



Innovation in point-of-care diagnostics for sepsis and bloodstream infections

Guest speakers: Till T. Bachmann, Amrita Sukrity, David Anderson
Moderator: Caroline Purslow (Nesta Challenges)
Host: Astrid Pentz-Murr (GARDP)



An online space to connect and support the antimicrobial discovery, research, and development community

THREE AIMS OF REVIVE:



Facilitate
learning



Connect
people



Knowledge
sharing

Webinar recordings

REVIVE

LIVE WEBINAR

26 November 2019, 9:30-11:00 (CET)
14:00-15:30 (IST), 19:30-21:00 (AEDT)

Innovation in point-of-care diagnostics for sepsis and bloodstream infections

Speaker: Till T. Bachmann, University of Edinburgh, United Kingdom

Amrita Sukriti, Sporexics, India

David Anderson, Binner Institute, Australia

Register now!

In collaboration with: nesto Challenges

LONGITUDE PRIZE

Innovation in point-of-care diagnostics for sepsis and bloodstream infections

26 November 2019

REVIVE

LIVE WEBINAR

7 November 2019, 17:00-18:30 CET

Converting Gram-Positive-Only Compounds into Broad-Spectrum Antibiotics

Speaker: Paul Hergenrother, University of Illinois

Register now!

GARDP

LIVE WEBINAR

3 October 2019, 17:00-18:30 CEST

Natural products antibiotics: from traditional screening to novel discovery approaches

Speaker: Olga Genilloud, Scientific Director, Fundación MEDINA, Spain

Recording available

REVIVE

LIVE WEBINAR

7 November 2019, 17:00-18:30 CET

Converting Gram-Positive-Only Compounds into Broad-Spectrum Antibiotics

Speaker: Paul Hergenrother, University of Illinois

Recording available

GARDP

LIVE WEBINAR

3 October 2019, 17:00-18:30 CEST

Natural products antibiotics: from traditional screening to novel discovery approaches

Speaker: Olga Genilloud, Scientific Director, Fundación MEDINA, Spain

Recording available

REVIVE

LIVE WEBINAR

10 September 2019, 17:00-18:30 CEST

Models for antimicrobial R&D: Advanced and complex in vivo models for infectious disease research

Speaker: Peter Warn, Evotec

Recording available

GARDP

LIVE WEBINAR

20 August 2019, 17:00-18:30 (CEST)

Models for antimicrobial R&D: Computational modelling for population PK and PKPD

Speakers: Lena Frimberg & Elisabet Nielsen, Dept of Pharmaceutical Biosciences, Uppsala University, Sweden

Recording available

REVIVE

LIVE WEBINAR

18 July 2019, 9:00-10:30 (CEST)

Enabling academia to fill the discovery gap – Learnings from industry and funders

Speaker: Ursula Theuretzbacher

Recording available

GARDP

LIVE WEBINAR

18 July 2019, 9:00-10:30 (CEST)

Enabling academia to fill the discovery gap – Learnings from industry and funders

Speaker: Ursula Theuretzbacher

Recording available

In collaboration with: CARB-X repair

REVIVE

LIVE WEBINAR

20 August 2019, 17:00-18:30 (CEST)

Models for antimicrobial R&D: Computational modelling for population PK and PKPD

Speakers: Lena Frimberg & Elisabet Nielsen, Dept of Pharmaceutical Biosciences, Uppsala University, Sweden

Recording available

GARDP

LIVE WEBINAR

18 July 2019, 9:00-10:30 (CEST)

Enabling academia to fill the discovery gap – Learnings from industry and funders

Speaker: Ursula Theuretzbacher

Recording available

revive.gardp.org/webinars

Today's speakers

Innovation in point-of-care diagnostics for sepsis and bloodstream infections



Till T. Bachmann
University of Edinburgh, UK



Amrita Sukrity
SpotSense, India



David Anderson
Burnet Institute, Australia



Moderator:
Caroline Purslow
Nesta Challenges, UK

Today's speakers



Till Bachmann is Professor of Molecular Diagnostics and Infection and Deputy Head of Infection Medicine at Edinburgh Medical School:Biomedical Sciences at the University of Edinburgh. Till is an expert in point of care (POC) detection, infectious diseases and antimicrobial resistance, conducting research at the interface of clinical microbiology and diagnostics.



Amrita Sukrity is the founder of Spot Healthcare Solutions Pvt Ltd which is a start-up in India working in the field of affordable diagnostics. The start-up aims to develop multiple solutions in the space of maternal and child health and is currently piloting an algorithm for detection and monitoring of neonatal sepsis.



David Anderson is Deputy Director (Partnerships) and co-head of the Global Health Diagnostics Laboratory at the Burnet Institute in Melbourne, Australia, where he has spent his entire professional career. His work has led to diagnostic innovations including the Visitect® CD4 POC test for monitoring of CD4+ T-cells in HIV, which serves as a paradigm for future cell-based POC tests including CD64 in sepsis and severe infection, and novel POC tests for liver disease.

LONGITUDE PRIZE

£10 Million Prize Fund
£8 Million payout

1 Winner

First past the post

5 year + international
prize

Funded by Nesta &
Innovate UK

nesta

A **£8 million global prize** that will reward a transformative, rapid, accurate, and affordable **point-of-care** diagnostic test that can significantly reduce antibiotic misuse or overuse, anywhere in the world.



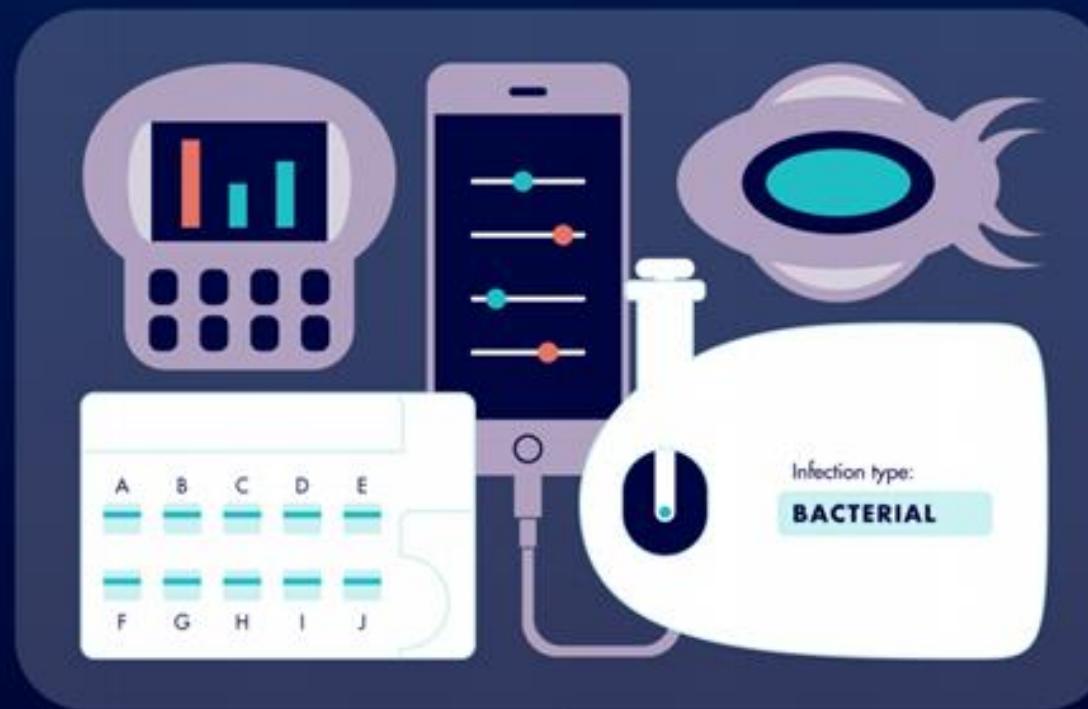
What do competitors need to do to win?



nesta

LONGITUDE PRIZE

WHAT KIND OF TEST COULD WIN THE LONGITUDE PRIZE?



ENVIRONMENTAL STABILITY

EASILY CARRIED

NO COLD CHAIN

NO MAINS POWER

THE WINNING TEST MUST BE...



NEEDED

Improve the antibiotic treatment decision of a globally occurring problem



ACCURATE

Eliminate harmful treatment decisions and give confidence to the user



AFFORDABLE

Affordable for purchase and use everywhere that it is needed



RAPID

Sample collection to result in less than 30 minutes



EASY TO USE

Can be used and interpreted anywhere in the world with minimal training



CONNECTED

Tests with built-in data recording and transmission will be favoured



SAFE

The benefits far outweigh any risks



SCALABLE

A plan for full-scale manufacture and distribution

Who are our teams?

