5 TOP PAPERS
IN CRITICAL CARE

Dr. David Lyness
Anaesthetist & Intensive Care Doctor
Belfast, Northern Ireland

EDUCATION IN ANAESTHESIA, CRITICAL CARE AND PAIN MEDICINE

propofology.com

ICU STUDIES FROM 2017

CHECK OUT WWW.THEBOTTOMLINE.ORG.UK FOR THE FULL REVIEWS & ROUND UP

www.propofology.com

TRICS-3

restrictive vs liberal red-cell transfusion in for cardiac surgery
This study adds to the growing body of evidence that restrictive transfusion protocols are not harmful in critically ill patients

SEYMOUR

In patients with severe sepsis or septic shock, does a faster time to completion of a 3 hour bundle of care, compared with a slower time, affect in hospital mortality? = Yes, a delay in the 3h bundle of care, increased mortality in a large cohort of patients

PRESERVE

Outcomes after Angiography with Sodium Bicarbonate and NAC
Sample = predominantly male patients with diabetes and chronic renal failure. The administration of sodium bicarbonate +/- NAC did not prevent the occurrence of major adverse events

DET02-AMI

Oxygen Therapy in Suspected Acute Myocar
This large MCRCT shows that supplemental ox
difference to outcomes in normoxic patients w
– other studies show trend to harm = use not

ATHOS 3

Angiotensin II for the Treatment of Vasodilator
Yes – it increased blood pressure
It will likely beco
More trials nee

TRANSFUSE

Age of Red
There is no
Also confir
the blood b

ICE-CUB 2

ICU patients ag
systematic ICU
Increased ICU
In-hospital mor

INPRESS

Individualized vs Sta
Organ Dysfunction A
Targeting individualis
undergoing surgery

ART

Effect of Lung Recruitment and T
PEEP on Mortality in Patients Wit
Confirms protective lung ventilati
and that an open lung approach w

SSP2

Effect of an Early Resuscitation
Sepsis and Hypotension.
Consistent with previous studies
appeared to be **harmful** in **Africa**
Alas, cannot translate well into a

ICU TRIALS part four

a compilation of

TRIAL
Bystander Efforts and 1-Year Out Cardiac Arrest
Effect of early tranexamic acid ad hysterectomy, and other morbidit partum haemorrhage (WOMAN): a randomised, double-blind, placeb
Reversal of trauma-induced coag coagulation factor concentrates (RETIC): a single-centre, parallel- randomised trial
Safety and Efficacy of Antiviral Th Cytomegalovirus Reactivation in Critically Ill Patients
Stress-Dose Corticosteroid Versu Cardiac Operations: A Randomize
Association of Postoperative High Levels With Myocardial Injury and Patients Undergoing Noncardiac
Immunoglobulin G for patients wi infection (INSTINCT)
Effect of Ularitide on Cardiovascu Failure
Intermittent noninvasive ventilatio patients with chronic respiratory randomized controlled trial (VHYP
Effects of restricting perioperative chloride on kidney injury in patien surgery: the LICRA pragmatic cor
Levosimendan for Hemodynamic Surgery
Effect of Intensive vs Moderate A Strategies Added to Lung-Protect Postoperative Pulmonary Compli
Effect of Dexmedetomidine on M Days in Patients Requiring Mecha Sepsis
Early, Goal-Directed Therapy for S Level Meta-Analysis

ICU TRIALS part three

a compilation of so

TRIAL
Safety of mechanical chest compressio devices AutoPulse and LUCAS in cardia arrest: a randomized clinical trial for no inferiority
Feasibility and Safety of Mild Therapeuti Hypothermia in Poor-Grade Subarachno Hemorrhage: Prospective Pilot Study
Efficacy and Safety of Combination The of Shenfu Injection and Postresuscitatio Bundle in Patients With Return of Spontaneous Circulation After In-Hospit Cardiac Arrest: RCT Assessor-Blinded
Effect of Depth and Duration of Cooling Death or Disability at Age 18 Months An Neonates With Hypoxic-Ischemic Encephalopathy
Early Use of N-acetylcysteine With Nitra Therapy in Patients Undergoing Primary Percutaneous Coronary Intervention for Segment–Elevation Myocardial Infarctio Reduces Myocardial Infarct Size (NACIA
Effectiveness of an exercise programme physical function in patients discharged hospital following critical illness: a randomised controlled trial (the REVIVE
Effect of Abdominal Ultrasound on Clini Care, Outcomes, and Resource Use Am Children With Blunt Torso Trauma
Randomized Trial of Icatibant for Angiot Converting Enzyme Inhibitor–Induced U Airway Angioedema
High-Flow Nasal Cannula Versus Conventional Oxygen Therapy in Emerg Department Patients With Cardiogenic Pulmonary Edema: RCT
A randomized trial of supplemental pare nutrition in underweight and overweight critically ill patients: the TOP-UP pilot tr
Intraoperative Infusion of Dexmedetomi for Prevention of Postoperative Delirium Cognitive Dysfunction in Elderly Patients Undergoing Major Elective Noncardiac Surgery
Discriminative Accuracy of Physician an Nurse Predictions for Survival and Func Outcomes 6 Months After an ICU Admis
A Multicenter, Randomized Trial of Ramped Position vs Sniffing Position During Endotracheal Intubation of Critic Adults
A pilot, prospective, randomized trial of

ICU TRIALS part two

a compilation of so

TRIAL
Enteral nutrition as stress ulcer proph critically ill patients: A randomized co exploratory study
Quality sleep using earplugs in the int the QUIET pilot randomised controlled
Continuous versus intermittent neuro blockade in patients during targeted t management after resuscitation from A randomized, double blinded, double trial
Effect of Ganciclovir on IL-6 Levels An Cytomegalovirus-Seropositive Adults Illness
Selepressin, a novel selective vasopre agonist, is an effective substitute for n in a phase IIa randomized, placebo-co septic shock patients
Prevention of Exposure Keratopathy i Patients: A Single-Center, Randomized Comparing Ocular Lubrication With Ba Lenses and Punctal Plugs
Intensive versus standard physical reh therapy in the critically ill (EPICC): a m parallel-group, randomised controlled
Targeted Temperature Management fo Hours and Neurologic Outcome After Cardiac Arrest
Evaluation of early administration of si the prevention and treatment of deliriu patients undergoing mechanical ventil a randomised, double-blind, placebo-c
The effect of low-dose furosemide in c patients with early acute kidney injury: randomized blinded controlled trial (th
Procalcitonin-guided decision making antibiotic therapy in neonates with sus onset sepsis: a multicentre, randomise trial (NeoPIns)
Non-invasive ventilation versus invasiv ventilation in patients with hypoxemic respiratory failure in an Intensive Care randomized controlled study
Efficacy and Safety of Spironolactone Failure - The ATHENA-HF Randomized
Faster Blood Flow Rate Does Not Impr in Continuous Renal Replacement The Randomized Controlled Trial

ICU TRIALS part one

a compilation of so

TRIAL
EAT-ICU Early goal-directed nutrition standard of care in adult inte care patients.
Early application of airway pr release ventilation may reduc duration of mechanical ventil in acute respiratory distress syndrome
Reconnection to mechanical ventilation for 1 h after a succ spontaneous breathing trial reduces reintubation in critic patients: MCRCT
Biomarker-based strategy fo discontinuation of empirical antifungal treatment in critica patients: RCT
MCRCT of lateral Trendelenb versus semirecumbent body position for the prevention of ventilator-associated pneum
Guidelines for the diagnosis management of critical illnes related corticosteroid insuffic (CIRCI) in critically ill patients
Immediate interruption of se compared with usual sedatio in critically ill postoperative patients (SOS-Ventilation): a randomised, parallel-group c trial
Nebulized Versus IV Amikacin Adjunctive Antibiotic for Hos and Ventilator-Acquired Pneu Postcardiac Surgeries: RCT
Transfusion Requirement in C Care Evaluation (TRIBE): A Multicenter Randomized Prospective Trial of Blood Transfusion in Major Burn Inj
Loxapine to control agitation weaning from mechanical ventilation
A pilot clinical trial of recomb human angiotensin-convertin enzyme 2 in acute respirator distress syndrome

