ratio of unbalanced to balanced crystalloid solutions consumed between the two periods (Figure 4, Table 4).

Temporal changes in colloid consumption

Total colloid sales per hospital admission decreased by 12% between 2012–2013 and 2013–2014 ($P = 0.02$). This was primarily driven by a huge reduction in the consumption of starch (Figure 4, Table 4).

Discussion

Key findings

Using regional and national fluid sales data as a surrogate measure of fluid consumption, we describe the first published estimate of IV fluid use at a national level, for two countries. We make several new and important observations. First, we show that the consumption of crystalloids across Australia and New Zealand is orders of magnitude greater than the consumption of colloids. Second, patterns of

Table 3. Intravenous fluid consumption 2013–2014, volumes per capita and volumes standardised to Australian and New Zealand overall values

Region	Crystalloid solutions*				Colloid solutions						Total fluids	
	Saline [†]	CSL	Acetate [‡]	U:B [§]	Total crystalloids	20% albumin [¶]	4% albumin ^{**}	Gelofusine ^{††}	Starch ^{‡‡}	N:S ^{§§}		Total colloids
Fluid sold, mL/capita												
NZ	275	85	96	1.51	457	0.22	1.38	1.14	1.52	0.6	4.27	461
Australia	314	178	12	1.65	504	0.64	4.96	1.99	0.24	2.51	7.83	511
ACT/NSW	324	205	13	1.48	542	0.69	3.78	0.76	0.43	3.77	5.66	548
VIC	284	190	3	1.47	478	0.59	5.12	2.12	0.13	2.54	7.96	486
QLD	370	186	26	1.75	582	0.66	7.34	1.18	0.2	5.82	9.38	592
WA	255	218	4	1.15	478	0.43	2.72	6.05	0.17	0.51	9.37	487
SA	347	168	6	1.99	521	0.81	7.12	3.87	0.08	2.01	11.88	533
TAS	394	250	2	1.57	646	0.69	4.1	1.22	0.01	3.89	6.02	652
NT	488	86	81	2.92	656	0.63	3.56	0.29	0	14.57	4.47	660
Australia and NZ	308	163	26	1.63	496	0.57	4.38	1.85	0.44	2.16	7.25	503
Fluid totals (ratios, standardised to Australian and New Zealand volumes)												
NZ	0.89	0.52	3.69	0.93	0.92	0.39	0.32	0.62	3.45	0.28	0.59	0.92
Australia	1.02	1.09	0.46	1.01	1.02	1.12	1.13	1.08	0.55	1.16	1.08	1.02
ACT/NSW	1.05	1.26	0.5	0.91	1.09	1.21	0.86	0.41	0.98	1.75	0.78	1.09
VIC	0.92	1.17	0.12	0.9	0.96	1.04	1.17	1.15	0.3	1.18	1.1	0.97
QLD	1.2	1.14	1	1.07	1.17	1.16	1.68	0.64	0.45	2.69	1.29	1.18
WA	0.83	1.34	0.15	0.71	0.96	0.75	0.62	3.27	0.39	0.24	1.29	0.97
SA	1.13	1.03	0.23	1.22	1.05	1.42	1.63	2.09	0.18	0.93	1.64	1.06
TAS	1.28	1.53	0.08	0.96	1.3	1.21	0.94	0.66	0.02	1.8	0.83	1.3
NT	1.58	0.53	3.12	1.79	1.32	1.11	0.81	0.16	0	6.75	0.62	1.31
Australia and NZ	1	1	1	1	1	1	1	1	1	1	1	1

