cRitical cAre opTimIzatiON of ALbumin ordEring (RATIONALE) in Alberta: A Critical Care SCN initiative.

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Objectives

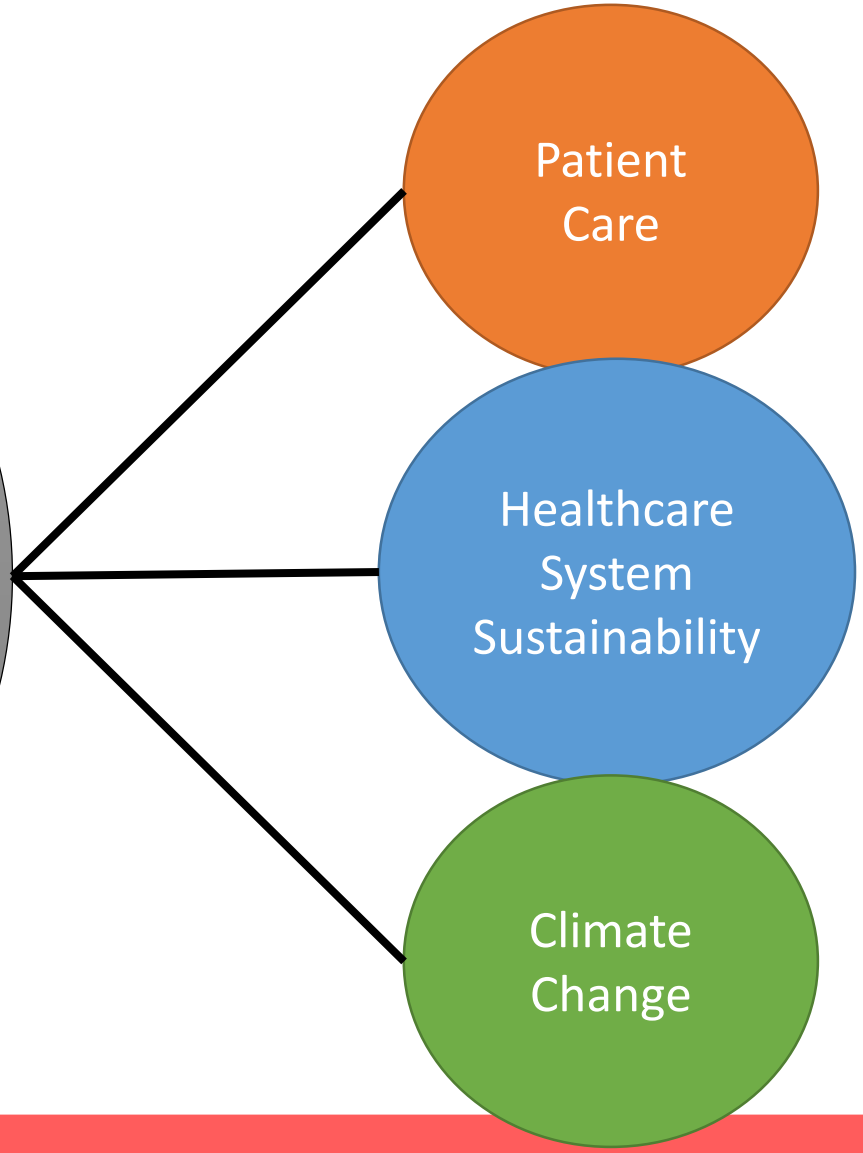
- To review the societal importance of reducing low-value care
- To review the evidence that underpins the use of albumin for fluid resuscitation – an exemplar low-value practice
- To introduce the RATIONALE study

What is Low-value Care?

- "An intervention in which **evidence suggests it confers no or very little benefit for patients**, or risk of harm exceeds probable benefit, or more broadly, the **added costs of the intervention do not provide proportional added benefits**."

Lancet 2017;390:191-202

Societal Importance of Reducing Low-value Care



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Patient Perspective

Example: Blood Product Use

- "As a potential recipient, I would only want to received blood if there were no other options because there are risks to receiving blood and I would want to ensure that blood is there for the people who really need it."

Anonymous blood donor, 2019

Blue Ribbon Panel

EDMONTON

'Alberta has a spending problem': Blue Ribbon Panel says health, education, public sector need change

Alex Antoneshyn Digital Journalist
@AAntoneshyn | Contact

Published Tuesday, September 3, 2019 11:11AM MDT
Last Updated Tuesday, September 3, 2019 6:40PM MDT

https://open.alberta.ca/dataset/081ba74d-95c8-43ab-9097-cef17a9fb59c/resource/257f040a-2645-49e7-b40b-462e4b5c059c/download/blue-ribbon-panel-report.pdf