For the actual reviews, refe
www.criticalcarereviews.
www.propofology.com

For the actual reviews, ref

THIS PRESENTATION IS AVAILABLE NOW
ON WWW.PROPOFOLOGY.COM/IAEM

+INFOGRAPHS
+SLIDES
+WEB LINKS

RETWEET & TALK ABOUT IT USING #18IAEM TO @GAS_CRAIC

SEE FULL DISCUSSIONS OF TRIALS AT WWW.PROPOFOLOGY.COM/IAEM

COI

NONE RELEVANT

#FOAMED

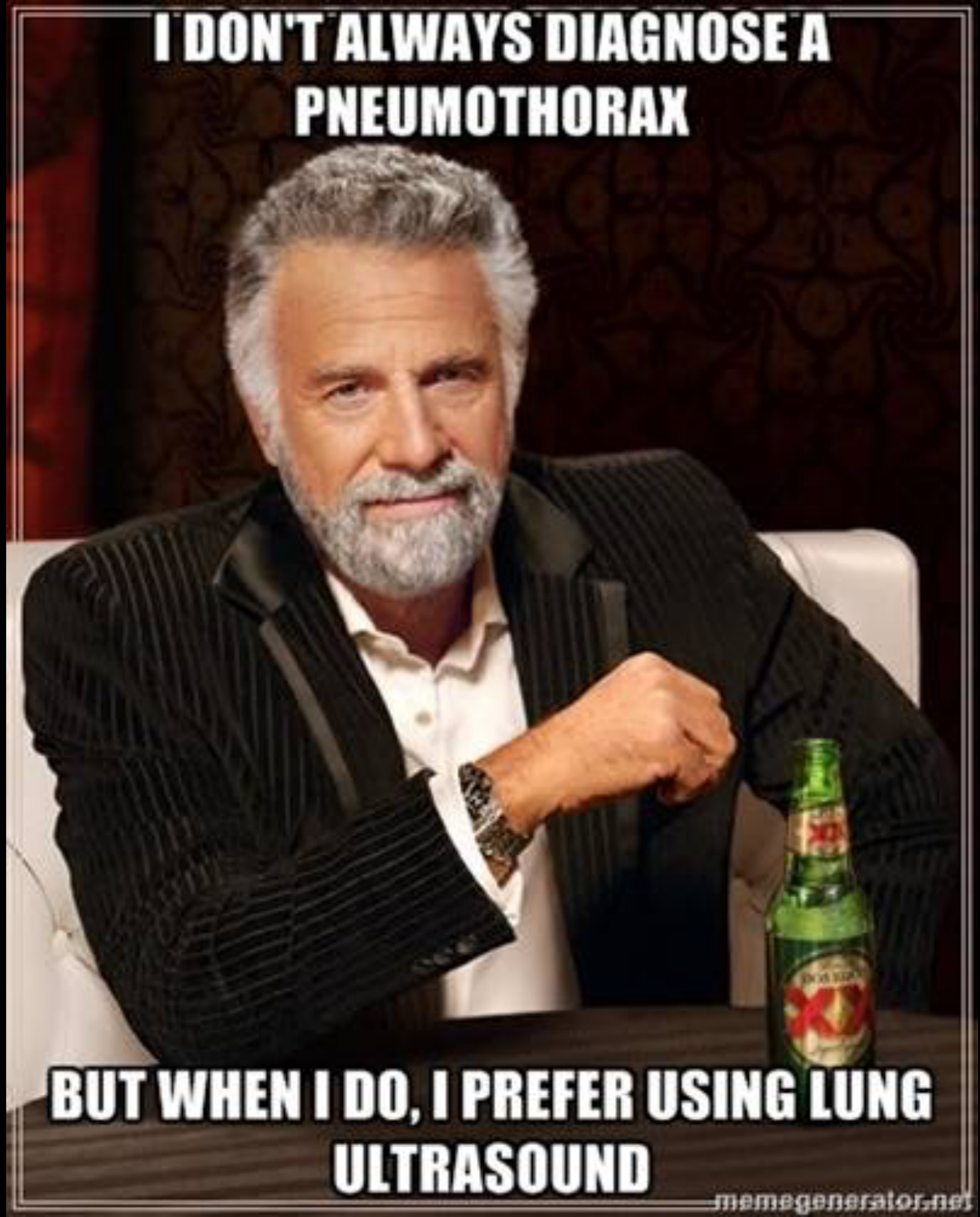
- FACULTY FOR EUROPEAN SOCIETY OF INTENSIVE CARE MEDICINE
- FOUNDING FACULTY OF COSMICC (SoMe) GROUP
- FACULTY OF INTERNATIONAL FLUID ACADEMY
- ONLINE SOCIAL MEDIA PROFILE = @GAS_CRAIC
- FOUNDER PROPOFOLOGY.COM
- NHS

in 20 mins

KETAMINE-

JUST SAY

NEIGH!!


I DON'T ALWAYS DIAGNOSE A PNEUMOTHORAX
BUT WHEN I DO, I PREFER USING LUNG ULTRASOUND
memegenerator.net

the papers

- personal preferences
- most influential
- most robust
- leading on to further study
- to highlight the INFOGRAPHICS

1. Paramedic-2
2. SHOC-ED
3. SALT-ED
4. BEAM (Bougie Study)
5. PAMP-ER

1. Paramedic-2

In adult patients with out-of-hospital cardiac arrest does the administration of ADRENALINE compared to placebo improve survival?

YES!

Important?

This trial provides the largest set of randomised data to date addressing this topic.

PARAMEDIC2

NEJM July 2018

G.D Perkins et al.,

Only pts who needed Adrenaline were eligible

↓

This means if you had ROSC earlier you were excluded

8014 patients were included

3999 got placebo

4015 got adrenaline

ONLY 21% INCLUDED HAD INITIAL SHOCKABLE RHYTHM

THIS IS AN OUT OF HOSPITAL CARDIAC ARREST TRIAL

IT TOOK A MEDIAN TIME OF ~6min 40sec FOR AMBULANCE TO ARRIVE

65% were male

35% were female

ADRENALINE OR PLACEBO GIVEN IN A MEDIAN TIME OF 21 MINS

THE OVERALL SURVIVAL AT 30 DAYS WAS 2.8%

8014 people → 7790 Died

↓

224 LIVED

Placebo	Adrenaline
94 survivors	130 survivors

This means 36 more people were alive in adrenaline group at 30days

↓

PRIMARY OUTCOME!

So the odds ratio for survival in adrenaline group = 1.39 (1.08-1.82 p=0.02)

@whistlingdixie4

BUT WHAT DID SURVIVAL LOOK LIKE?

ADRENALINE GROUP

10%

n = 128 patients alive at hospital discharge (more survivors)

PLACEBO GROUP

n = 91 patients alive at hospital discharge (less survivors)

- severe DISABILITY
- MODERATE OR MODERATELY SEVERE DISABILITY
- NONE, NO SYMPTOMS OR NO SIGNIFICANT DISABILITY

TO PREVENT ONE DEATH AT 30 DAYS (IRRESPECTIVE OF NEUROLOGICAL OUTCOME YOU NEED TO TREAT **112** PATIENTS WITH ADRENALINE (this is the NNT)

THE NNT FOR BYSTANDER CPR IS JUST **15** PATIENTS

THE NNT FOR EARLY DEFIBRILLATION WHERE INDICATED IS JUST **5** PATIENTS

TLDR

- **Large, pragmatic, good trial**
- **OOHCA survival rates are abysmal**
- **Better access to defibs and bystander CPR needed**

Adrenaline improved survival but at the expense of poorer neurological outcome.