CSL = compound sodium lactate. NZ = New Zealand. ACT = Australian Capital Territory. NSW = New South Wales. VIC = Victoria. QLD = Queensland. WA = Western Australia. SA = South Australia. TAS = Tasmania. NT = Northern Territory. * Australian, NZ, and Australian + NZ crystalloid values adjusted to account for national sales to veterinary agencies. † 0.9% sodium chloride solution. ‡ PlasmaLyte (proprietary acetated solution). § Ratio of unbalanced to balanced crystalloid solution consumption. ¶ 20% human albumin solution. ** 4% human albumin solution. †† 4% succinylated gelatin solution. ‡‡ 6% hydroxyethyl starch + 10% pentastarch. §§ Ratio of natural (albumin) to synthetic (gelatin and starch) colloid consumption.

fluid consumption are highly variable across Australia and New Zealand, with different crystalloids and colloids being used in different proportions and different total volumes in different regions in an apparently chaotic fashion. Acetated solutions, albumin solutions and 6% HES solutions, in particular, show massive regional variations in consumption over the study periods. Third, the ratio of unbalanced to balanced crystalloid consumption is falling in every region, suggesting that there is a widespread increasing preference for such balanced solutions over saline. Fourth, we show significant reductions in the sale of colloid solutions over a 2-year period, and a two-thirds decrease in the consumption of starch solutions, a finding congruent with recent trials showing toxicity.