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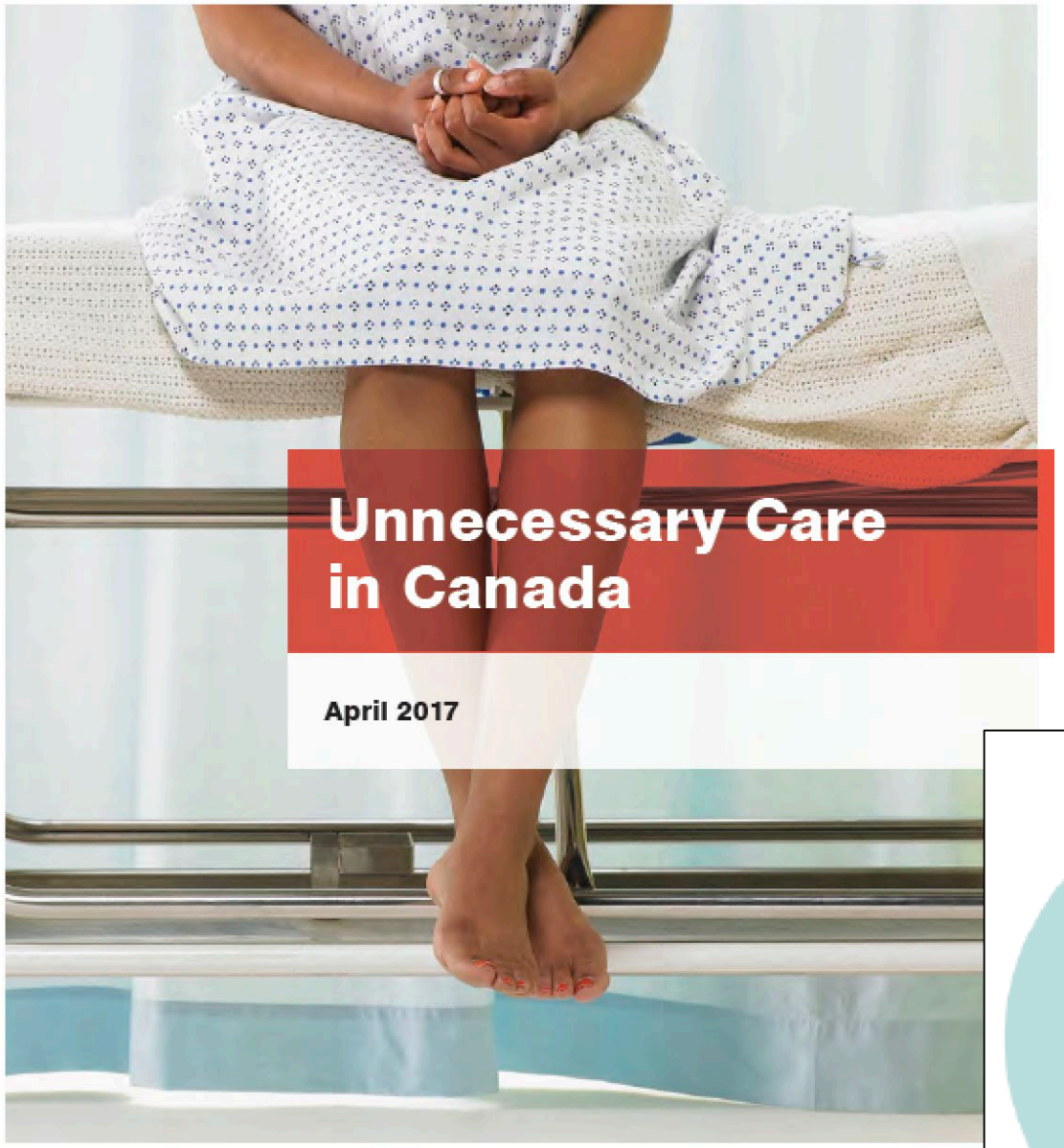

Unnecessary Care in Canada

April 2017

C3 Research Network

Canadians have

1 million+

potentially unnecessary medical tests and treatments each year.

of patients indicated in the 8 selected Choosing Wisely Canada recommendations had tests, treatments and procedures that **are potentially unnecessary**.

Choosing Wisely Canada™

Canadian Institute for Health Information
Institut canadien d'information sur la santé

Healthcare is responsible for ~5% global greenhouse gas emissions

RESEARCH ARTICLE

Life cycle environmental emissions and health damages from the Canadian hea… system: An economic-environme… epidemiological analysis

Matthew J. Eckelman[1], Jodi D. Sherman[2], Andrea J. MacNeill[3]*

How health care contributes to climate change

Cite as: *CMAJ* 2019 April 8;191:E403-4. doi: 10.1503/cmaj.109-5722

Posted on cmajnews.com on Mar. 19, 2019.

The 2019 report of The *Lancet* Countdown on health and climate change: ensuring that the health of a child born today is not defined by a changing climate

1. PLoS Med 2018;15:e1002623; 2. CMAJ 2019;191:E403-4; 3. Lancet 2019;394:1836-78

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Clinicaltrials.gov Identifier: NCT04187534

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Albumin is an Exemplar Low-Value Practice

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- **Albumin is a blood product** voluntarily donated by the public
- Commonly used intravenous fluid, however…
  - **STRONG EVIDENCE for NO BENEFIT** to albumin use in majority of patients, and HARM in others
- Inappropriate use puts **patients at risk** and contributes to **unnecessary healthcare spending** ($2.2M in Alberta in 2018)
- **Glass bottles and plastic tubing** contribute considerably to **unnecessary healthcare waste**

What Does Science Tell Us We SHOULD Do with Albumin?