57 Teams

19 UK

13 India

10 US

3 Australia

3 Sweden



LONGITUDE PRIZE

longitudeprize.org

@longitude_prize
www.facebook.com/longitudeprize



Innovation in point-of-care diagnostics for sepsis and bloodstream infections

Introduction

Till T. Bachmann

Infection Medicine, Edinburgh Medical School: Biomedical Sciences
University of Edinburgh



GARDP Webinar 26 November 2019





Introduction & Contact

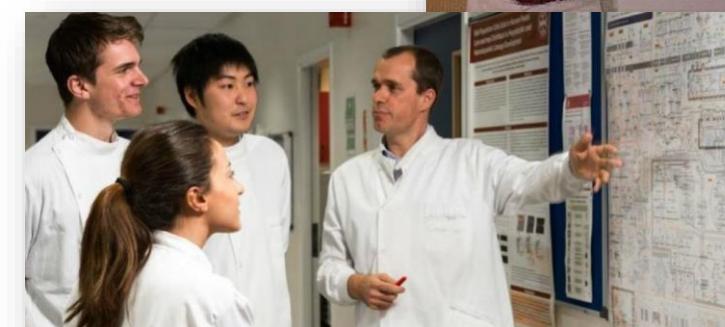
Till T. Bachmann, PhD FRSB

- Deputy Head of Infection Medicine
- Professor of Molecular Diagnostics and Infection
- Programme Director Clinical Microbiology and Infectious Diseases
- University of Edinburgh Programme Director Zhejiang University – University of Edinburgh Institute Dual PhD
- **Longitude Prize Judge** (Advisory Panel Member)

Infection Medicine
University of Edinburgh Medical School: Biomedical Sciences
Chancellor's Building
49 Little France Crescent
Edinburgh EH16 4SB

till.bachmann@ed.ac.uk
www.pathwaymedicine.ed.ac.uk

 @BachmannTill

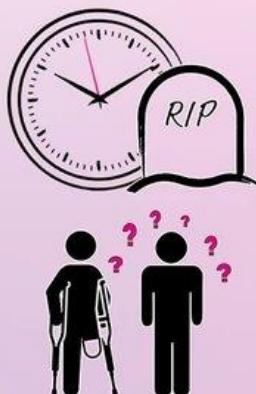


WORLD SEPSIS DAY INFOGRAPHICS

A GLOBAL HEALTH CRISIS



27 000 000 - 30 000 000 people per year develop sepsis



7 000 000 - 9 000 000 die
- 1 death every 3.5 seconds

Survivors may face lifelong consequences

Infographic 2/21



Global Sepsis Alliance

www.world-sepsis-day.org
www.global-sepsis-alliance.org

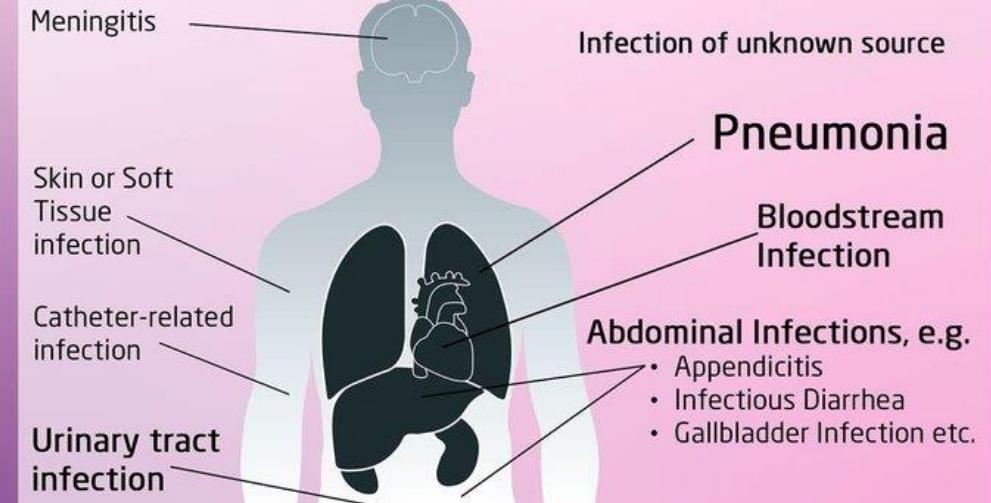
September | World
13 | Sepsis
2018 | Day



WORLD SEPSIS DAY INFOGRAPHICS

SOURCES OF SEPSIS

The Most Common Sources of Sepsis



Infographic 3/21



Global Sepsis Alliance

www.world-sepsis-day.org
www.global-sepsis-alliance.org

September | World
13 | Sepsis
2018 | Day

Rapid Appropriate Antimicrobial Therapy is Essential for Survival

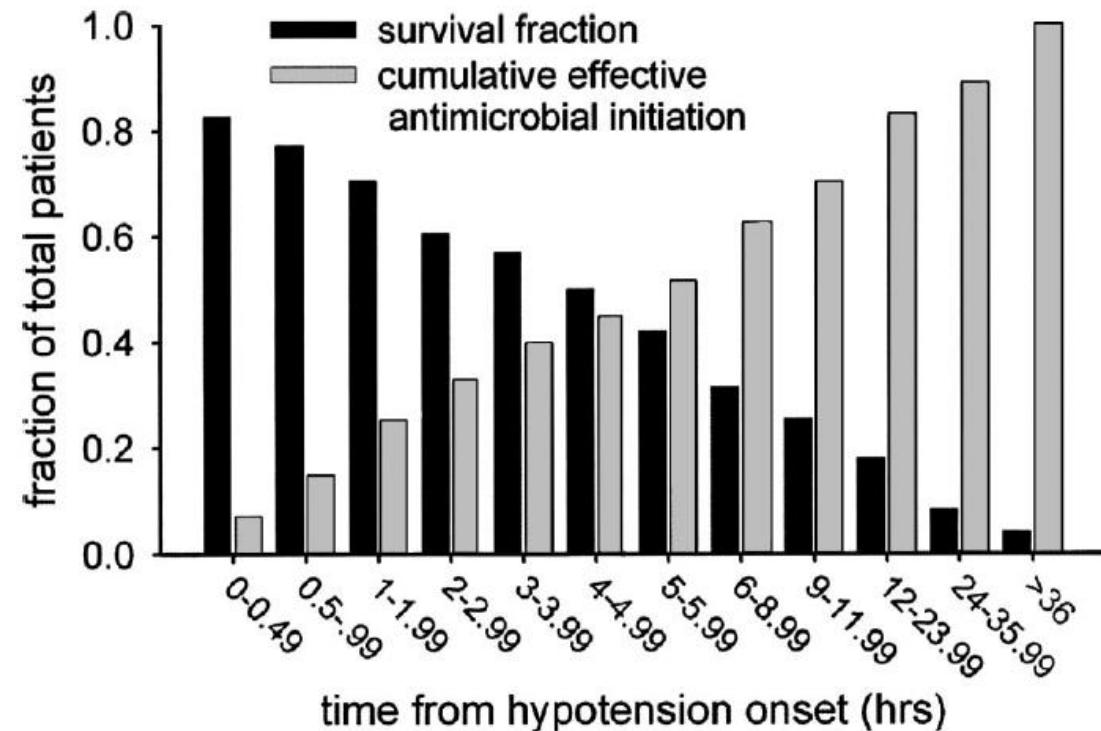


Figure 1. Cumulative effective antimicrobial initiation following onset of septic shock-associated hypotension and associated survival. The x-axis represents time (hrs) following first documentation of septic shock-associated hypotension. *Black bars* represent the fraction of patients surviving to hospital discharge for effective therapy initiated within the given time interval. The *gray bars* represent the cumulative fraction of patients having received effective antimicrobials at any given time point.

Clinical Response to Sepsis - Sepsis 6 Bundle

Action (complete ALL within 1 hour)

Why we do this

1. Administer oxygen

Aim to keep saturations >94%
(88-92% if at risk of CO₂ retention e.g. COPD)

To improve the oxygen content of the blood, and therefore its delivery to the tissues

4. Give IV fluids

If hypotensive/ lactate >2 mmol/l, up to 30ml/kg
Give 500ml stat if not hypotensive and lactate normal

To improve preload to the heart by correcting hypovolaemia, improving cardiac output and BP

2. Take blood cultures

At least a peripheral set. Consider e.g. CSF, urine, sputum. **Think source control!** Call surgeon/ radiologist if needed

To help identify pathogens, to determine likely source of infection & guide antimicrobial therapy

5. Check serial lactates

Corroborate high VBG lactate with arterial sample
If lactate >4 mmol/L, recheck after each 10ml/kg challenge and call Critical Care

High lactate indicates hypoperfusion- response of lactate helps to guide resuscitation

3. Give IV antibiotics

According to Trust protocol
Consider allergies prior to administration

To control the underlying infection, removing the trigger for immune overreaction