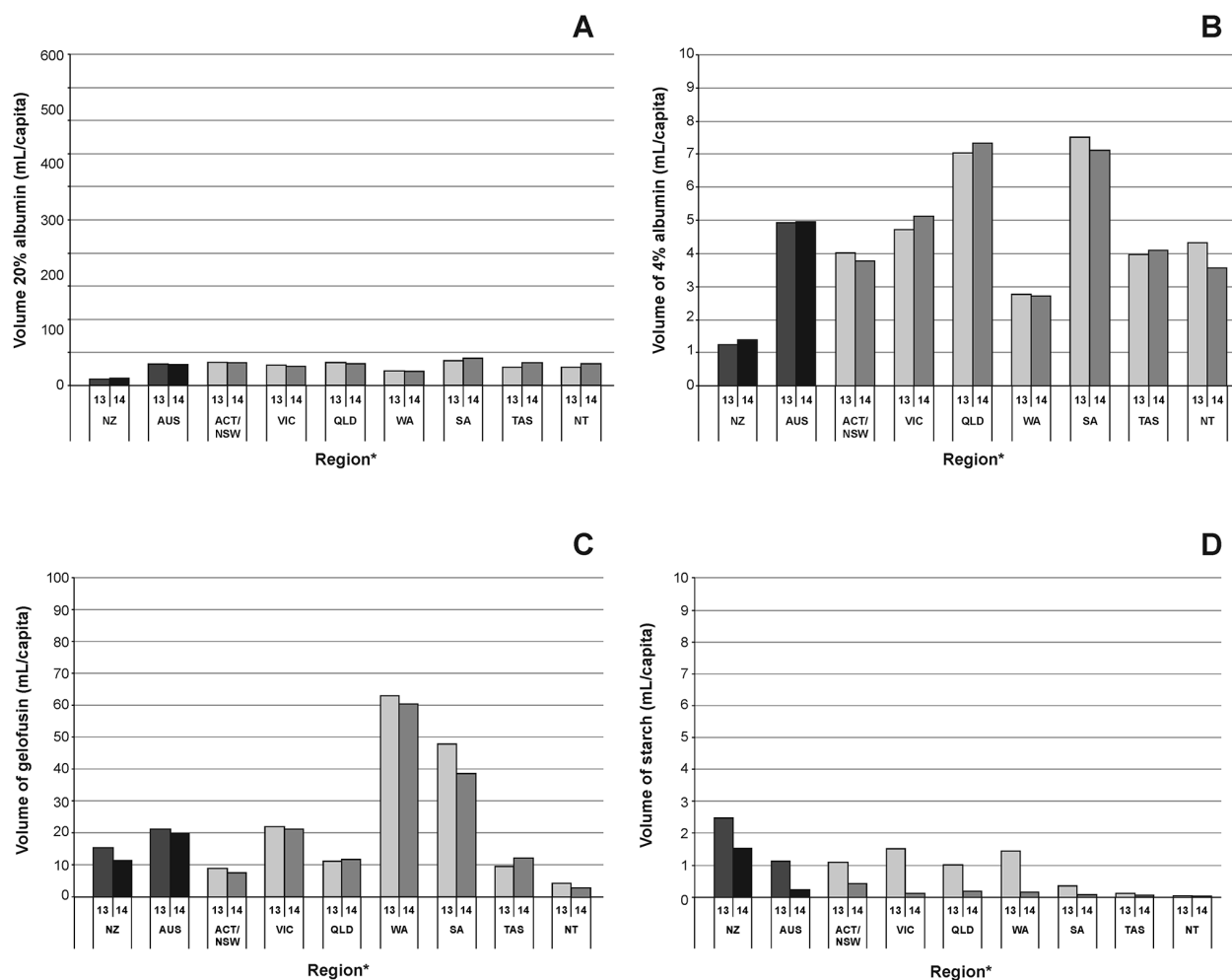
Study findings in context

To our knowledge, this is the first published description of fluid administration at a bi-national level across two entire

health services. The National Health Service of the United Kingdom spends about £156 million on IV fluids each year,⁹ and the only previously published estimate of IV fluid sales in the medical literature¹⁰ suggests that the UK purchases 10 million litres of saline annually. In Australia and New Zealand, more than 13 million litres are purchased, despite having a combined population less than half the size, while the US purchases 200 million litres.¹⁰ We were unable to identify information in the medical literature about temporal trends in fluid sales or use at a national level in the US.

Our description of fluid consumption patterns shows significant regional variation in IV fluid use. Such an inconsistent approach to fluid use has been described tangentially in other contexts. In 1994, world consumption of colloid solutions was 48.33 million units. Of these, 31.4% were albumin solutions (37.7% in New Zealand and 71.6% in Australia in 2013–2014); 44.9% were dextrans and starches (35.7% in New Zealand and 3.1%

Figure 3. Regional consumption of colloid solutions in Australia and New Zealand, by fluid type (estimated by sales per capita), 2012–2013 and 2013–2014