Conditions with EVIDENCE of BENEFIT

- **Large-volume therapeutic paracentesis** (5L ascitic fluid or more)
  - Meta-analysis of RCTs: OR (mortality) 0.64 (95% CI 0.41 – 0.98)

- **Spontaneous bacterial peritonitis**
  - Meta-analysis of RCTs: OR (mortality) 0.34 (95% CI 0.19 – 0.60)

- **Therapeutic plasmapheresis**

1. Hepatology 2012;55: 1172 *2. Clinic Gastroenterol Hepatol*;2013;11: 123

Conditions with EVIDENCE of NO BENEFIT

- **Hypovolemia**
- **Sepsis**
- Traumatic brain injury (HARM – increased mortality)
- Acute ischemic stroke (HARM – increased ICH, pulm edema)

No Benefit in Patients with Hypovolemia

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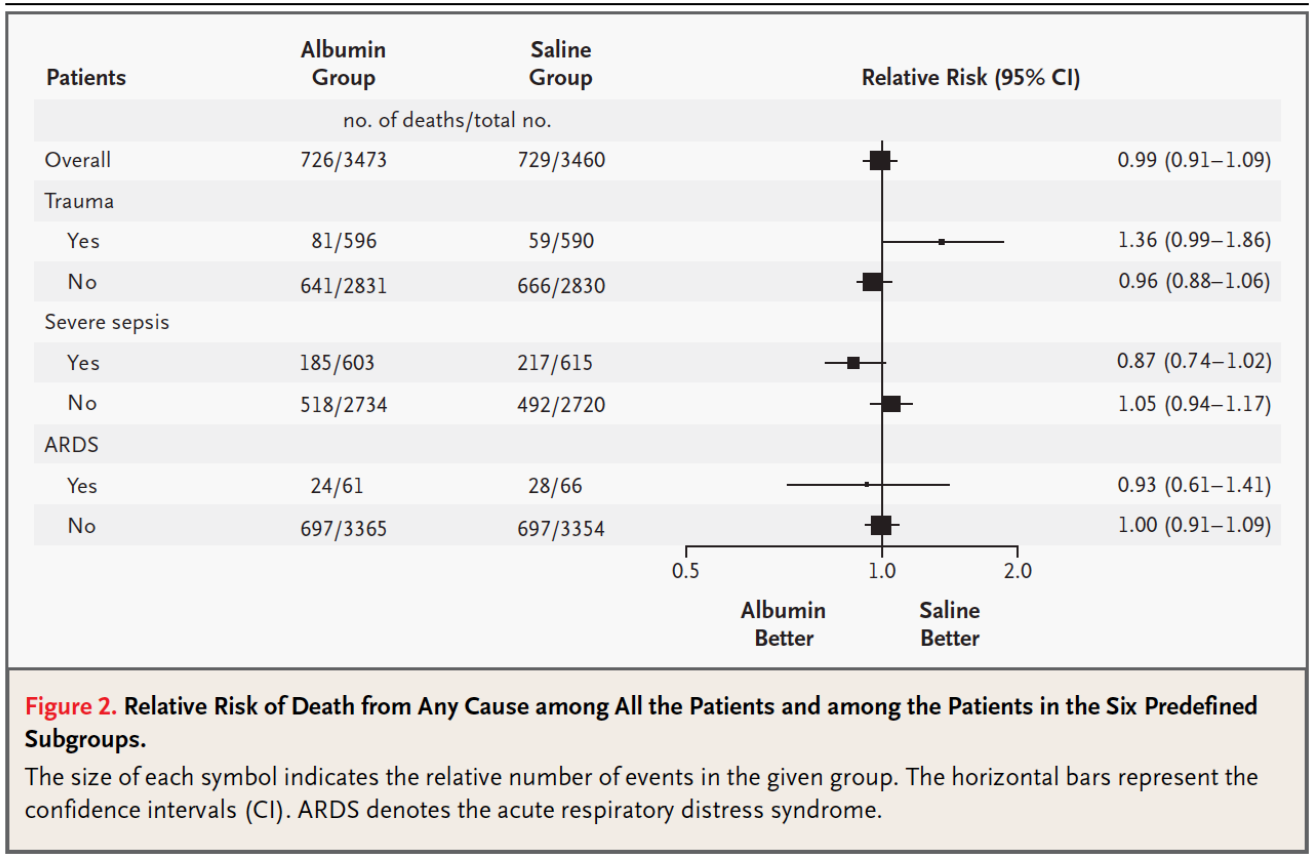
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

A Comparison of Albumin and Saline for Fluid Resuscitation in the Intensive Care Unit

The SAFE Study Investigators*



Patients	Albumin Group	Saline Group	Relative Risk (95% CI)
	no. of deaths/total no.		
Overall	726/3473	729/3460	0.99 (0.91–1.09)
Trauma			
Yes	81/596	59/590	1.36 (0.99–1.86)
No	641/2831	666/2830	0.96 (0.88–1.06)
Severe sepsis			
Yes	185/603	217/615	0.87 (0.74–1.02)
No	518/2734	492/2720	1.05 (0.94–1.17)
ARDS			
Yes	24/61	28/66	0.93 (0.61–1.41)
No	697/3365	697/3354	1.00 (0.91–1.09)

Figure 2. Relative Risk of Death from Any Cause among All the Patients and among the Patients in the Six Predefined Subgroups.

The size of each symbol indicates the relative number of events in the given group. The horizontal bars represent the confidence intervals (CI). ARDS denotes the acute respiratory distress syndrome.

