Ambulance Victoria

Pre Hospital IV Antibiotic Administration in Sepsis

A Future Ambulance Victoria Randomised Controlled Trial…

Daniel Cudini – Clinical Support Officer | Critical Care Paramedic
BEx Sci, BEmergHlth (Paramedic), Grad Dip EmergHlth (ICP), MPA

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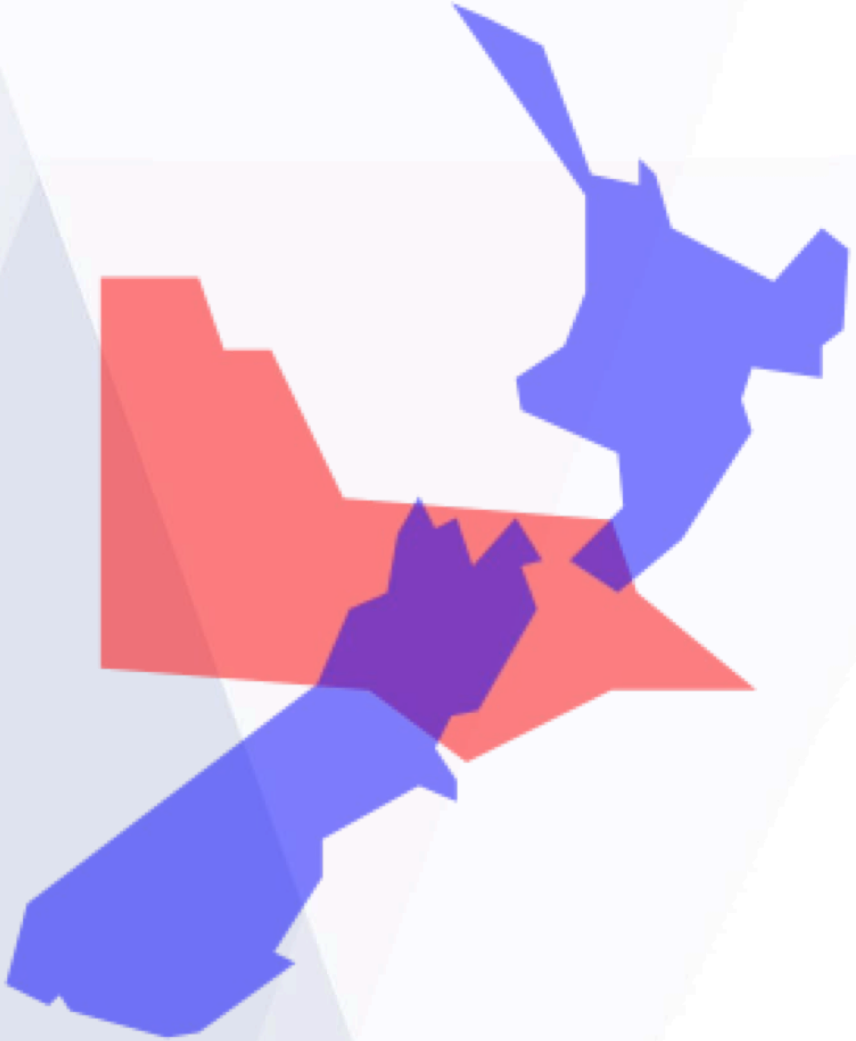
Ambulance Victoria

Victoria
227,416 km²



New Zealand
270,467 km²

Quote

"Sepsis is like beauty,

we know it when we see it,

but we can't actually define what it is"

Unknown Source, FOAM - 2017

A Future Randomised Controlled Trial…

The **PASS** Trial – Phase 2

PARAMEDIC **A**NTIBIOTICS FOR **S**EVERE **S**EPSIS

A Future Randomised Controlled Trial…

Why is a trial such as this important?

Pre Hospital IV Antibiotic Administration in Sepsis

The International Burden of Sepsis

Time To First Antibiotic Dose

Extending Point of Care (POC) Medicine into the Pre Hospital Setting

The International Burden of Sepsis

- One of most **frequent causes of ED attendance worldwide**, with an **annual incidence in adults of up to 300 cases per 100,000** population.[1-4]
- **Sepsis** is recognised by the **WHO as a global health priority.**[5]
- **Mortality** ⇧⇧⇧ with **delays to treatment.**[6,7]
- ⇧⇧⇧ **incidence** in the **elderly** and **chronically ill.**[6,7]

Sepsis Facts!

Patients with **sepsis** have a hospital mortality rate **(20% – 50%)** that greatly exceeds that seen in **myocardial infarction**, **stroke** and **traumatic injury**.[6,7]

Time to First Antibiotic Dose

Duration of hypotension before initiation of effective antimicrobial therapy is the critical determinant of survival in human septic shock*

Anand Kumar, MD; Daniel Roberts, MD; Kenneth E. Wood, DO; Bruce Light, MD; Joseph E. Parrillo, MD; Satendra Sharma, MD; Robert Suppes, BSc; Daniel Feinstein, MD; Sergio Zanotti, MD; Leo Taiberg, MD; David Gurka, MD; Aseem Kumar, PhD; Mary Cheang, MSc

Survival was 82.7% if effective antimicrobials were administered within 30 mins of initial evidence of hypotension **77.2% in the second half hour** and **42.0% in the sixth hour**.[8]

Time to First Antibiotic Dose

It has been shown that mortality increases by 7.6 % for every hour of delay in starting antibiotic therapy after the onset of hypotension.