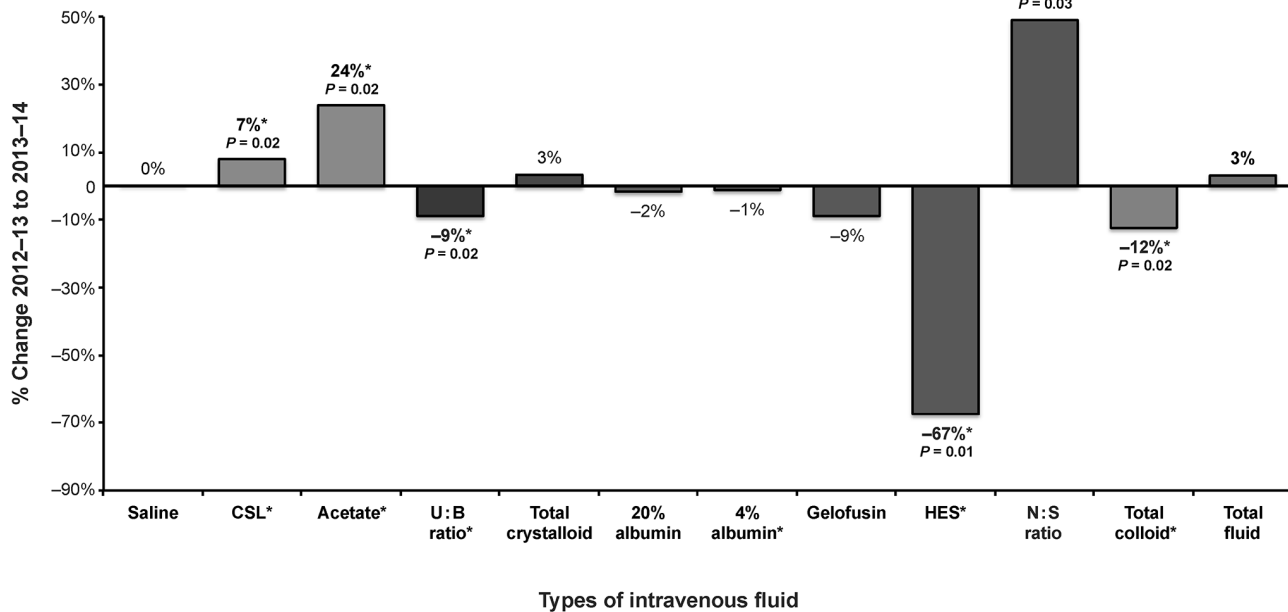


A. 20% albumin = 20% human albumin solutions. **B.** 4% albumin = 4% human albumin solutions. **C.** Gelofusins = 4% succinylated gelatin solutions. **D.** Starch = 6% hydroxyethyl starch + 10% pentastarch. 13 = 2012–2013. 14 = 2013–2014. * NZ = New Zealand. AUS = Australia. ACT = Australian Capital Territory. NSW = New South Wales. QLD = Queensland. WA = Western Australia. SA = South Australia. TAS = Tasmania. NT = Northern Territory.

in Australia); 9.3% were gelatins (26.8% in New Zealand and 25.5% in Australia); and 4.9% were other solutions.¹¹ By comparison, the UK over the same period consumed 1.54 million units of colloid, 68% of which were gelatins.¹¹ An international cross-sectional study of fluid resuscitation in 391 intensive care units showed marked international variability in the types of fluid used in the acute care setting.⁶ Recent Australian and New Zealand studies of paediatric emergency physicians¹² and adult emergency physicians and intensivists¹³ also confirm that this inconsistency is likely to exist at an individual, as well as a regional, level. There is a marked paucity of information on the preferences of prescribing specialists outside these areas, although similar variability is likely to be present on general adult medical and surgical wards.^{14–18}

The use of balanced or buffered solutions is not new,^{19–24} but the administration of such quantities of salt had been of concern since the inception of IV fluid experimentation.²⁵ Recent evidence has highlighted the potential adverse physiological, and possibly clinical, effects of excess sodium²⁶ and chloride administration.^{10,27–31} The use of balanced solutions has been shown, on meta-analysis of small trials of surgical patients, to be safe and associated with an improved perioperative metabolic profile when compared with non-physiological solutions.³² To our knowledge, ours is the first high-level demonstration of a changing, widespread bi-national preference for balanced crystalloid fluids over saline, a finding that is consistent with recent reports of changing preferences for resuscitation fluids in ICUs in Australia and New Zealand.³³

Figure 4. Temporal percentage changes in overall fluid consumption by fluid type in Australia and New Zealand, 2012–2013 and 2013–2014



Relative difference between fluid consumption as measured by fluid sales, by fluid type, between 2012–13 and 2013–14. Saline = 0.9% sodium chloride solution. CSL = compound sodium lactate. Acetate = PlasmaLyte (proprietary acetated solution). U:B ratio = ratio of unbalanced to balanced crystalloid consumption. 20% Albumin = 20% human albumin solution. 4% Albumin = 4% human albumin solution. Gelofusine = 4% succinylated gelatin solution. HES = 6% hydroxyethyl starch. N:S ratio = ratio of natural (albumin) to synthetic (gelatin and starch) colloid consumption. * $P < 0.05$ for change over all regions between the two time points.