NEJM 2004;350:2247-56

What About Patients with Sepsis?

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ORIGINAL ARTICLE

Albumin Replacement in Patients with Severe Sepsis or Septic Shock

Pietro Caironi, M.D., Gianni Tognoni, M.D., Serge Masson, Ph.D., Roberto Fumagalli, M.D., Antonio Pesenti, M.D., Marilena Romero, Ph.D., Caterina Fanizza, M.Stat., Luisa Caspani, M.D., Stefano Faenza, M.D., Giacomo Grasselli, M.D., Gaetano Iapichino, M.D., Massimo Antonelli, M.D., Vieri Parrini, M.D., Gilberto Fiore, M.D., Roberto Latini, M.D., and Luciano Gattinoni, M.D., for the ALBIOS Study Investigators*

- **1818 adult patients with sepsis randomized to 20% albumin and crystalloid OR crystalloid alone**
- **Open-label RCT targeting [albumin] >= 30 g/L in intervention group**
- **Primary outcome: 28-day mortality**

NEJM 2014;370:1412-21

- **Albumin group had significantly better physiology:**
  - Higher MAP
  - Lower HR
  - Higher [albumin]
  - Lower daily net fluid balance

- **No difference in survival**

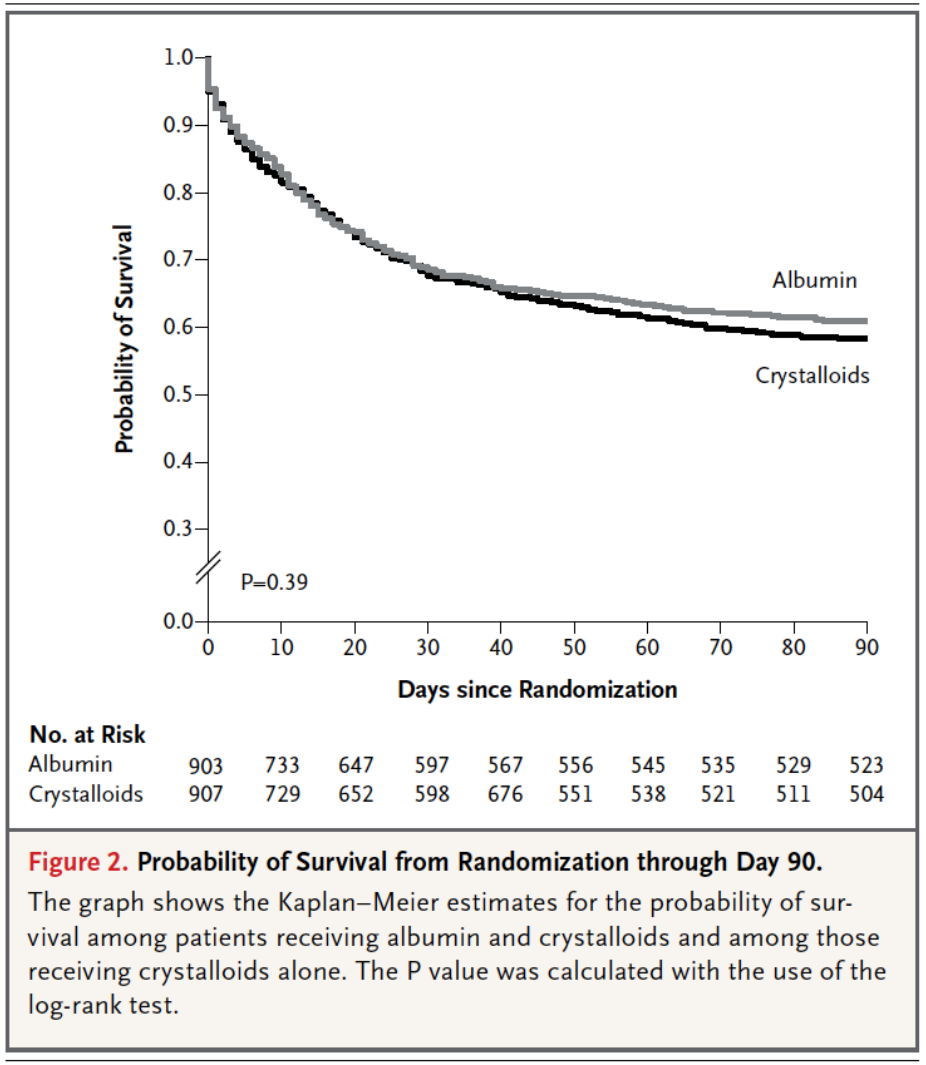

Figure 2. Probability of Survival from Randomization through Day 90.
The graph shows the Kaplan–Meier estimates for the probability of survival among patients receiving albumin and crystalloids and among those receiving crystalloids alone. The P value was calculated with the use of the log-rank test.

NEJM 2014;370:1412-21

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NEJM 2014;370:1412-21

Why Limited Effect of Albumin on Clinical Outcomes?