6. Measure urine output

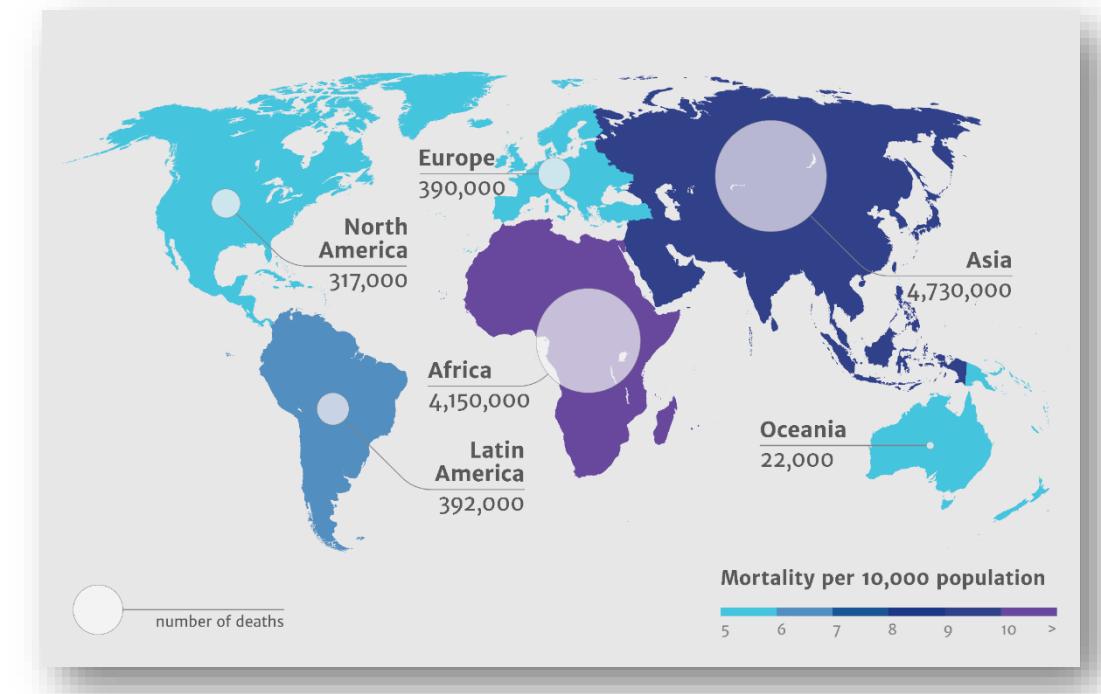
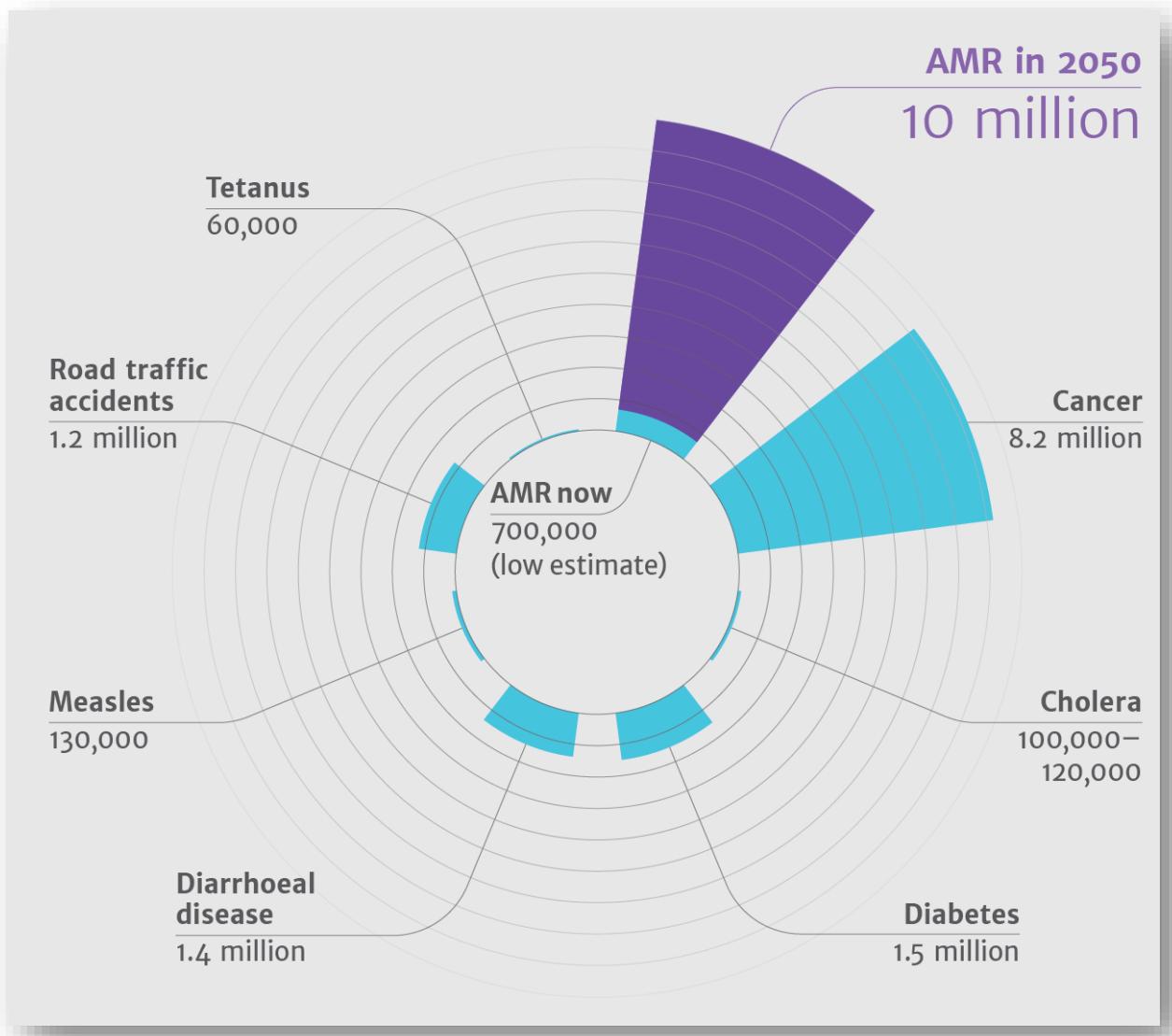
May require urinary catheter
Ensure fluid balance chart commenced & completed hourly

Urine output falls if the patient is hypovolaemic, also provides an indicator of adequate cardiac output

Diagnostics

Antibiotics

The Global Threat of Antimicrobial Resistance



TACKLING ANTIMICROBIAL RESISTANCE ON TEN FRONTS

<http://amr-review.org>



Public
awareness



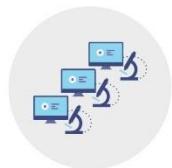
Sanitation
and hygiene



Antibiotics in
agriculture and
the environment



Vaccines and
alternatives



Surveillance



Rapid
diagnostics

There has been **very little progress** on the review's central and most expensive recommendations for transforming research and development incentives for antibiotics, vaccines and **diagnostics**.

Review of Progress on Antimicrobial Resistance: Background and Analysis,
Charles Clift, Centre on Global Health Security | October 2019, Chatham House

innovation fund

coalition for action



“I call on the governments of the richest countries to mandate now that **by 2020**, all **antibiotic prescriptions** will need to be informed by up-to-date surveillance information and a **rapid diagnostic test** wherever one exists.”

AMR Review May 19, 2016 – Tackling Drug-Resistant Infections Globally: final report and recommendations