Colloid solutions have been used in acute care for a century³⁴ and there has long been controversy about their role.^{35–36} However, given the modern understanding of microvascular fluid dynamics,³⁷ the intravascular persistence of colloids is likely to be limited. It is also possible that fluid resuscitation itself may disrupt the glycocalyx, further altering the transvascular equilibrium in states of acute illness.³⁸ Clinical evidence has shown that replacement of colloids with crystalloids occurs with a 1:1.3 ratio instead of the 1:3 ratio that has been postulated by advocates of the traditional Starling hypothesis.⁵

We show that in Australia and New Zealand, the use of colloid solutions is falling,³³ primarily due to decreased consumption of starch-containing fluids in response to large, randomised controlled trials conducted in Australia and New Zealand,³⁹ and elsewhere,^{40,41} showing harm.⁴² For the first time, we show the effect of these studies in real terms across the entire health service as evidence of translation of research into widespread practice.

Study implications

Our findings imply that there are unexplained major regional practice variations in the use of fluids. Acetated solutions, albumin solutions, and 6% HES solutions, in particular, show massive regional variation in consumption over the periods

of the study, with threefold differences within Australia and up to sixfold differences between Australia and New Zealand. This implies that regional factors overcome evidence-based considerations.^{39,42,43}

The ratio of unbalanced to balanced crystalloid use is falling in every region, which implies that there is a widespread shift away from saline use. This shift, involving millions of litres and probably thousands to millions of patient exposures, leads us to believe that large, double-blind, randomised controlled trials are needed to define whether such changes are justified.⁴⁴ New physiological solutions are in development for use in humans, and these will require extensive testing before being introduced.⁴⁵

Finally, the significant reduction in the sale of artificial colloid solutions and the two-thirds decrease in the consumption of starch solutions show that clinicians do respond to high-quality evidence when present. These changes are also high-level, bi-national evidence of translation of research into practice. They also show the impact and value of the National Health and Medical Research Council-funded Crystalloid versus Hydroxyethyl Starch Trial (CHEST) in driving practice change, with the 20 000 L decrease in starch use leading to approximately \$460 000 in annual savings in health care expenditure in Australia alone.^{39,42}

Table 4. Changes in fluid consumption in Australia and New Zealand between 2012–2013 and 2013–2014, by fluid type, estimated by sales per capita

Region	Crystalloid solutions*				Colloid solutions							
	Saline†	CSL	Acetate‡	U:B§	Total crystalloids	20% albumin¶	4% albumin**	Gelofusine††	Starch‡‡	N:S§§	Total colloids	Total fluids
NZ	+13.6%	+25.0%	+14.3%	-5.0%	+16.3%	+10.0%	+12.2%	-26.0%	-38.5%	+66.7%	-21.5%	+15.5%
Australia	-2.2%	+6.6%	+33.3%	-9.3%	+1.4%	-1.5%	+0.6%	-6.1%	-78.8%	+46.8%	-11.3%	+1.0%
ACT/NSW	-0.6%	+9.0%	+18.2%	-9.8%	+3.2%	0.0%	-6.2%	-14.6%	-60.6%	+57.7%	-15.4%	+3.2%
VIC	-7.5%	-2.1%	0.0%	-5.8%	-5.2%	-3.3%	+8.2%	-3.6%	-91.4%	+76.4%	-12.2%	-5.3%
QLD	-4.4%	+8.1%	+36.8%	-3.8%	+0.9%	-7.0%	+4.3%	+6.3%	-80.2%	+59.0%	-5.0%	+0.9%
WA	-1.9%	+6.9%	+33.3%	-8.7%	+2.4%	-4.4%	-1.8%	-4.1%	-88.4%	+24.4%	-14.7%	+1.9%
SA	+15.3%	+12.0%	+50.0%	+2.1%	+14.3%	+6.6%	-5.4%	-19.2%	-77.1%	+24.8%	-11.5%	+13.6%
TAS	-2.0%	+6.8%	0.0%	-8.2%	+1.3%	+21.1%	+3.5%	+27.1%	-92.9%	-5.1%	+6.9%	+1.4%
NT	+3.4%	+4.9%	+170.0%	-30.8%	+12.3%	+14.5%	-17.8%	-31.0%	na	+24.6%	-15.7%	+12.1%
Australia, NZ	0.0%	+7.9%***	+23.8%***	-8.9%***	+3.3%	-1.7%	+1.2%	-8.9%	-67.4%***	49.0%***	-12.4%***	+3.1%