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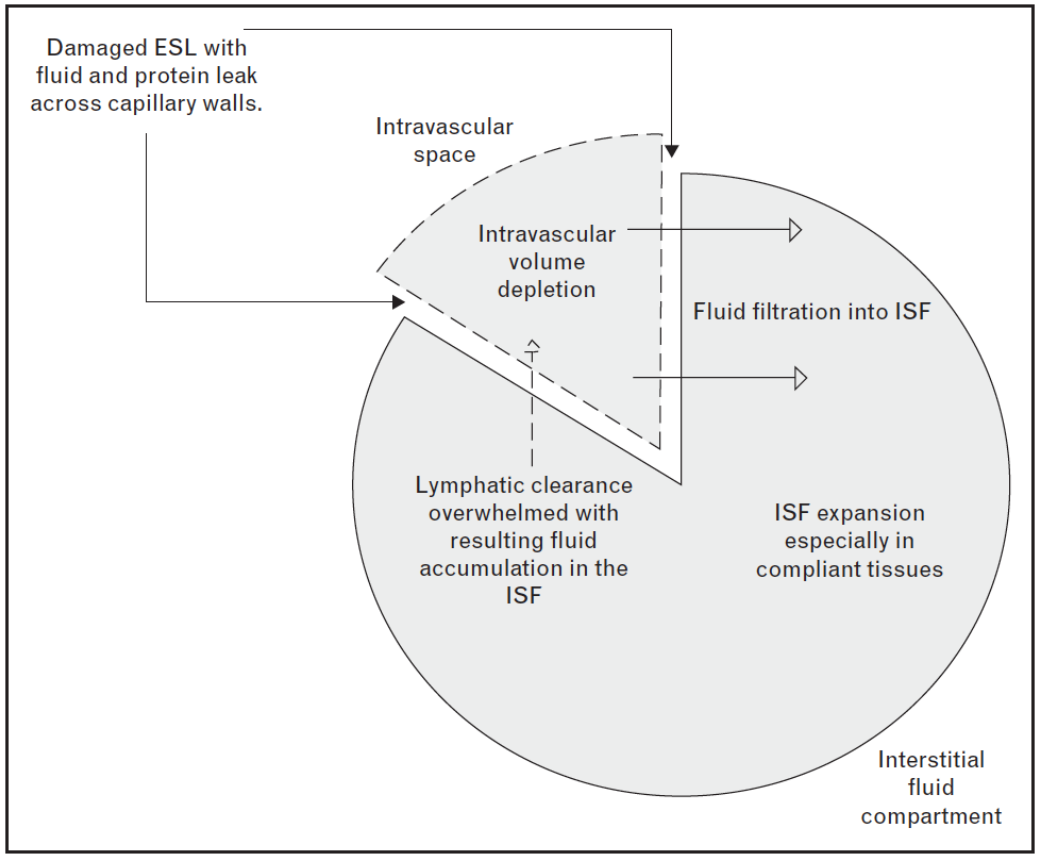
- **Endothelium is compromised** during any systemic inflammatory state (infection, injury, etc.)
- **Increased vascular permeability** and **escape of albumin** into tissues
- Fluid accumulates in compliant interstitial spaces (lung, muscle, skin, GI)



Curr Opin Crit Care 2012;18: 350

Hydroxyethyl Starches Provide Proof of Systemic Inflammation and Colloidal Leak…

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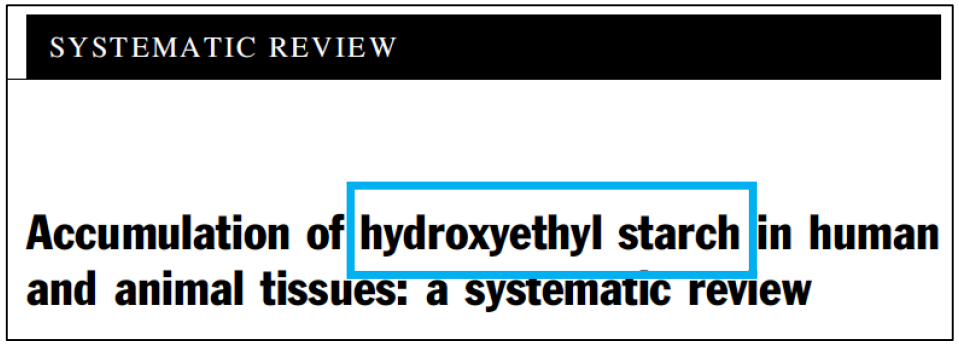
SYSTEMATIC REVIEW

Accumulation of hydroxyethyl starch in human and animal tissues: a systematic review

- 37 human studies; **635 patients**
- Most common sites of HES deposition – skin, **kidneys**, liver, bone marrow
- **HES deposition proportional to dose, but also seen at lowest doses**

Intensive Care Med 2014;40: 160

If HES Leaks into Tissues, Why Can't Albumin?