Tackling antimicrobial resistance 2019–2024

The UK's five-year national action plan

Published 24 January 2019



Contained and controlled

The UK's 20-year vision for antimicrobial resistance

Published 24 January 2019

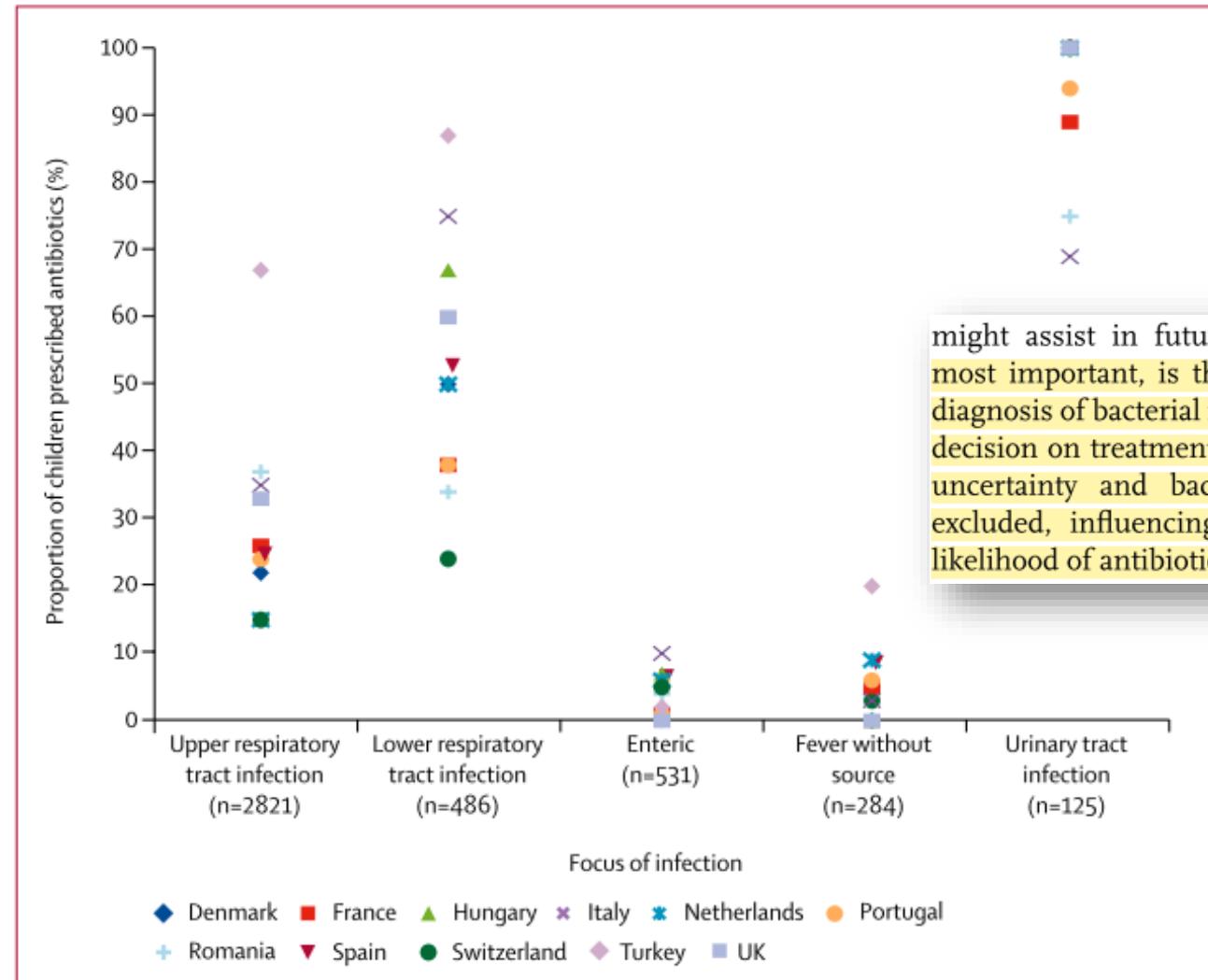
“... be able to report on the percentage of prescriptions supported by a diagnostic test or decision support tool by **2024**.”

For Dx: UK AMR Diagnostics Collaborative

Variability of **Antibiotic Prescription** for Febrile Children



<https://www.theguardian.com/society/2013/jun/25/a-and-e-emergency-medicine>



might assist in future studies. Second, and probably most important, is the lack of a gold standard for the diagnosis of bacterial respiratory tract infections. When a decision on treatment is made, there is often diagnostic uncertainty and bacterial causes can often not be excluded, influencing diagnostic assessment and the likelihood of antibiotic prescription.⁵

Figure 3: Variability in antibiotic prescription across countries for the most frequent foci of infection in 4560 children without comorbidities

Unmet Need in Clinical Microbiology

Blood

~ 10 CFU/mL

~ 1,000,000 CFU/mL



Pathogen



Drug Resistance



Therapy



Rapid Diagnostic

- Therapy Decision Support
- Patient Management
- Surveillance
- Drug Development



The **Diagnostic Spectrum** in Clinical Microbiology

Phenotypic

- Gram staining
- Culture
- Biochemistry

Non phenotypic

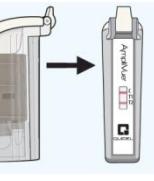
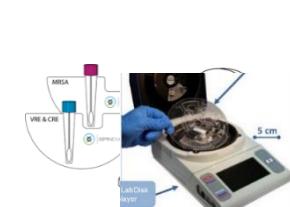
- Immunoassays
- Molecular
- Mass Spectrometry
- Imaging
- Sequencing

Host Response

- Biomarkers
- Gene expression

Specimen - Culture
Whole Blood - Blood Culture
Automation, Integration, Sample to Answer
ID, ID/AST, AMR
Lab - POCT

Some Molecular Diagnostic Systems in Use or With Potential for Infectious Disease Diagnostics

www.drw-ltd.comwww.biocartis.comwww.cepheid.comwww.nanosphere.comwww.molecular.roche.comwww.check-points.comwww.curetis.comwww.alere-i.comwww.alere.comwww.biomerieux-diagnostics.comwww.luminexcorp.comwww.stat-dx.comwww.bosch-vivalytic.comwww.blink-dx.comwww.twistdx.co.ukwww.quidel.comwww.optigene.comwww.meridianbioscience.comwww.mybixhealth.comwww.genefluidics.comwww.daktaridx.comwww.genmarkdx.comwww.mobidiag.comwww.nanoporetech.comwww.dnae.co.ukwww.rheonix.comwww.corisbio.comwww.genepoc-diagnostics.comspindia.dewww.chipcare.cawww.quantumdx.comwww.cubedlabs.comwww.genedriveplc.comwww.ivd-plattform.dewww.bigteclabs.comgbscience.com

WHO AMR Diagnostics Landscape & Gap Analysis

Table 1. Gaps in syndromic testing at Level I and Level II healthcare facilities*

Purpose	Syndromes	Fever without a known source	Sepsis	Sore throat, cough, URTI	TB ¹	Pneumonia, LRTI	Diarrhea	Visible skin/soft tissue infection	Wounds (traumatic and chronic)	Urethral and vaginal discharge	UTI
Level I											
Bacteria vs other	A	NA	NA	A	A	A	A	NA	NA	NA	A ³
Bacterial ID (culture, RDT, ..)	NA	NA	NA	A, B	NA	A, B	NA	NA	NA	A, B	NA
Antibiotic Susceptibility	NA	NA	NA	NA	NA	NA	NA	NA	NA	A, B	NA
Resistance Testing	NA	NA	NA	NA	NA	NA	NA	NA	NA	A, B	NA
Level II											
Bacteria vs other	A	NA	NA	A	A	A	A	A	A	NA	A ³
Bacterial ID	B, C	B, C	B, C	A, B, C	A, B, C	B ² , C	A, B, C	A, B, C	A, B	A, B	A, B, C
Antibiotic Susceptibility	B, C	B, C	B, C	C	A, B, C	B, C	B ² , C	B, C	B, C	B, C	A, B, C
Resistance Testing	B, C	B, C	B, C	C	A, B, C	B, C	B ² , C	B, C	B, C	B, C	C
If test desired	Available						Not fully available or ideal				Not available

A Reduce unnecessary antibiotic prescriptions, B Guidance for appropriate treatment of drug-resistant infections, C Surveillance

*Based on informal consensus of participants attending the Technical Consultation on In Vitro Diagnostics for AMR.

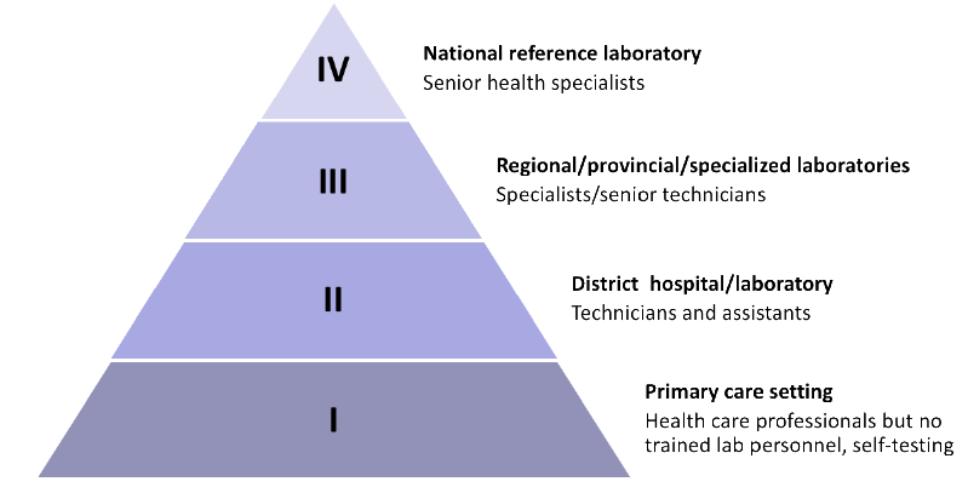
Notes:

¹ MTB, the cause of human tuberculosis, was not subjected to review for inclusion in this prioritization exercise as it is already a globally established priority. And although priority TPPs to stimulate product development have been developed, more innovative new TB diagnostics are urgently needed. The section on TB was provided by the WHO Global TB Programme.

² In case it is needed in special populations.