CSL = compound sodium lactate. NZ = New Zealand. ACT = Australian Capital Territory. NSW = New South Wales. VIC = Victoria. QLD = Queensland. WA = Western Australia. SA = South Australia. TAS = Tasmania. NT = Northern Territory. na = not applicable. * Australian, NZ, and Australian + NZ crystalloid values adjusted to account for national sales to veterinary agencies. † 0.9% sodium chloride solution. ‡ PlasmaLyte (proprietary acetated solution). § Ratio of unbalanced to balanced crystalloid solution consumption. ¶ 20% human albumin solution. ** 4% human albumin solution. †† 4% succinylated gelatin solution. ‡‡ 6% hydroxyethyl starch + 10% pentastarch. §§ Ratio of natural (albumin) to synthetic (gelatin and starch) colloid consumption. *** $P < 0.05$ for change over time, across NZ, ACT/NSW, VIC, QLD, WA, SA, TAS, NT.

Limitations

Ours was an ecological study using census and government data, so had the limitations associated with this study design. We were unable to identify from this ecological data where these fluids were used, and there is likely to be significant variation between the fluids consumed in operating theatres and those consumed on the ward or in the emergency department or ICU. We do not know the factors that might have influenced the purchasing of fluids at a regional or individual hospital level, and the complexities of health care procurement make controlling for such factors nearly impossible. However, such factors may include emerging evidence, staff preference, changes in pricing or marketing strategy, and local or national changes in policy.

Given that we used proprietary sales data as a surrogate for actual use, our results may not accurately reflect the administration of fluids. However, it is unlikely that significant quantities of fluid are purchased but not used, and this methodology is unlikely to introduce significant bias. By using a per-capita rather than a per-hospital admission approach to consumption, and by correcting for veterinary sales where we were able to, we aimed to limit additional bias.

Conclusions

Ours was the first study of IV fluid sales as a surrogate of consumption at a bi-national level across two entire health services. We found that use was highly variable in Australia and New Zealand, with different crystalloid and colloid

solutions being used in different proportions and different total volumes in different regions in a seemingly chaotic fashion. We found major regional variations in consumption of acetated solutions, albumin solutions and 6% HES solutions in particular over the study period. A widespread increasing preference for balanced solutions over saline was suggested by the falling ratio of unbalanced to balanced crystalloid use. Finally, we showed significant reductions in the consumption of starch solutions, a finding that fits with recent concerns about its safety. Our findings provide an up-to-date, bi-national insight into this fundamental component of medical practice across health services; imply that there is a need for trials comparing balanced solutions with saline; and provide a benchmark for the assessment of translation of research into practice.

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Competing interests

The Avant Doctor in Training Research Scholarship Program funds Neil Glassford's research salary. Rinaldo Bellomo has received

unrestricted research grants from Baxter Healthcare. Craig French is the current co-chair of the National Blood Authority (NBA) Working Group, Patient Blood Management Guidelines and a member of the Australian Red Cross Blood Service (ARCBS) Advisory Committee. Johan Mårtensson has received travel grants from Gambro/Baxter International. Glenn Eastwood has no competing interests to declare.

Author contributions

Data integrity and accuracy: Neil Glassford had full access to all data in the study and is responsible for integrity and accuracy of data and analysis. Concept and design: all authors. Data acquisition: Glassford, Bellomo and French. Data analysis and interpretation: all authors. Drafting of the manuscript: Glassford, Bellomo and Bailey. Critical revision of the manuscript: all authors. Statistical analysis: Glassford, Bellomo and Bailey. Funding: Glassford and Bellomo. Administrative, technical or material support: Glassford, Eastwood and Bellomo. Study supervision: Glassford and Bellomo.

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