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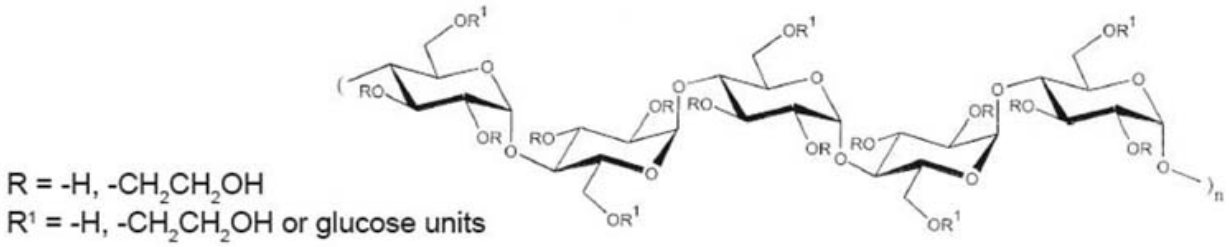
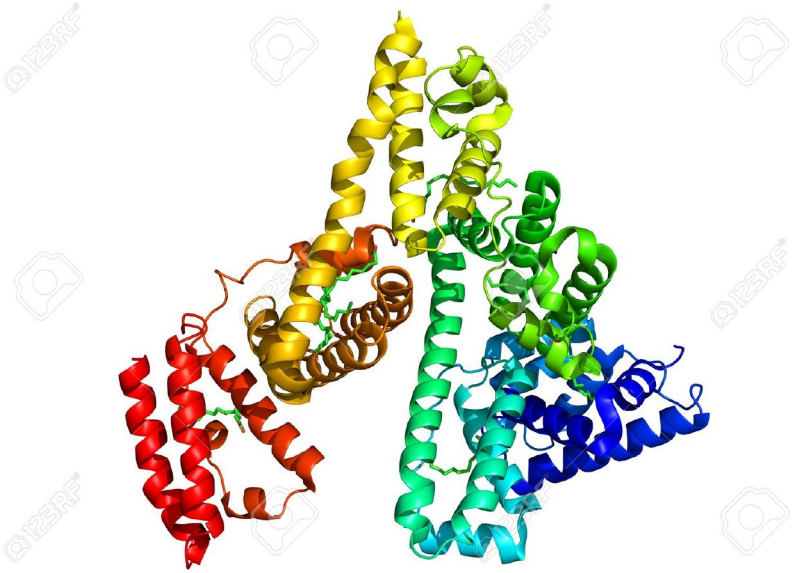
Voluven: 6% HES (130/0.4)
Mean MW = 130,000 Da



Albumin
Mean MW = 65,000 Daltons



Conditions where EVIDENCE is LESS CLEAR

- **Hepatorenal syndrome**
- **Diuretic resistance and hypovolemia**
- ARDS
- Burns
- Post-op cardiac surgery

Diuretic Resistance and Hypoalbuminemia

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Co-administration of furosemide with albumin for overcoming diuretic resistance in patients with hypoalbuminemia: A meta-analysis ☆

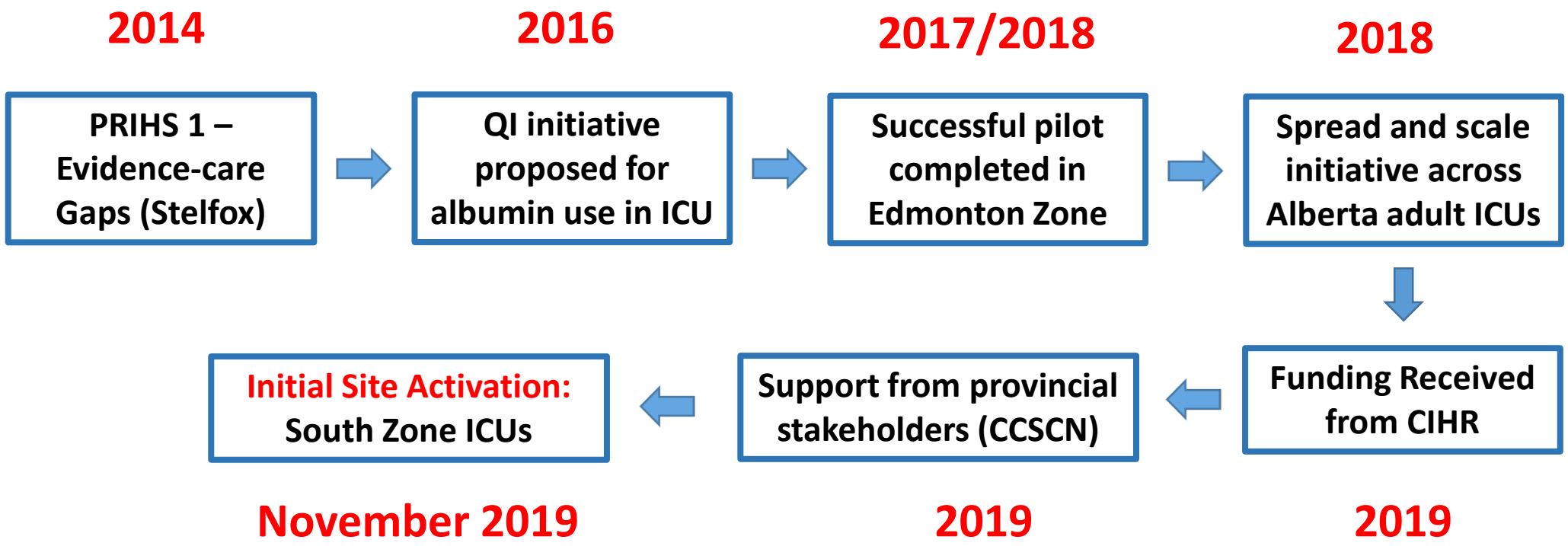
Georgios D. Kitsios, MD PhD [a,b,*], Paolo Mascari, MD PharmD [a], Riad Ettunsi, MD MSc [a], Anthony W. Gray, MD [a]