³ Infection marker.

https://www.who.int/medicines/access/antimicrobial_resistance/en/





Emerging BSI Tests & Technologies

FDnews Device Daily Bulletin
Medical Devices / Submissions and Approvals
T2 Biosystems Earns CE Mark for Antibiotic Resistance Diagnostic
Nov. 22, 2019



www.t2biosystems.com
Josephson L et al Angew Chem 2001

London, UK and Carlsbad, CA, USA – 2 November 2018 – A rapid new diagnostic platform that harnesses the power of semiconductor DNA sequencing, promises to revolutionise the ability of physicians to treat antimicrobial resistant infections. DNAe achieves major milestone in a novel clinical sequencing platform, successfully completing the first phase of its \$51.9 million contract with US government's BARDA



www.dnae.com

FDA clears Accelerate Diagnostics' infection test
by Amirah Al Idrus | Feb 24, 2017 9:20am



www.acceleratediagnostics.com



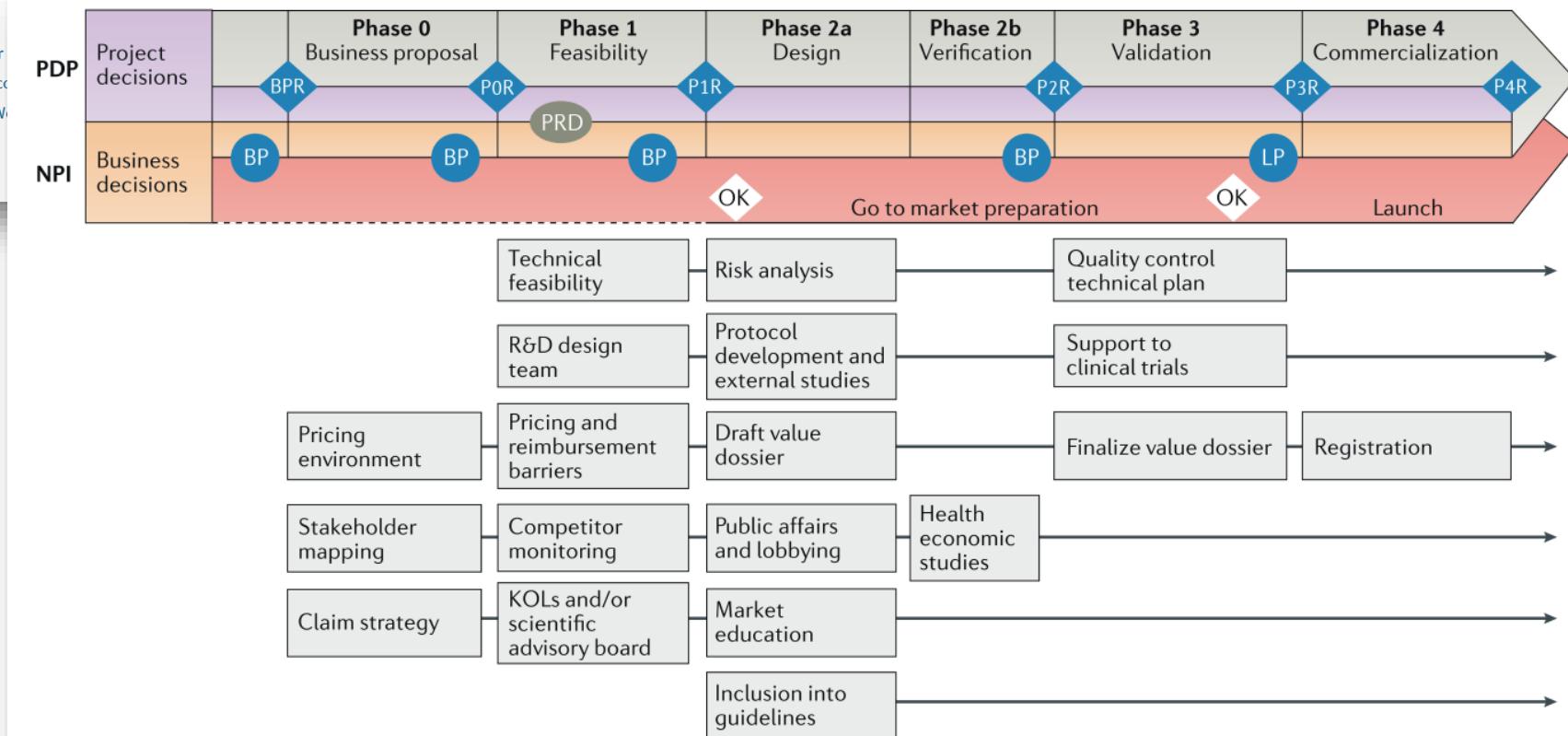
Commercial Pathway to Develop Antimicrobial Susceptibility Testing Systems

Consensus Statement | OPEN | Published: 17 October 2018

Developmental roadmap for antimicrobial susceptibility testing systems

Alex van Belkum , Till T. Bachmann, Gerd Lüdke, Jan Gorm Lisby, Gunnar Karsten Becker, John P. Hays, Neil Woodford, Konstantinos Mitsakakis, Jacob Harald Peter, John H. Rex, Wm. Michael Dunne Jr & the JPIAMR AMR-RDT Working Group on Antimicrobial Resistance and Rapid Diagnostic Testing

Nature Reviews Microbiology (2018) | Download Citation 





Many **Thanks** for Your Attention

Visit our Surveys

AMR Diagnostics-Teaching and Training

<https://edin.ac/2Qk37Vb>

AMR Diagnostics Teaching & Training Resource

<https://edin.ac/376Vd7N>

Creating point-of-care diagnostics for neonatal sepsis.

Amrita Sukrity
Founder, SpotSense
GARDP-REVIVE Webinar 26th Nov 2019



Making Healthcare Simple

Current diagnostics landscape for neonatal sepsis.