Kumar et al, Crit Care Med; 2006

Time to First Antibiotic Dose

The Impact of Timing of Antibiotics on Outcomes in Severe Sepsis and Septic Shock: A Systematic Review and Meta-analysis

Sarah A. Sterling, MD, W. Ryan Miller, MD, Jason Pryor, MD, Michael A. Puskarich, MD, and Alan E. Jones, MD

Reviewed the Impact of **Timing of Antibiotics on Outcomes in Severe Sepsis** and **Septic Shock** showed **no significant mortality benefit** of administering antibiotics **within 3 hours of ED triage** or **within 1 hour of shock recognition**.

Extending POC Medicine into the Pre Hospital Setting

STEMI – Pre Hospital 12 Lead ECG / Thrombolysis

Trauma – Pre Hospital Red Cell Concentrate

Stroke – Pre Hospital CT / Thrombolysis

Sepsis – ???

Extending POC Medicine into the Pre Hospital Setting

"The PHANTASi Trial"

Pre Hospital ANTibiotics Against SepsIs

Prehospital antibiotics in the ambulance for sepsis: a multicentre, open label, randomised trial

Nadia Alam, Erick Oskam, Patricia M Stassen, Pieternel van Exter, Peter M van de Ven, Harm R Haak, Frits Holleman, Arthur van Zanten, Hien van Leeuwen-Nguyen, Victor Bon, Bart A M Duineveld, Rishi S Nannan Panday, Mark H H Kramer, Prabath W B Nanayakkara, on behalf of the PHANTASi Trial Investigators and the ORCA (Onderzoeks Consortium Acute Geneeskunde) Research Consortium the Netherlands*

Alam Nadia et al, Lancet; 2017

Extending POC Medicine into the Pre Hospital Setting

Pre Hospital ANTibiotics Against SepsIs

- Prospective non blinded RCT
- **28-day mortality**, hospital length of stay, admission to intensive or medium care unit (ICU/MC). Follow up of one year.
- **n = 2698 patients** (**1535** in the **intervention group** and **1137** in the **usual care group**).
- At day 28, 120 **(8%) patients had died** in the **intervention group** and 93 **(8%) had died** in the **usual care group**.

Extending POC Medicine into the Pre Hospital Setting

Conclusion…

Pre hospital antibiotics did not lead to improved survival, regardless of illness severity.

Alam Nadia et al, Lancet; 2017

The PASS Trial - Phase 2

Primary Hypothesis:

In patients who have severe community-acquired sepsis when evaluated by paramedics, pre-hospital administration of 2 g IV ceftriaxone will result in a **significant reduction in time to appropriate antibiotic treatment, compared with standard care.**

The PASS Trial - Phase 2

Propose that the initiation of **antibiotics pre-hospital will result in an absolute reduction in time to antibiotics of at least 60 minutes** (control: 120 minutes, intervention: 30 minutes, SD: 30 minutes).

The PASS Trial - Phase 2

Secondary Hypotheses:

- Paramedics will be able to accurately identify severe community-acquired sepsis
- Pre-hospital ceftriaxone administration will result in minimal adverse events, and cover the majority of bacterial pathogens.
- Administration of pre-hospital antibiotic therapy will not result in a significant increase in scene times.

The PASS Trial - Phase 2

Inclusions:

- Adults (age ≥ 18 years)
- History suggestive of infection
- **One Red Flag present:**
  - **Responds only to voice or pain/unresponsive;**
  - **Systolic BP ≤ 90 mmHg or drop > 40 mmHg from normal;**
  - **HR > 130 per minute; RR ≥ 25 per minute;**
  - **Needs oxygen to keep SpO2 ≥ 92%;**
  - **Non-blanching rash/mottled/ashen/cyanotic;**
  - **Not passed urine in last 18 hours;**
  - **Recent chemotherapy**
- Transport to a participating hospital

The PASS Trial - Phase 2

Exclusions:

- Female known to be pregnant
- Suspected allergy to cephalosporins
- Suspected meningococcal infection (will receive ceftriaxone as standard care)
- Deranged clinical parameters considered likely to be from a non-infective cause (such as dehydration, acute coronary syndrome, trauma, anaphylaxis)
- Already receiving IV antibiotics (“Hospital in the home” patients)
- Cystic Fibrosis
- Transplant recipient

The PASS Trial - Phase 2

Eligible patients will be enrolled
(Estimated sample size of 100 patients 50 in each arm, statistical power > 95%)

Peripheral blood culture drawn

Patient will be randomised to either paramedic administered 2g IV ceftriaxone or standard care.

The PASS Trial - Phase 2

If the Phase 2 RCT demonstrates:

- Paramedics can accurately identify sepsis
- Pre-hospital intervention results in a significant reduction in the time to appropriate antibiotic treatment

Provide a robust rationale to undertake a larger interventional study exploring mortality and morbidity outcomes

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- Associate Professor Andrew Udy CI
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- Associate Professor Michael Stephenson AI

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theAlfred
Part of AlfredHealth

Peninsula Health

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Contact Details

Daniel Cudini – Clinical Support Officer | Critical Care Paramedic
BEx Sci, BEmergHlth (Paramedic), Grad Dip EmergHlth (ICP), MPA

daniel.cudini@ambulance.vic.gov.au

Phone: +61 409 186 795