PARAMEDIC 2

Perkins et al., NEJM JUL 2018

DISTRIBUTION OF MODIFIED RANKIN SCALE AT 3 MONTHS *

Adrenaline Group

+ 3888 patients dead (97.5%)

Placebo Group

+ 3905 patients dead (98.1%)

No symptoms
NO significant, or
slight disability

moderate or
moderate
severe Disability

Severe Disability

*absolute patient numbers from table S3

Strengths

- Pragmatic design, large numbers, randomised patients
- Good internal validity due to rigorous methodology (less bias)
- Good external validity (generalisability)
  - Multiple ambulance services across UK
  - Balanced baseline characteristics
  - Analysis adjusted for measured covariates.

FRAGILITY INDEX….

The **fragility index** is a number indicating how many patients would be required to convert a trial from being statistically significant to not significant

Although statistically significant, the fragility index with respect to 30 day mortality is only 6.

- SEVEN patients randomised but **not included** in this primary outcome, **<u>it is possible that the statistical significance could be lost had these 7 been included in the analysis.</u>**

Patient Focused

Outcomes clinical and patient centred

- During design of trial 280 lay people were consulted on personal views
- Of these, 95% prioritised long-term survival with a favourable neurological outcome over short-term (hours – days) survival.

However…

- Primary outcome was mortality, not neurological outcome
- Power to detect meaningful differences in neuro outcome is low
- There was significant loss to follow-up for the secondary outcomes
  - 20 (18.2%) in the placebo group and 29 (18.2%) in the adrenaline group were lost at 3 months
    - May be attrition bias.

2. SHOC-ED

In selected non-trauma patients presenting to the ED with undifferentiated hypotension, does a standardised point-of-care ultrasound protocol, compared with usual care, improve 30 day or hospital survival?

AUTHORS SAID:

In ED patients with undifferentiated hypotension, the addition of a point of care ultrasound protocol **did not** translate to additional benefit.

SHOC-ED

Annals of Emergency Medicine
An International Journal

Atkinson PR et al
Ann Emerg Med. 2018 Oct;72(4):478-489

@wilkinsonjonny

Benefit of POCUS

- POCUS protocols are commonly used in the ER for initial management of undifferentiated hypotension
- Little published evidence for mortality benefit

Why look at this?

- Single centres report using POCUS in shock Mx with improvement in both diagnostic accuracy and mortality
- US directs changes in Mx in up to 50% of patients
- No multi centre prospective randomised control trials of POCUS in shock in the emergency department

Research Question

- Does Point-of-Care Ultrasonography Improve Clinical Outcomes in Emergency Department Patients With Undifferentiated Hypotension?

RCT

- International
- 6 centers
- N.America and S.Africa

Inclusion

- Hypotensive patients
  - Systolic BP <100mmHg
  - Shock index (systolic BP/HR) >1

Intervention

- Early POCUS + standard care
- Standard care without POCUS

Diagnoses recorded at 0 and 60mins

Primary Outcome

- Survival to 30 days or to hospital discharge

Secondary Outcomes

- Included initial treatment and investigations,
- Admissions
- Length of stay

- There were significant differences in final diagnoses in the North American and South African cohorts:
  - Much more sepsis in South African than in North American group (71% vs 42%)
  - More severe dehydration in North America vs South Africa(20% vs 3%)

Primary Outcome

270

136 POCUS | **134** Std Care

104 survived **76.5%** | **102** survived **76.1%**

Secondary Outcomes

- Median Vol fluid (1609ml vs 1683 ml)
- Hospital admission rates (81% vs 83%)
- Inotrope administration (12% vs 9%)
- CT scanning (26% vs 24%)
- ICU admission rates (18% vs 14%)
- ICU LOS (7.16 vs 5.14 days)

Higher mortality in South African sites but still no significant benefit from POCUS

CRITICALCARE NORTHAMPTON.COM
REVIEWING CRITICAL CARE, JOURNALS & FOAMed

PROBLEMS

1. CONVENIENCE SAMPLE
2. EXCLUDED DEFINITIVE DIAGNOSIS (AAA, ECTOPIC ETC)
3. >50% PATIENTS WITH OCCULT SEPSIS
4. TRIAL TERMINATED EARLY… thus…

PROBLEMS

347 assessed, 273 enrolled (138 POCUS, 135 Control)

Assuming a 30% baseline mortality, they needed a 400 sample size to provide 80% power to detect a 10% difference in primary outcome…

PROBLEMS….

1. **There is a difference between being ‘accredited’ and ‘accredited and confident’ with POCUS**

2. **Pragmatically, there will be large differences in practice (leading to CT etc)**

3. **No availability of images to review retrospectively….**

3. SALT-ED

Every day, over 1 million patients are administered IV fluids in hospital…. yet still a lack of evidence to favour one crystalloid over the other….

3. SALT-ED

In non-critically ill adult patients admitted to hospital from the ED, does the administration of a balanced crystalloid solution compared with normal saline, reduce hospital free days to day 28?

**“What’s Hartmann’s solution?
Is that the one you can’t give in sepsis?”**

- Anonymous Foundation Doctor

**“No, we absolutely don’t stock Hartmann’s.
That’s Surgical Fluid.”**

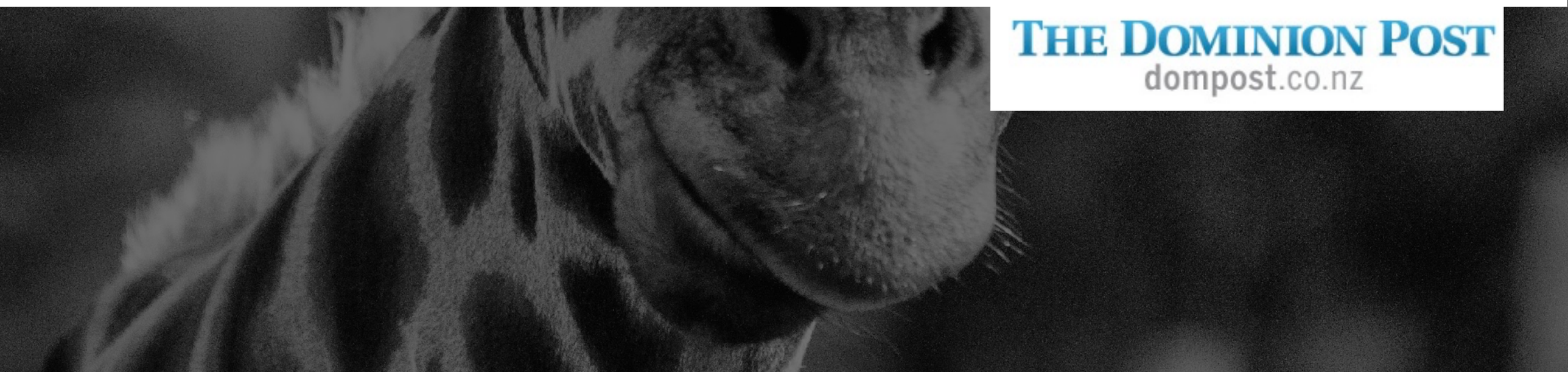
- Anonymous Medical Ward Staff

GOOD Q - CONFUSING AREA

- Sheer variety, variability and lack of senior stewardship
- 5% Dextrose? ‘NORMAL’ saline? CSL? Hartmann’s? Plasmalyte?
- A good starting question - highlights a lot of ‘fluid problems’…
- **Re-prescribing Syndrome**

Atomic Taniwha 9 hours ago

It's interesting isn't it. Last week I had a friend in hospital who came close to dying. They went in with a problem and were put on fluids. And fluids. And fluids. And fluids. They put on nearly 10Kg in 48 hours and no one was the wiser. In the end, my friend called her sister who couldn't find a doctor or nurse or anyone else would listen. Out of desperation she suggested that perhaps calling 111 would elicit a better response. Six staff promptly arrived and the problem was resolved. She had been in bed, sick, sweating, for 72 hours and the staff were not able to organise the basics of a shower.