- 8 RCTs, n = 96 patients included in data synthesis
- 5 of 8 studies focused on nephrotic syndrome

- **231cc increased urine volume after 8 hours NOT maintained at 24h**

J Crit Care 2014; 29:253

The Making of RATIONALE



Successful Pilot Initiative in Edmonton ICUs

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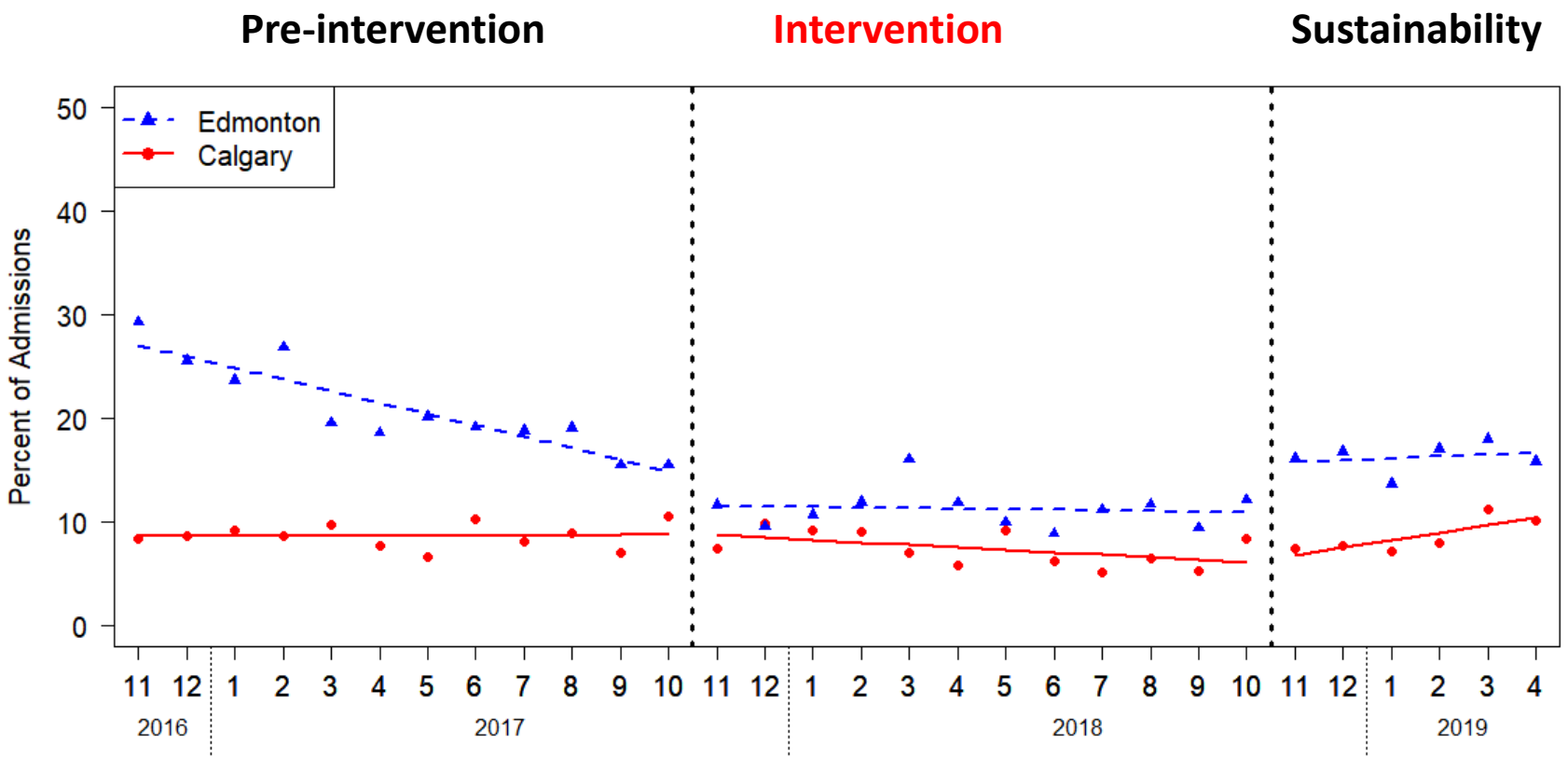
- **Similar multi-modal QI intervention**
  - Implemented in 6 Edmonton Zone adult ICUs in November 2017
  - 5 Calgary Zone adult ICUs served as controls

- **Controlled interrupted time series analysis**

- **eCritical served as the 'registry' for data**
  - Analytic population = adult ICU admissions without an evidence-based indication for albumin fluid resuscitation (TPE, SBP, therapeutic paracentesis)

  - Primary outcome = proportion of study population that received at least 1 unit of albumin

Primary Outcome: Albumin Pilot Initiative



Intervention ICUs: 47% RR in any albumin use

Control ICUs: 14% RR in any albumin use

Data analyses courtesy Dr. Andrea Soo

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RATIONALE - Methods

- **Setting:** 16 adult ICUs in Alberta
- **Population:** All adult patients admitted to study ICUs
- **Design:** registry-based, stepped-wedge quality improvement intervention trial

- **Quality improvement intervention (KT piece)**
  - Co-developed by working group members; tailored to target ICUs

- **Primary Outcome:** proportion of patients without evidence-based indication for albumin who receive ≥ 1 unit of albumin during ICU