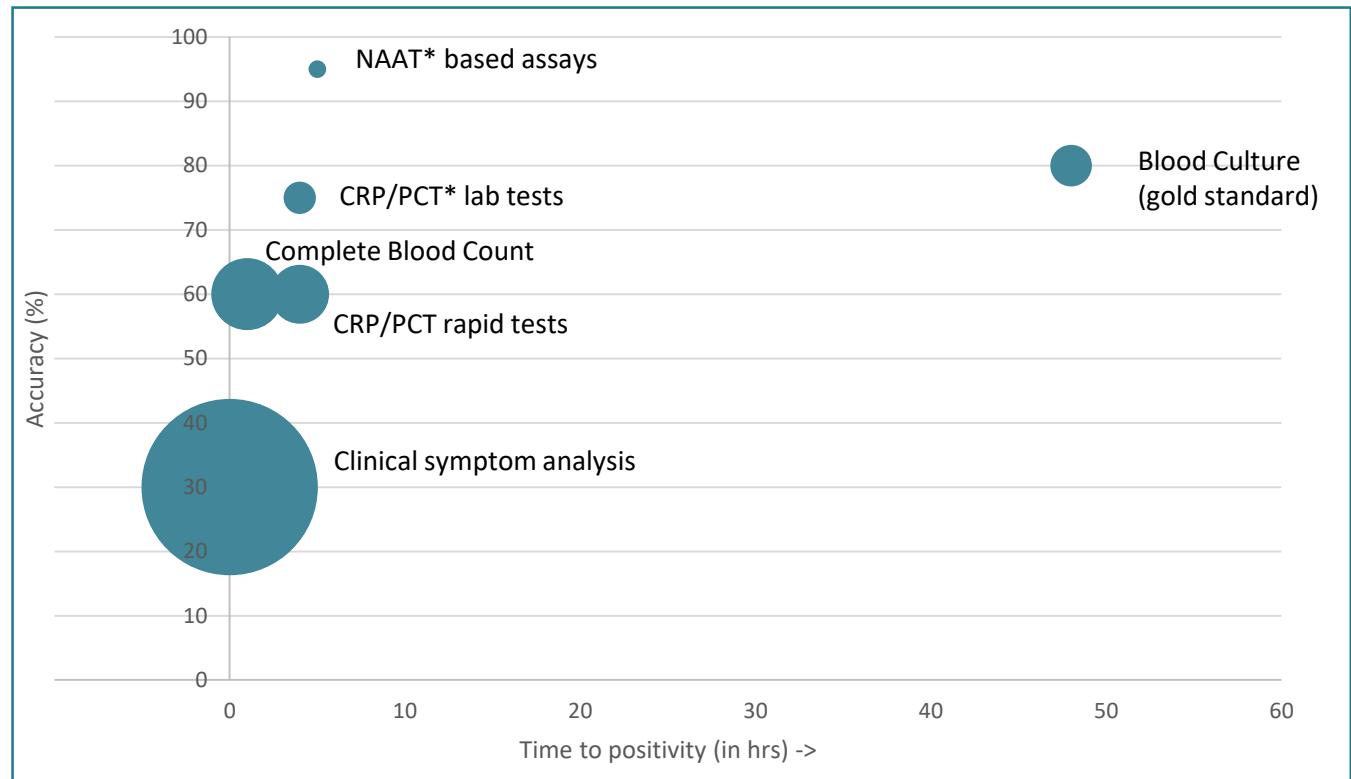
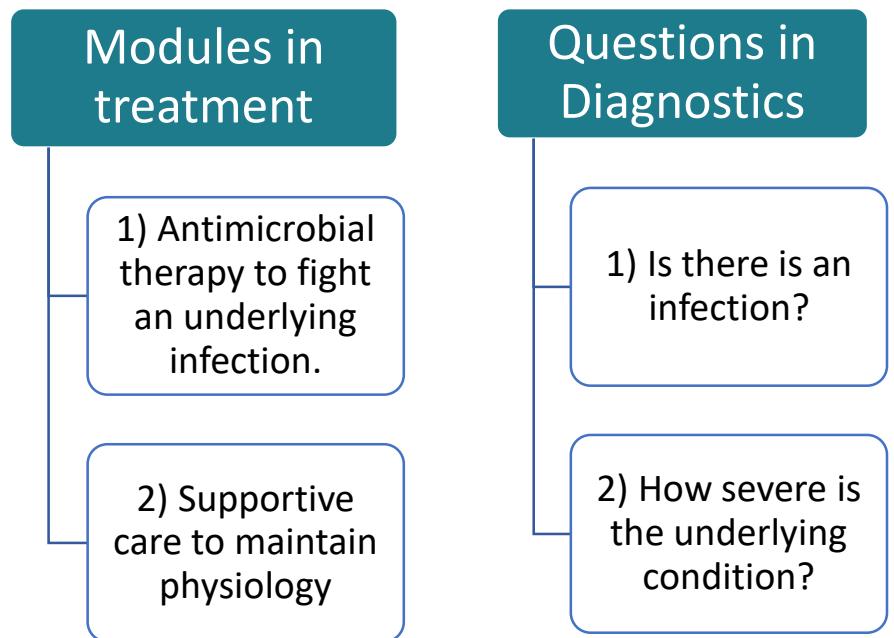
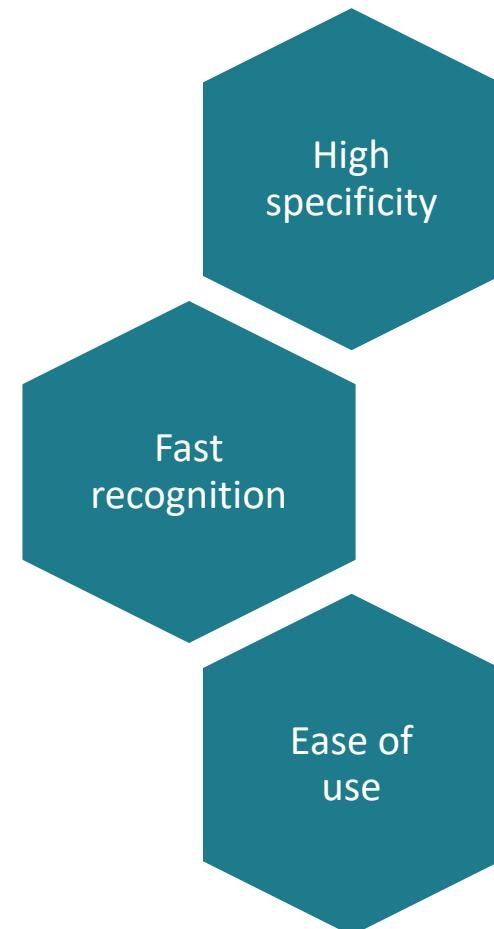


Chart 1: Current diagnostic protocols, their Time-to-positivity, accuracy and accessibility parameters. The radius of bubbles indicate accessibility of these tests at community health level.

*NAAT - nucleic acid amplification test
CRP - C-reactive protein
PCT - Procalcitonin

Requirements for a point-of-care test to be used at the community.



- Most sepsis protocols focus on initiating treatment within 60 min of presentation of sepsis.
- Newborns with sepsis who are treated with antibiotics within 60 min of presentation have significantly better outcomes than those with delayed treatment.

- Blood culture, considered a gold standard for sepsis can indicate false negatives in 20-40% of sepsis cases.
- While physicians do want to know the causative organism, the choice of antibiotics doesn't always depend on the result.
- Prolonged early empirical antibiotic therapy is also known to be associated with increased risk of sepsis, NEC* and death.

- The delay in start of therapy is very often attributed to a delay in referral, especially when clinical presentation isn't conclusive for sepsis.
- After start of treatment, continuous monitoring is a challenge as frequent blood draws are not advisable.

*NEC – Necrotizing enterocolitis

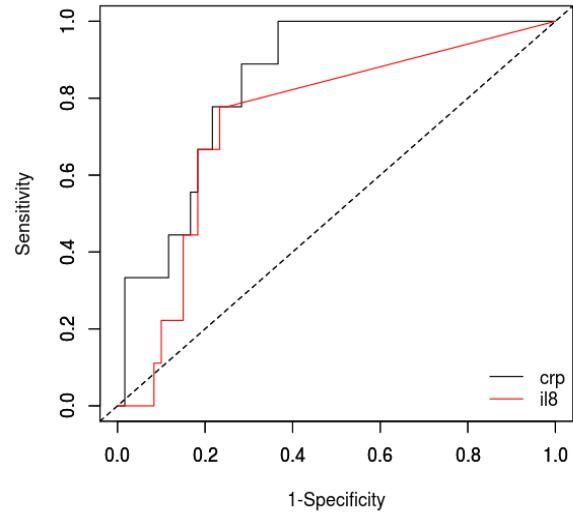
Understanding the role of Interleukin 8/IL8 (CXCL8) in neonatal immunology.

Why did we choose IL8 as our 'biomarker of choice'?

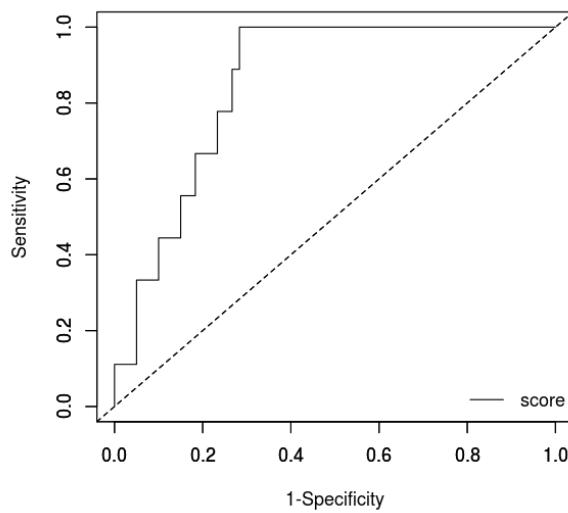
- There isn't a significant physiological change in IL8 production based on gestational age at birth.
- IL8 production is evident in babies with gestational age as low as 23 weeks and then remains mostly stable for healthy newborns.
- Previous literature has shown a marked rise in IL8 production which precedes a rise in C-Reactive Protein aiding in fast recognition of sepsis.
- Some previous studies have shown that IL8 can be correlated with severity of sepsis.

However, in case of early onset sepsis

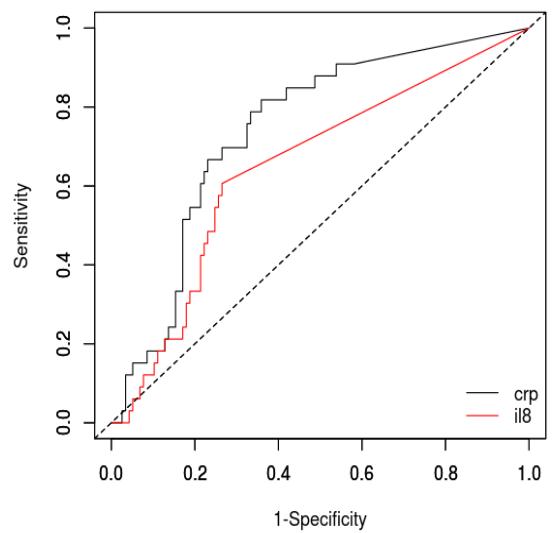
- Significantly lower amounts of monocytes and neutrophils are seen to be recruited during infection.
- A reduction in expression of adhesion molecules is also noticed leading to difficulties in migration of neutrophils to the site of infection.
- IL8 production can still be very readily seen to be provoked by antigen receptor engagement of T cells in preterm infants, but levels remain low for first 3 days.