THE DOMINION POST
dompost.co.nz

SINK OR SWIM?

A NEW IV FLUID PROTOCOL

Dr. Jonny Wilkinson & Dr. David Lyness

the propofology PODCAST

IV FLUIDS

DRUG, DOSE, DURATION & DE-ESCALATION

IV fluids are drugs, they must be dosed accordingly with a duration and plan for de-escalation.

Assess your patient using: clinical judgement, vital signs and fluid balance including urine output.

1. PATIENT'S VOLUME STATUS — HYPO/HYPER/EUVOLAEMIC
2. WHAT IS THE PATIENT'S WEIGHT? (WITHIN 4 DAYS)
3. U&E WITHIN PAST 24H — GET ONE!
4. INPUT/OUTPUT IN PAST 24H (BALANCE CHARTS)
5. CALCULATE

Hyponatraemia	Hypernatraemia	Hypokalaemia	Hyperkalaemia
Serum Na^+ < **135 mmol/L**	Serum Na^+ > **145 mmol/L**	Serum K^+ < **3.5 mmol/L**	Serum K^+ > **5.5 mmol/L**
Establish underlying cause of hyponatraemia. Correct hyponatraemia slowly to prevent complications. **SEEK SENIOR ADVICE** ***Seek expert advice before considering hypertonic saline (1.8% NaCl)***	Encourage oral intake if possible. Correct hypernatraemia slowly to prevent complications. **SEEK SENIOR ADVICE** Manage as per NGH guidelines on the intranet. **DO NOT USE FLUIDS CONTAINING SODIUM**	Check ECG for changes **MILD (3.0 – 3.4)** Sando-K 2 tablets TDS Kay Cee L 25ml TDS Check level in 3 days **MODERATE (2.5 – 2.9)** Sando-K 2 tablets QDS Kay Cee L 25ml QDS Check level in 3 days **SEVERE (<2.5)** IV Replacement using 40mmol KCl in fluids BD or TDS Check level the next days Check serum Mg^{2+} level	***MEDICAL EMERGENCY*** Assess using **ABCDE** approach Send VBG **AND** laboratory sample to confirm Check ECG for changes **MILD (5.5–5.9)** Repeat in 6 hours in unwell patients or daily if stable Review medications & diet **MODERATE/SEVERE (>6)** Give 10ml Calcium Gluconate 10% IV over 3-5 mins via large vein. Give 10units Actrapid IV in 100ml of 20% glucose over 15 – 30 mins. Give 10-20mg nebulised salbutamol. **SEEK SENIOR ADVICE** Manage as per NGH guidelines on the intranet

Resuscitation	Maintenance
Give a **STAT** crystalloid fluid bolus (up to 500ml in less than 30 minutes). Re-assess the patient using **ABCDE approach** and monitor **urine output**. If no response ➔ Repeat fluid bolus as above. If adequate response ➔ Initiate maintenance fluids and monitor the patient Re-assess the patient using **ABCDE approach.** If inadequate response **after 2000ml of fluid boluses** ➔ Escalate to a senior member of the team.	Normal daily IV fluid and electrolyte requirements: **IV Water Volume:** 1.25 ml/Kg/hr **Na*/K*/Cl-:** 1 mmol/Kg/day **Glucose:** 50 – 100 g/day **Urine Output:** 0.5 – 1 ml/kg/hr Review excess losses from fluid chart If patient requires IV fluids for more than 24 hours the patient will require **daily monitoring of U&E's**.

Fluid Status — Clinical Signs	
Hypovolaemia	**Hypervolaemia**
Thirst	
Hypotension (Systolic BP < 100)	
Tachycardia (HR > 90)	
Tachypnoea (RR > 20)	Peripheral oedema
Delayed capillary refill time (CRT > 2s)	Pulmonary oedema
Cold shutdown peripheries	Raised JVP
Reduced urine output (UO < 0.5 ml/kg/hr)	
Altered Urea: Creatinine ratio	

Dr. Jonny Wilkinson - Anaesthetics/ICU - Northampton, UK
Dr. David Lyness - Anaesthetics/ICU - Belfast, UK

ifa international fluid academy

propofology.com

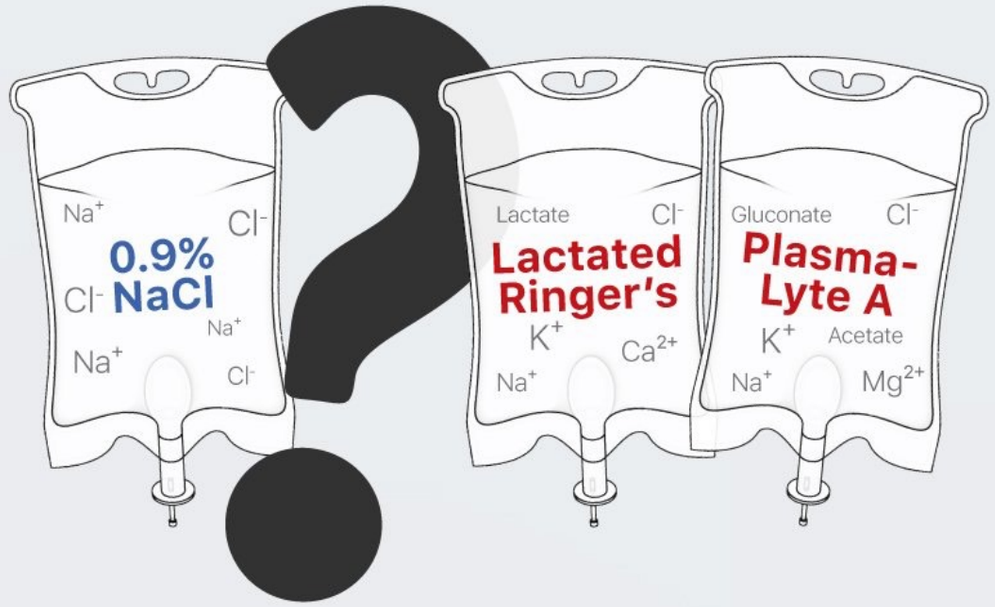
CriticalCareNorthampton.com

https://www.ncbi.nlm.nih.gov/m/pubmed/26575163/

infographic by Tommaso Scquizzato[1] @tscquizzato

Balanced Crystalloids vs. Normal Saline

Both balanced crystalloids and saline are used for intravenous fluid administration in critically and non-critically ill adults, but it is not known which results in better clinical outcomes.



in non-critically ill adults

SALT-ED trial[2]

single-center, pragmatic, multiple-crossover trial comparing balanced crystalloids with saline in adults admitted in the ED and hospitalized outside an ICU

13,346
adult patients enrolled in 16 months who received at least 500 ml of crystalloids

Balanced	Saline
6,708 ml	6,639 ml
Lactated Ringer's	

lower Cl^- and higher HCO_3^- concentrations
less episodes of hyperchloremia or acidemia

results

1. **Hospital-Free Days**
   days alive after discharge before day 28
   Balanced **25 days** / Saline
2. **MAKE30**
   Major Adverse Kidney Events at 30 days
   In-hospital mortality, new RRT and persistent renal dysfunction
   Balanced **4.7%** / Saline **5.6%**

AKI stage ≥ 2 and In-hospital mortality
Balanced ≈ Saline

conclusion

No difference in hospital-free days between treatment with BC and NS.