Clinicaltrials.gov Identifier: NCT04187534

Multi-modal QI Intervention

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- **Tailored to specific barriers/facilitators**
  - **Clinical champions:** within each ICU, working group discussions
  - **Education:** departmental rounds; education to residents, RNs; education tools provided to units (CNEs, websites, posters)
  - **Process change:** develop/modify **order sets** specific to albumin
  - **Audit and feedback:** monthly basis for 1-year post-intervention, facilitated feedback sessions with PLP
  - **Sustainability:** support for specialty training content updates

- **Design: s**tepped-wedge quality improvement intervention

Clinicaltrials.gov Identifier: NCT04187534

Albumin Order Sheet

Indication sections

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Albumin Indication and Evidence Summary:

Condition	Summary	References	Recommendation
Conditions for which albumin has Evidence of BENEFIT			
☐ Large-volume therapeutic paracentesis (Greater than or equal to 5L ascitic fluid)	Decreased mortality	Meta-analysis: Hepatology 2012;55:1172	***Concentration:*** 25% ***Amount:*** 100-150 cc for first 5L, then 25cc for each additional liter
☐ Spontaneous bacterial peritonitis	Decreased mortality	Meta-analysis: Clinic Gastroenterol Hepatol 2013;11:123	***Concentration:*** 25% ***Amount:*** 1.5g/kg day 1; 1.0g/kg day 3
Conditions for which albumin has Evidence of NO BENEFIT			
☐ Hypovolemia	No effect on morbidity or mortality	SAFE study: NEJM 2004;350:2247 Meta-analysis: Cochrane Database Syst Rev 2011;11:CD001208	Recommend not using
☐ Sepsis	No effect on morbidity or mortality	ALBIOS study: NEJM 2014;370:1412 Meta-analysis: BMJ 2014;349:g4561	Recommend not using
☐ Traumatic Brain Injury	Increased mortality	SAFE-TBI study: NEJM 2007;357:874	Avoid use
☐ Acute Ischemic Stroke	Increased morbidity	ALIAS 1 and 2 studies: Stroke 2016;47:2355	Avoid use
Conditions for which Evidence is LESS CLEAR			
☐ Hepatorenal syndrome	Improved renal function	1 prospective, non-randomized study: Hepatology 2002;36:941	None
☐ Post-operative liver transplantation	Unclear effect	No RCTs; small observational studies with conflicting results	None
☐ Burn resuscitation	Possibly increased mortality	Meta-analysis 4 small RCTs, 205 patients: Cochrane Database Syst Rev 2011;11:CD001208	None
☐ Post-operative cardiac surgery	Unclear effect	2 RCTs conflicting results: BJA 2014;112:255; Anesthesiology 2016;124:1001	None
☐ ARDS	Unclear effect	2 small RCTs, albumin co-administered with furosemide infusion improved P/F Crit Care Med 2002;30:2175 Crit Care Med 2005;33:1681	None
☐ Other* *(Describe)*: _____ _____ _____			

*There may be other clinical circumstances not adequately examined in existing research wherein the most responsible physician may feel albumin is indicated. Please indicate here.

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Albumin Order Sheet – Cost/Order Section

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Fluid Resuscitation Costs (AHS 2019)

Albumin		Crystalloid	
Concentration, volume	Cost per bottle	Type	Cost per bag
25%, 100 mL (25 grams)	$59.91	0.9% Saline (500 mL)	$1.21
25%, 50 mL (12.5 grams)	$29.96	0.9% Saline (1000 mL)	$1.30
5%, 500 mL (25 grams)	$59.91	Ringer's lactate (1000 mL)	$1.66
5%, 250 mL (12.5 grams)	$29.96	Plasmalyte A (1000 mL)	$1.87

Albumin Prescription:

Concentration and volume per bottle: ☐ 5%, 250 mL ☐ 25%, 100 mL ☐ Other _____

Number of bottles: _____ (total) Frequency: _____ (e.g. Once, q6h)

Physician Signature _____ Date/Time: _____

20965 (Rev2019-10)

Audit and Feedback

- **Bi-monthly feedback** on albumin utilization at 'ICU-level'
- Albumin administration data obtained from eCritical
- Facilitated feedback session with Physician Learning Program, **following intervention implementation**

Intervention Goals

- **50% relative reduction in evidence-incongruent albumin use** by end of intervention
- Estimated to **save approximately $350,000* annually** in actual healthcare dollars (*likely underestimate…)
- **Develop and test infrastructure for future Provincial ICU appropriateness initiatives**…

Take Away Points

- We have a duty to be **responsible stewards of healthcare resources** – patients, healthcare systems, climate change
- Albumin fluid resuscitation represents an excellent place to test a system for appropriateness initiatives in Alberta ICUs (**RATIONALE**)
- Let's begin the 2020s by **decreasing care practices we know to be low-value**, studying the effects of those we think may be low-value, and design **systems of care that enable not inhibit evidence-based care**

Acknowledgements

- **Personnel:**
  - RATIONALE working group and steering committee members
  - **YOU for your attendance today and willingness to participate in this initiative**

- **Infrastructure:** Critical Care Strategic Clinical Network; all adult critical care units in Alberta, Physician Learning Program

- **Funding:** Canadian Institutes of Health Research; Critical Care Strategic Clinical Network