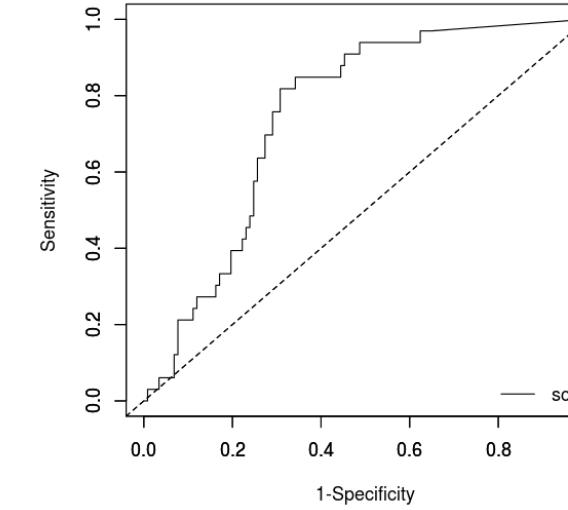
ROC curve for salivary IL8 and salivary CRP for late onset bacteremia on the first screening test.



ROC curve for combined score for late onset bacteremia on the first screening test.



ROC curve for salivary IL8 and salivary CRP for late onset bacteremia across all tests (after antibiotics have begun).



ROC curve for combined score for late onset bacteremia across all tests (after antibiotics have begun).

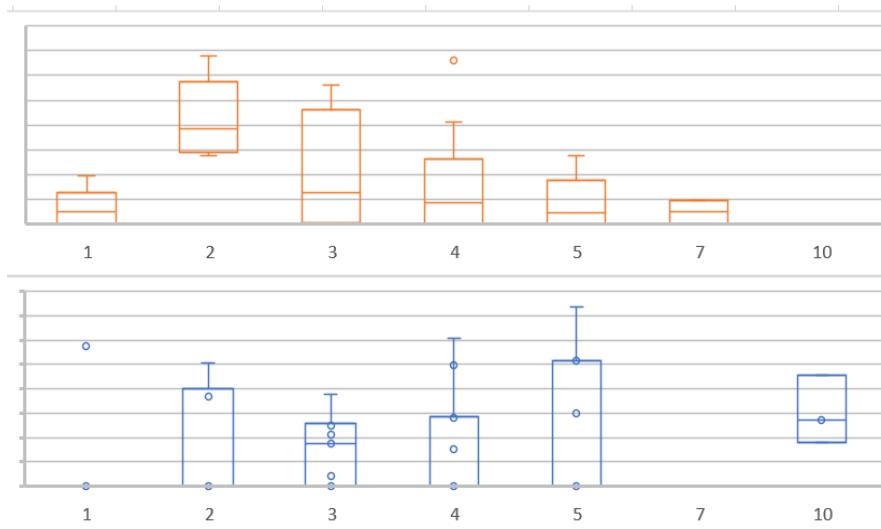
Predicting late onset culture positive sepsis (bacteremia) using a combined score of salivary IL8 and salivary CRP.

What are some of the trends for early onset sepsis?

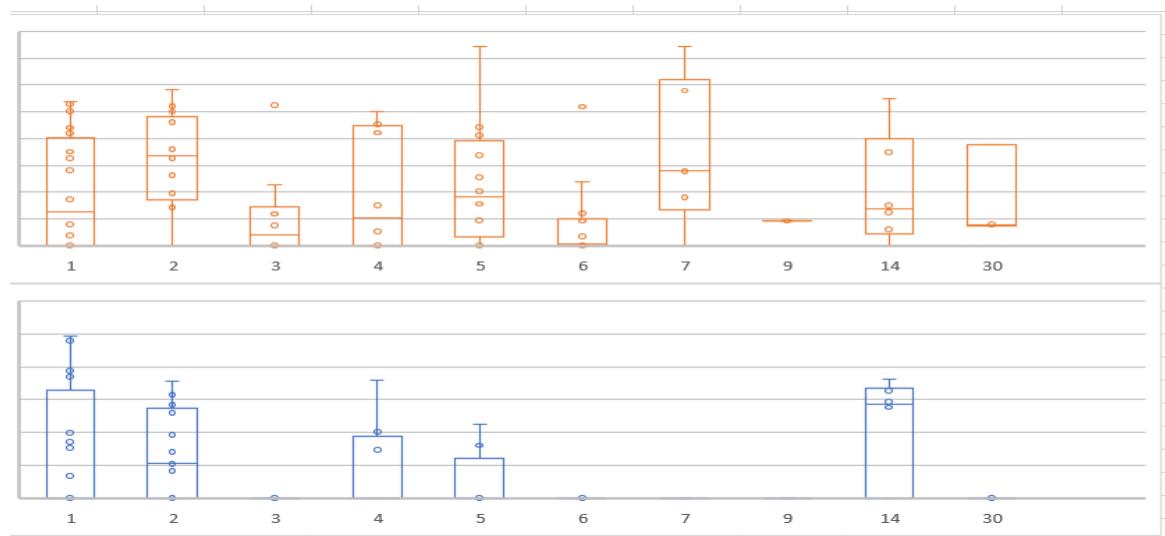
Variation of salivary IL8 and salivary CRP levels with gestational age

Parameter	P-value
Gestational age and salivary IL8 levels	0.0045
Gestational age and salivary CRP levels	0.0002

Variation of salivary IL8 and salivary CRP levels with physiological age

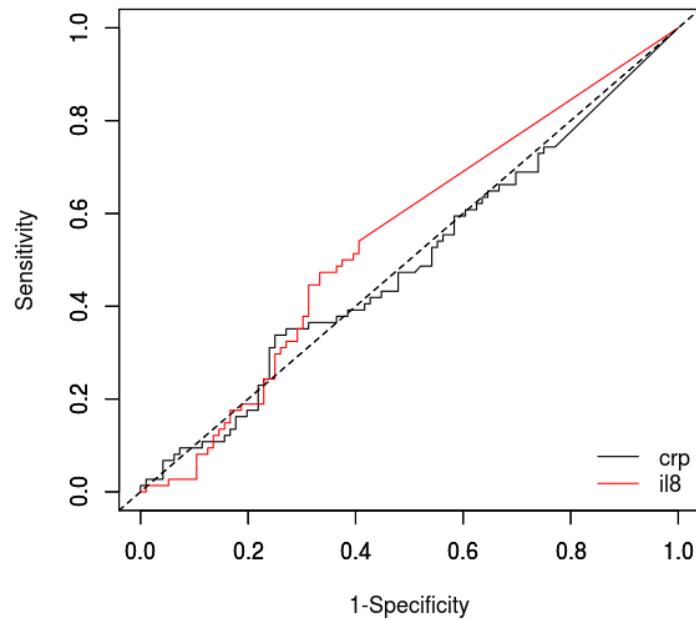


Variations across CRP (top) and IL8 (bottom) levels against physiological age for healthy babies without any comorbidities.

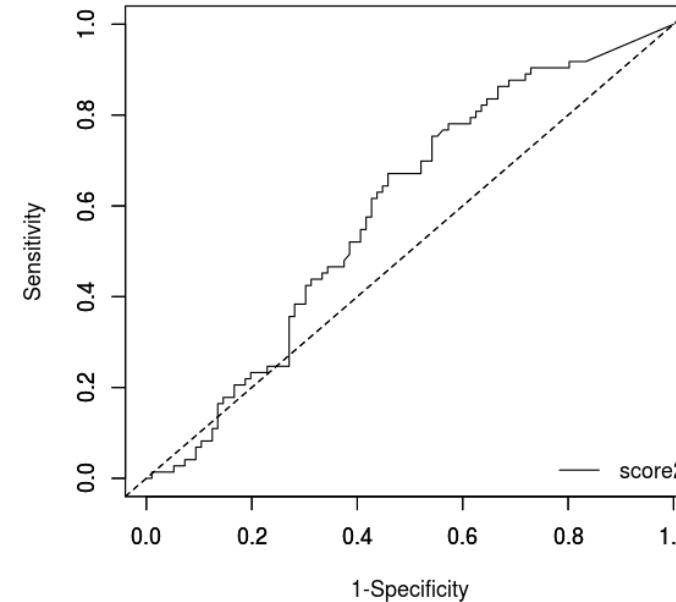


Variations across CRP (top) and IL8 (bottom) levels against physiological age for babies with early onset sepsis.

Predicting early onset culture-positive sepsis (bacteremia) using a combined score of salivary IL8 and salivary CRP.



ROC curve for salivary IL8 and salivary CRP for early onset sepsis across all tests (after antibiotics have begun).

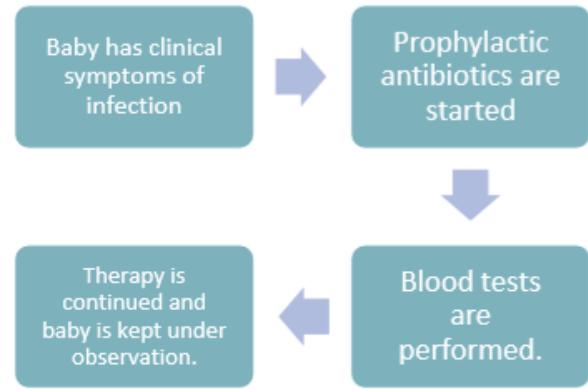


ROC curve for combined score for early onset sepsis across all tests after adjusting for gestational and physiological age (after antibiotics have begun).