Stage ≥ 2 AKI patients or those with borderline renal failure or hyperchloremia had the largest benefit from balanced crystalloids.

in critically ill adults

SMART trial[3]

pragmatic, cluster-randomized, multiple-crossover trial comparing balanced crystalloids with saline in adults admitted in 5 ICU

15,802
adult patients enrolled in 16 months randomized to NS or BC

Balanced	Saline
7,942 ml	7,860 ml

- **34.3%** on ventilator
- **26.4%** on vasopressors
- **14.7%** are septic
- **8.8%** have TBI

results

1. **MAKE30**
   Major Adverse Kidney Events at 30 days
   In-hospital mortality, new RRT and persistent renal dysfunction
   Balanced **14.3%** / Saline **15.4%**
2. **In-hospital mortality**
   before ICU discharge or at 30 days
   Balanced **25.2%** / Saline **29.4%**

Receipt of new renal replacement therapy
Balanced **2.5%** / Saline **2.9%**

No difference in ICU-free days, ventilator-free days, vasopressor-free days, RRT-free days

conclusion

The use of balanced crystalloids resulted in a lower rate of MAKE30 than the use of saline.

The largest benefit appears to be in the septic subset of patients with a NNT of 20.

[1]Vita-Salute San Raffaele University, Milan - Faculty of Medicine and Surgery, contact at t.scquizzato@studenti.unisr.it
[2]Self WH et al. Balanced Crystalloids Versus Saline in Noncritically Ill Adults. NEJM 2018
[3]Semler MW et al. Balanced Crystalloids Versus Saline in Critically Ill Adults. NEJM 2018

appeared first on www.empillsblog.com empills

@WILKINSONJONNY

CRITICALCARE NORTHAMPTON.COM
REVIEWING CRITICAL CARE JOURNALS & FOAMED

The Issue

Intravenous isotonic crystalloids are commonly given in the ED, on hospital wards, intensive care units (ICUs), and operating rooms.

N Saline very commonly used!

- Supraphysiologic chloride concentration of saline may contribute to kidney injury and impair a patient's ability to recover from severe illness
- Hartmanns (109 mmol per liter) and Plasma-Lyte A (98 mmol per liter), are more similar to that of human plasma

NON-ICU Population?

- Multitude of comparator trials in ICU, few in acutely ill patients without organ failure or other critical illness
- Comprises a large patient population, routinely treated with intravenous fluids

The ED!

- Investigation into IV balanced solutions Vs IV N Saline among non-critically ill adults
- Hypothesis - balanced crystalloids would result in earlier hospital discharge and a lower incidence of major adverse kidney events than saline?

RCT

- Vanderbilt University Medical Center ED
- Pragmatic
- Unblinded
- Multiple-crossover trial

The Trial

Patients admitted to the ED received either balanced crystalloids or N Saline

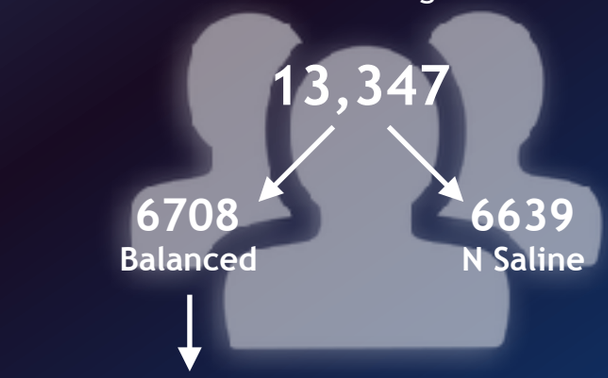
Primary Outcome

- Hospital-free days to day 28
- Composite of in-hospital death and hospital LOS defined as the number of days alive and out of the hospital between the index emergency department visit and 28 days later

Secondary Outcomes

- M.A.K.E within 30 days
  - Composite of death, new renal-replacement therapy, or persistent renal dysfunction at the earliest of hospital discharge or 30 days after the index emergency department visit
- AKI > stage 2
- In-hospital death

1079ml **ave volume received**
88.3% received assigned fluid



Hartmmans (95.3%)
Plasma-Lyte A (4.7%)

Lower Cl- and higher HCO3- then saline group
Less academia and hyperchloraemia

Primary Outcome

Hospital Free Days
No difference - 25 days in each group — P=0.41

Death
Balanced = 1.4%
Saline = 1.5% — P=0.89

Secondary Outcomes

M.A.K.E within 30 days
Balanced = 4.7%
Saline = 5.6%; — P=0.01

New RRT, AKI >stage 2 and in hospital deaths no significant difference seen

- Those with borderline renal failure or hyperchloraemia appeared to have the largest benefit from balanced crystalloids for avoiding M.A.K.E within 30 days and AKI
- Stage 2 or higher AKI patients faired better with balanced crystalloids Vs saline with lower M.A.K.E incidence within 30 days 28.0% Vs 37.6% — P=0.001

The NEW ENGLAND JOURNAL of MEDICINE

Self et al. Feb 2018. DOI: 10.1056/NEJMoa1711586

Also…

- CSL group blood results showed lower chloride, lower rates of acidaemia & higher bicarbonate levels vs 0.9% Saline Group.

STRENGTHS

- Important and RELEVANT for routine, clinical practice
- Pragmatic design = very few patients were excluded from the study
- **More than 85% of patients received the allocated intervention**
- Patient focused primary outcome
- The RCT design = minimal baseline imbalances between the groups
- **<u>The high quality of data analysis = useful for future studies.</u>**

Weaknesses

Surrogate marker to assess M.A.K.E (major adverse kidney event) = serum creatinine

Does this translate to a patient benefit?

(SMART AND SALT-ED CONCUR M.A.K.E IS LOWER WITH BC'S)

Weaknesses

- Single study centre design

- The type of fluid administered in the ED was unblinded
  = ?physician bias in amount & timing

- No evaluation was made of fluid administration following hospital admission!!
  = ?impact of 1 litre of fluid given in the ED?

- Fewer patients in the balanced salt solution arm (83.8%) received the allocated study fluid, versus 92.8% in the saline group.

SALT-ED

- **Results need to be replicated in a multi-centre RCT before any conclusions about the proposed deleterious effects of 0.9% sodium chloride administration can be drawn.**

4. PAMP-ER

In severely injured patients at risk for haemorrhagic shock, does prehospital plasma resuscitation, compared with standard-care resuscitation

(not including plasma administration)

reduce 30-day mortality?

PAMPER

The NEW ENGLAND JOURNAL of MEDICINE

Sperry JL et al N Engl J Med 2018; 379:315-326

Clinical Question

- In severely injured patients at risk for haemorrhagic shock, does prehospital plasma resuscitation, compared with standard-care resuscitation (not including plasma administration), reduce 30-day mortality?

Context

- Bleeding in trauma, traditionally managed with the prehospital infusion of crystalloids,
  - Component transfusion started once patient arrives in hospital.
- Recent evidence that suggests the early institution of blood components may help prevent trauma coagulopathy, downstream traumatic shock, and improve outcomes

Plasma arm

- 2 units thawed plasma initiated in prehospital setting by air transport team before any other fluid.
- After this goal directed resuscitation with crystalloids or RBC's until arrival in ED

RCT

- Phase 3
- 27 centres
- Cluster-randomized trial
- Team in ambulances screened and enrolled patients

Inclusion:

- Blunt or penetrating trauma
- Transported to trauma centre from scene or from outside referral ED
- At risk of haemorrhagic shock, as defined by at least one episode of:
  - Hypotension (systolic blood pressure <90mmHg) and tachycardia (HR>108/min)
  - Severe hypotension (systolic blood pressure <70mmHg)

Exclusion:

- >90yr or <18yr / Unable to establish IV or IO access / Isolated fall from standing / documented C-spine injury / prisoner / pregnant / Traumatic cardiac arrest >5 minutes / Penetrating brain injury / Isolated drowning or hanging / >20% TBSA burns / Admitted to an outside referral hospital
- Patient or family member objected to participation in the trial at the scene

Randomisation

- Randomisation was of air medical services / not individual patients.
- Block randomized for 1mth at a time to:
  - Plasma arm
  - Standard care (control) arm

@wilkinsonjonny

501

230 Plasma | **271 Std. Care**

Primary Outcome

30 day mortality

- Plasma - 23%
- Std Care - 33%

P=0.03

Secondary Outcomes

- 24hr mortality 13.9% vs 22.1% (NS)
- In-hosp. mortality 22.2 % vs 32.5% (NS)
- Median 24hr Vol. RBCs 3 vs 4 (NS)
- Median 24hr Vol. crystalloid 4388 320) vs 4500 (9NS)
- Vasopressors received in first 24hours 45.2% vs 50.9% (NS)
- Multiorgan failure 63.0% vs 57.6% (NS)
- Median initial INR lower 1.2 vs 1.3 **P<0.001**

Goal Directed arm

- Targeting BP >90 (not standardised but guided by local protocol

CRITICALCARE NORTHAMPTON.COM
REVIEWING CRITICAL CARE, JOURNALS & FOAMed

Author Conclusions

In **patients at risk for haemorrhagic shock,** the administration of thawed plasma during prehospital air medical transport was **safe and resulted in lower 30-day mortality and a lower median PTT ratio than standard-care resuscitation.**

Strengths

- **Multi centre, RCT**
- **Majority of trauma related deaths due to haemorrhage occur early - good PHC question**
- **Primary analysis adjusted to account for prehospital crystalloid and RBC transfusion differences - reducing confounding.**

Strengths

- Relevant population = high proportion having haemorrhage that required transfusion and surgery
- Intervention = simple to deliver and would be reproducible in systems already with capacity to deliver blood products
- **<u>Early separation of the KM</u>** effect makes its treatment effect more plausible (particularly if trauma deaths have early mortality).

Weaknesses

- No mention of the use of prehospital TXA
- Economic analysis not performed
- Resuscitation protocols were not standardised - local protocols.

Weaknesses

- The total volume given prehospital was not reported
- Likely similar in both groups
- BP & HR similar.

Allocation	Crystalloid (mls)	Plasma (mls)	RBC (% transfused)	Prehospital total (mls)
Plasma	500	600	26%	?Similar
Crystalloid	900	0	42%	?Similar

Why?

Unclear mechanism of action

- **The large mortality benefit appears to have occurred very early and a 8.2% mortality difference by 24hours?**
- **The difference in INR (1.2 vs 1.3) = statistically significant but unlikely to account for all of this mortality difference**
- **Other potential mechanisms (?less crystalloid given, less RBCs, anti-inflammatory effects) not clarified.**

So...

- **The early (prehospital) initiation of plasma results in a significant fall in mortality in patients at high risk of bleeding without a significant increase in harm**

- **Further blinded studies are needed to confirm this benefit, and to test its applicability in different trauma systems.**

5. BEAM

In patients with at least ONE difficult airway characteristic, is the First-Pass Intubation success rate increased by using a ‘Bougie-First’ technique vs ETT & Stylet?

BOUGIE USE IN EMERGENCY AIRWAY MANAGEMENT (BEAM)

propofology.com
Dr. David Lyness
@Gas_Craic

Q: In patients admitted to the emergency department with difficult airway characteristics undergoing orotracheal intubation with a Macintosh laryngoscope blade, does a bougie facilitate higher first-attempt intubation success than an endotracheal tube + stylet?

INCLUDED: >18yo , EMERGENCY ORAL ETT PLACEMENT IN ED, USE OF A STANDARD MAC BLADE
EXCLUDED: PRISONERS, PREGNANT LADIES, KNOWN DISTORTION OF UPPER AIRWAY ANATOMY, USE OF HYPERANGULATED BLADES

Driver et al. JAMA. 2018

- 757 PATIENTS --> ETT for respiratory arrest, difficulty breathing, or airway protection
- 380 of the patients randomized had at least one difficult airway characteristic
- Bougie 1st Intubation = 381 patients (198 had a difficult airway characteristic)
- ETT + Stylet 1st Intubation = 376 patients (182 had a difficult airway characteristic)

No difference between groups for any intubation related complications including pneumothorax, aspiration, dental trauma, direct airway trauma, or oesophageal intubation

There were 3 oesophageal intubations with the endotracheal tube and stylet versus 0 with the bougie (p=0.08).

Primary OUTCOME: FPS in patients with at least 1 difficult airway characteristic
(i.e. body fluids obscuring the laryngeal view, airway obstruction or oedema, obesity, short neck, small mandible, large tongue, facial trauma, or need for cervical immobilization)

FPS was defined as successful endotracheal tube placement with the first device passed (bougie or endotracheal tube + stylet) during the first laryngoscope insertion

Secondary OUTCOMES:
FPS in all patients. FPS success without hypoxemia.
First attempt durationEsophageal intubation
Hypoxemia (i.e. SpO2 <90% or if the attempt began with a saturation <90%, and absolute decrease in desaturation of >10%)

OUTCOMES	BOUGIE 1ST	ETT + STYLET 1ST	95% CI	P VALUE	NNT
1ST ATTEMPT SUCCESS IN A PATIENT WITH AT LEAST 1 DIFFICULT AIRWAY CHARACTERISTIC	96%	82%	8-20%	<0.001	7
1ST ATTEMPT SUCCESS IN ALL PATIENTS	98%	87%	7-14%	0.001	9
Median Duration of 1st Intubation Attempt	38sec	36sec	-1 - 4%	0.24	NA
Incidence of Hypoxaemia	13%	14%	-6-4%	0.67	NA

Some Thoughts

- Best study to date
- Outcomes were clearly better with the bougie
- Single-center study - where they (in previous 2017 study) use bougie first already for >80% of first attempts!
- Best selection of patients to study - more ‘routine cases’ not airway horrendoplasties
- Mirrors my own thoughts.

IRISH ASSOCIATION FOR EMERGENCY MEDICINE

propofology.com

Dr. David Lyness
@Gas_Craic

TOP 5 STUDIES IN CRITICAL CARE FOR IAEM 2018

SHOC-ED

IN NON-TRAUMA PT'S WITH UNDIFFERENTIATED HYPOTENSION DOES A STANDARDISED POCUS PROTOCOL VS USUAL CARE, IMPROVE 30day OR HOSPITAL SURVIVAL? DIAGNOSES RECORDED AT 0 AND 60MINS

ATKINSON et al. Ann Emerg Med 2016

SOUTH AFRICAN & NORTH AMERICA. 270 PATIENTS. SIMILAR OVERALL SURVIVAL RATES OF 76.5% & 76.1%.
HIGHER MORTALITY IN S.A. HOSPITALS. MUCH MORE SEPSIS IN S.A. (71% VS 42%) AND MORE SEVERE DEHYDRATION IN NORTH AMERICA (20% VS 3%)

SECONDARY OUTCOMES... MEDIAN VOLUME OF FLUIDS INFUSED, HOSPITAL ADMISSION RATES, INOTROPE ADMINISTRATION, CT SCANNING, ICU ADMISSION AND ICU LENGTH OF STAY WERE QUITE SIMILAR...

SO THE ANSWER IS NO... BUT WEAKNESSES INCLUDED: EARLY TRIAL TERMINATION, CONVENIENCE SAMPLING, EXCLUSION OF DEFINITIVE DIAGNOSES LIKE AAA/ECTOPIC, >50% WITH OCCULT SEPSIS & TRIAL MAY NOT HAVE REFLECTED MANY PRACTITIONERS PRACTICE.

IE) NO SIGNIFICANT DIFFERENCES IN FINAL DIAGNOSES IN N.A. OR S.A. COHORT.

PARAMEDIC-2

IN ADULT PATIENTS WITH OOHCA DOES THE ADMINISTRATION OF ADRENALINE VS PLACEBO, IMPROVE SURVIVAL? OVERALL SURVIVAL WAS AT 2.8%....

PERKINS et al. NEJM 2018.

8014 PATIENTS INCLUDED, 3999 GOT PLACEBO, AND 4015 GOT ADRENALINE. 65% MALE, 35% FEMALE. 7790 DIED. 224 LIVED.

@30 DAY MARK --> PLACEBO GROUP = 94 SURVIVORS & ADRENALINE GROUP = 130 SURVIVORS.

suggests epinephrine improves 30 day-mortality but it may be at the cost of worse neurological outcome

THIS TRIAL PROVIDES, PROBABLY, THE LARGEST SET OF RCT DATA TO DATE ON THE TOPIC.
GOOD CLINICAL QUESTION - HAS BEEN ASKED FOR YEARS!
MEDIAN TIME OF 6MIN 40SECS FOR AMBULANCE TO ARRIVE. LARGE NETWORK OF AMBULANCE SERVICES ACROSS UK PARTICIPATED.
ADRENALINE OR PLACEBO GIVEN IN MEDIAN TIME OF 21MINS.
TO PREVENT ONE DEATH AT 30 DAYS (IRRESPECTIVE OF NEUROLOGICAL OUTCOME) - YOU NEED TO TREAT 112 PATIENTS.
THE NNT FOR BYSTANDER CPR IS JUST 15 PATIENTS!! THE NNT FOR EARLY DEFIB IS 5 PATIENTS!!
95% OF 280 LAY PEOPLE CONSULTED PRIORITISED LONG-TERM SURVIVAL WITH A FAVOURABLE NEUROLOGICAL OUTCOME OVER SHORT TERM (HOURS/DAYS) SURVIVAL

POTENTIALLY A FRAGILE STUDY. IF THE 7 PATIENTS NOT INCLUDED IN PRIMARY ANALYSIS HAD BEEN, THERE MAY HAVE BEEN NO STATISTICAL DIFFERENCE..

PAMP-ER

In severely injured patients at risk for haemorrhagic shock, does prehospital plasma resuscitation, compared with standard-care resuscitation (not including plasma administration), reduce 30-day mortality?

SPERRY et al. NEJM. 2018

authors concluded that plasma reduced 30day mortality, that it was safe and lowered median PTT ratio

MULTI-CENTRE, RCT, GOOD QUESTION, PRIMARY ANALYSIS ADJUSTED TO ACCOUNT OF PHC CRYSTALLOID AND RBC TRANSFUSION DIFFERENCES - REDUCING CONFOUNDING
RELEVANT STUDY POPULATION THAT REQUIRED TRANSFUSION AND SURGERY... + INTERVENTION WAS RELATIVELY SIMPLE AND COULD BE GENERALISABLE.
EARLY SEPARATION OF KEPLAN-MEYER CURVE = TREATMENT EFFECT MORE PLAUSIBLE.
NO MENTION OF PRE-HOSPITAL USE OF TXA HOWEVER.... AND RESUS PROTOCOLS WERE NOT STANDARDISED....
TOTAL FLUID VOLUMES GIVEN PREHOSPITALLY WERE NOT ACCUMULATED - BUT ARE LIKELY SIMILAR IN BOTH GROUPS...
THERE IS AN UNCLEAR MECHANISM OF ACTION... BUT A LARGE MORTALITY BENEFIT APPEARS TO INFLUENCE A 8.2% MORTALITY DIFFERENCE BY 24HOURS.
FURTHER BLINDED STUDIES ARE NEEDED TO CONFIRM BENEFIT AND SEE HOW OTHER TRAUMA SYSTEMS FARE.

THERE SEEMS TO INDEED BE A SIGNIFICANT FALL IN MORTALITY IN PATIENTS WITH A HIGH RISK OF BLEEDING WITHOUT SIGNIFICANT INCREASE IN HARM FROM TRANSFUSION

SALT-ED

In non-critically ill adult patients admitted to the hospital from the Emergency Department, does the administration of a balanced salt solution compared with normal saline, reduce hospital free days to day 28?

SELF et al. NEJM. 2018 LOOK AT 'SMART TRIAL' FOR CRITICALLY ILL PATIENTS

authors concluded NO difference in hospital-free days between treatment with balanced crystalloid vs 'normal' saline
However - in secondary outcomes - BC group associated with less 'major adverse kidney events' and more favourable biochemistry results.

Important and relevant Q. Pragmatic design. Over 85% of patients got their allocated intervention. Patient-focused primary outcome.
CLEAR DIFFERENCE BETWEEN DIFFERENT COHORT ELECTROLYTE LEVELS.... SODIUM, CHLORIDE, BICARBONATE AND ACIDAEMIA. Lower chloride, less acidaemia and higher bicarb in BC group)
Minimal baseline imbalances between groups. Good, HIGH-quality data lends itself to being used in future larger trials.

13,347 patients total! 95% of the balanced crystalloid group got Harmann's solution.
No evaluation made of fluid POST hospital administration!!!! ??what really is the impact of 1L of either crystalloid in the ED when looking at hospital stay?
There were fewer patients in the BC group vs Saline.
The type of fluid administered was UNBLINDED. Single study centre.

BOUGIE INTUBATION

DRIVER. 2018. JAMA

In patients admitted to the emergency department with difficult airway characteristics undergoing orotracheal intubation with a Macintosh laryngoscope blade, does a bougie facilitate higher first-attempt intubation success than an endotracheal tube + stylet?

RCT. In 757 adults, bougie use resulted in significantly higher first-attempt intubation success than an endotracheal tube + stylet (96% vs 82%) for those with a difficult airway characteristic.

3768 assessed --> 2938 excluded --> 2785 NOT INTUBATED --> 73 met criteria but not randomised --> 757 enrolled but only 380 had difficult a/w characteristic

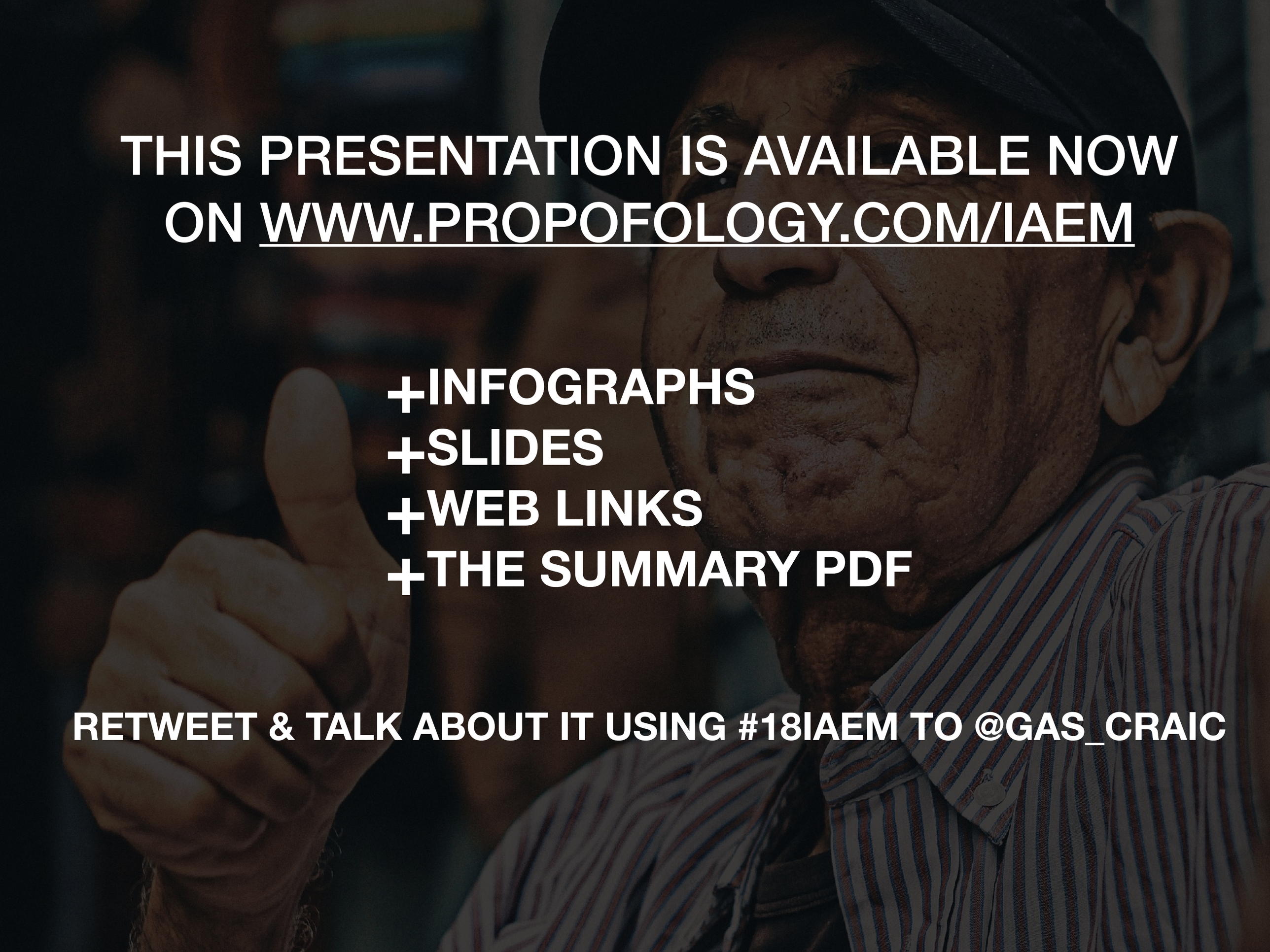
This is the best study we have to date examining this issue in ED.
Outcomes were clearly better with the bougie, BUT single-centre study,
The degree to which providers are trained and comfortable with a bougie could significantly impact the generalizability of these results.

*Bias towards bougie/selection bias - protocol violation - 8% of the intubations that were supposed to be done with a stylet were actually done with a bougie, compared to 2% of intubations randomized to a bougie being performed with an endotracheal tube....
this group might be more skilled with the bougie than other groups considering they use a bougie on the first attempt 80% of the time. (Driver 2017)

VISIT WWW.PROPOFOLOGY.COM/IAEM FOR THE FULL SUMMARIES

THANKS TO

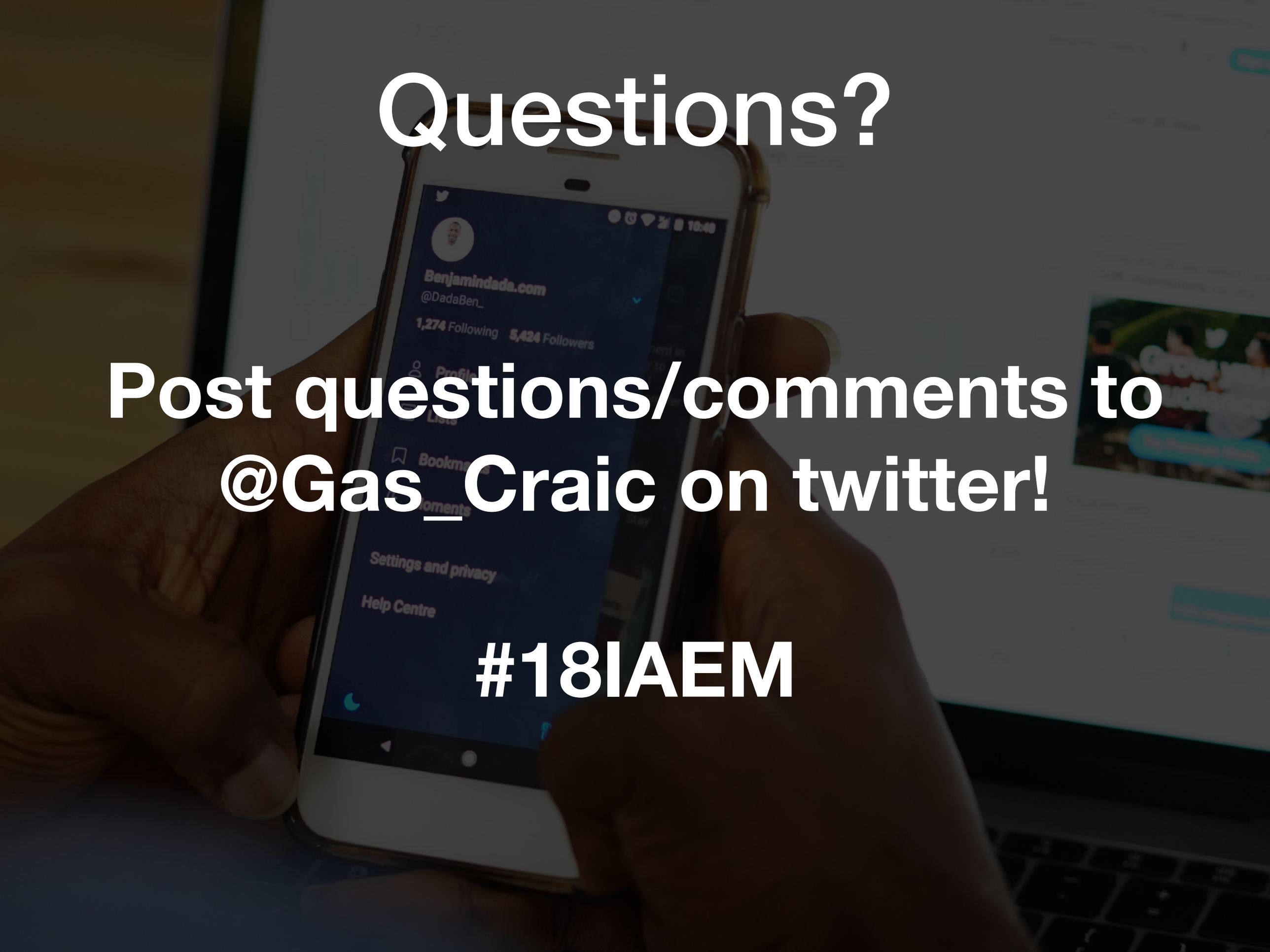
- **Dr. Jonny Wilkinson @wilkinsonjonny**
- **Dr. Aoife Abbey @whistlingdixie4**
- **Dr. Tomasso Scquizzato @tsquizzato**



THIS PRESENTATION IS AVAILABLE NOW
ON WWW.PROPOFOLOGY.COM/IAEM

+INFOGRAPHS
+SLIDES
+WEB LINKS
+THE SUMMARY PDF

RETWEET & TALK ABOUT IT USING #18IAEM TO @GAS_CRAIC



Questions?

Post questions/comments to @Gas_Craic on twitter!

#18IAEM