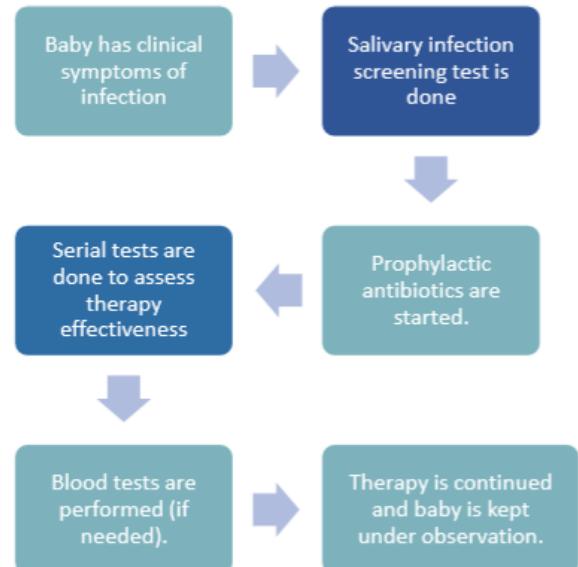
For early onset, especially for babies who are 48 hours old, a CRP and IL8 salivary test may not work for screening and should be used in addition with clinical symptom analysis.

Where do we go from here?

Current 'standard-of-diagnostic' for neonatal sepsis



Proposed 'standard-of-diagnostic' for neonatal sepsis



Some unanswered questions

- Would there be a difference in the cut-off points based on demography/ethnicity of the newborn?
- How do we separate out the effects arising from developmental immune disorders?
- What clinical parameter should be compared to quantitatively define the severity of sepsis?.

Thank You

Going against the Flow: towards a lateral flow, point of care test for sepsis/severe infections

A/Prof David Anderson, Deputy Director, Burnet Institute



GARDP Webinar, 26 November 2019

“Going against the Flow” – can we use lateral flow technology (POC) instead of Flow Cytometry to measure cell-associated biomarkers?

- **CD4 T-cells (Visitect® CD4 and Visitect® CD4 Advanced Disease – Omega Diagnostics, UK)**
 - CE Mark approval, and recent Global Fund endorsement for procurement of the CD4 Advanced Disease test

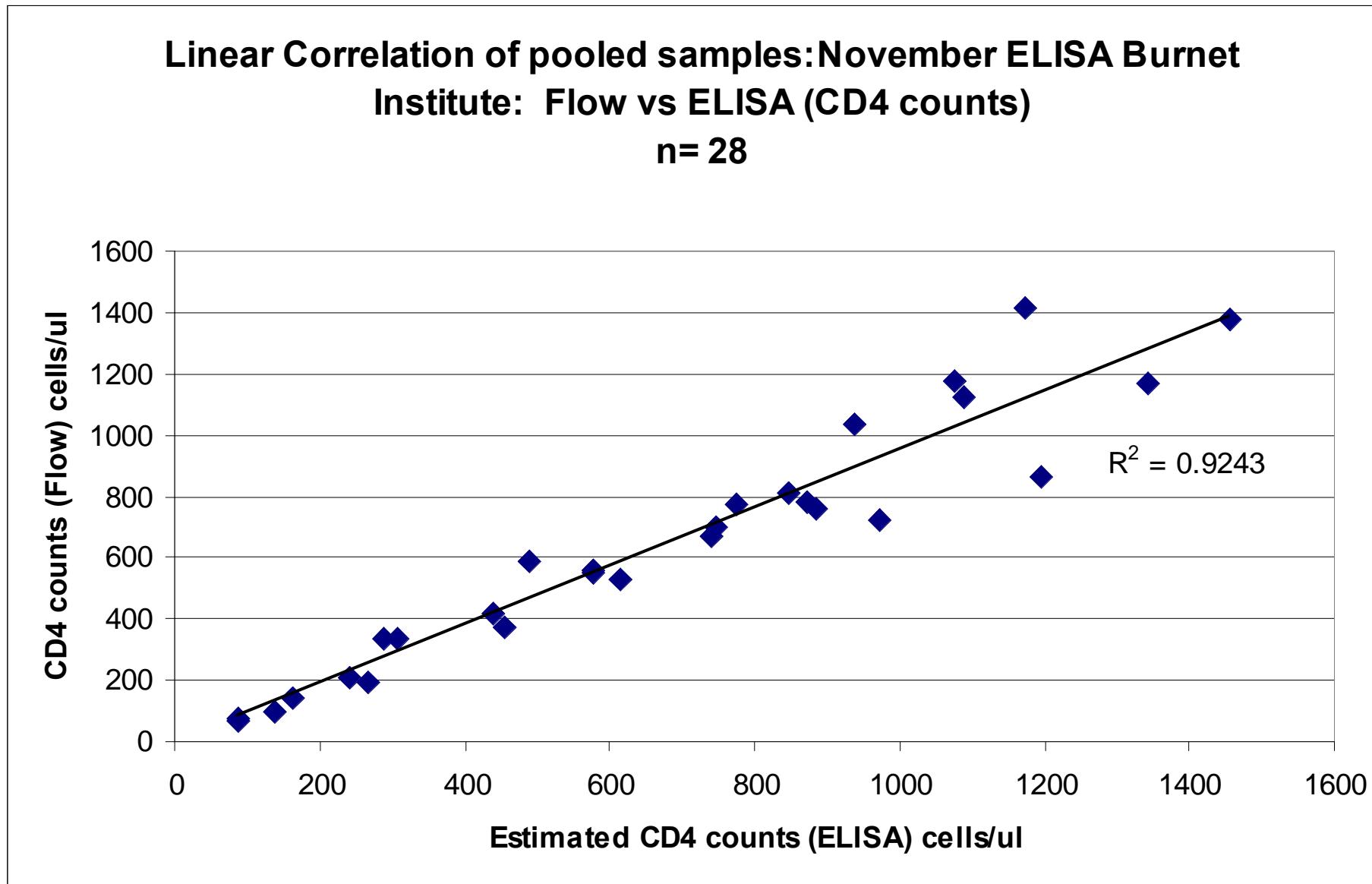


- **Neutrophil CD64 as a marker of sepsis/severe infections**
 - Well documented as a sepsis biomarker using flow cytometry, with elevated levels of CD64 on both neutrophils and monocytes during severe infections, but available flow cytometry test based on neutrophils only

From Visitect® CD4 to sepsis/severe infections

- Burnet R&D that led to the Visitect® CD4 T-cell tests (Omega Diagnostics) solved two critical questions that are also relevant to our development of a test for sepsis/severe infection:
 - 1) Can you measure cell-associated molecules in lateral flow, as an alternative to Flow Cytometry?
 - 2) Can you remove monocytes from whole blood in a lateral flow device?

1. Measuring cell-associated antigen (CD4) vs Flow



CE Mark and commercial launches of tests in 2017 (350 cutoff) and 2019 (200 cutoff, Advanced Disease). Global Fund endorsement of Advanced Disease test for procurement in 2019



RESEARCH ARTICLE

Open Access



CrossMark

Qualitative assessment of South African healthcare worker perspectives on an instrument-free rapid CD4 test

Fiona Scorgie^{1*}, Yasmin Mohamed^{2,3}, David Anderson², Suzanne M. Crowe², Stanley Luchters^{2,3,4,5} and Matthew F. Chersich^{1,5} 

IMMUNOASSAYS



Field Performance and Diagnostic Accuracy of a Low-Cost Instrument-Free Point-of-Care CD4 Test (Visitect CD4) Performed by Different Health Worker Cadres among Pregnant Women

Stanley Luchters,^{a,b,c} Karl Technau,^d Yasmin Mohamed,^{a,b} Matthew F. Chersich,^{c,e} Paul A. Agius,^{a,b} Minh D. Pham,^a Mary L. Garcia,^a James Forbes,^f Andrew Shepherd,^f Ashraf Coovadia,^d Suzanne M. Crowe,^{a,g} David A. Anderson^a

^aBurnet Institute, Melbourne, Victoria, Australia

^bDepartment of Epidemiology and Preventive Medicine, Monash University, Melbourne, Victoria, Australia

^cInternational Centre for Reproductive Health, Department of Public Health and Primary Care, Ghent University, Ghent, Belgium

^dEmpliveni Services and Research Unit, Department of Paediatrics & Child Health, Rahima Moosa Mother and Child Hospital, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa

^eWits Reproductive Health and HIV Institute, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa

^fOmega Diagnostics, Ltd, Omega House, Alva, Scotland

^gThe Alfred Hospital and Department of Infectious Diseases, Monash University, Melbourne, Victoria, Australia

>90% accuracy for the Visitect® CD4 and CD4 Advanced Disease test using visual readout in multiple trial sites across India, UK, and Sub-Saharan Africa

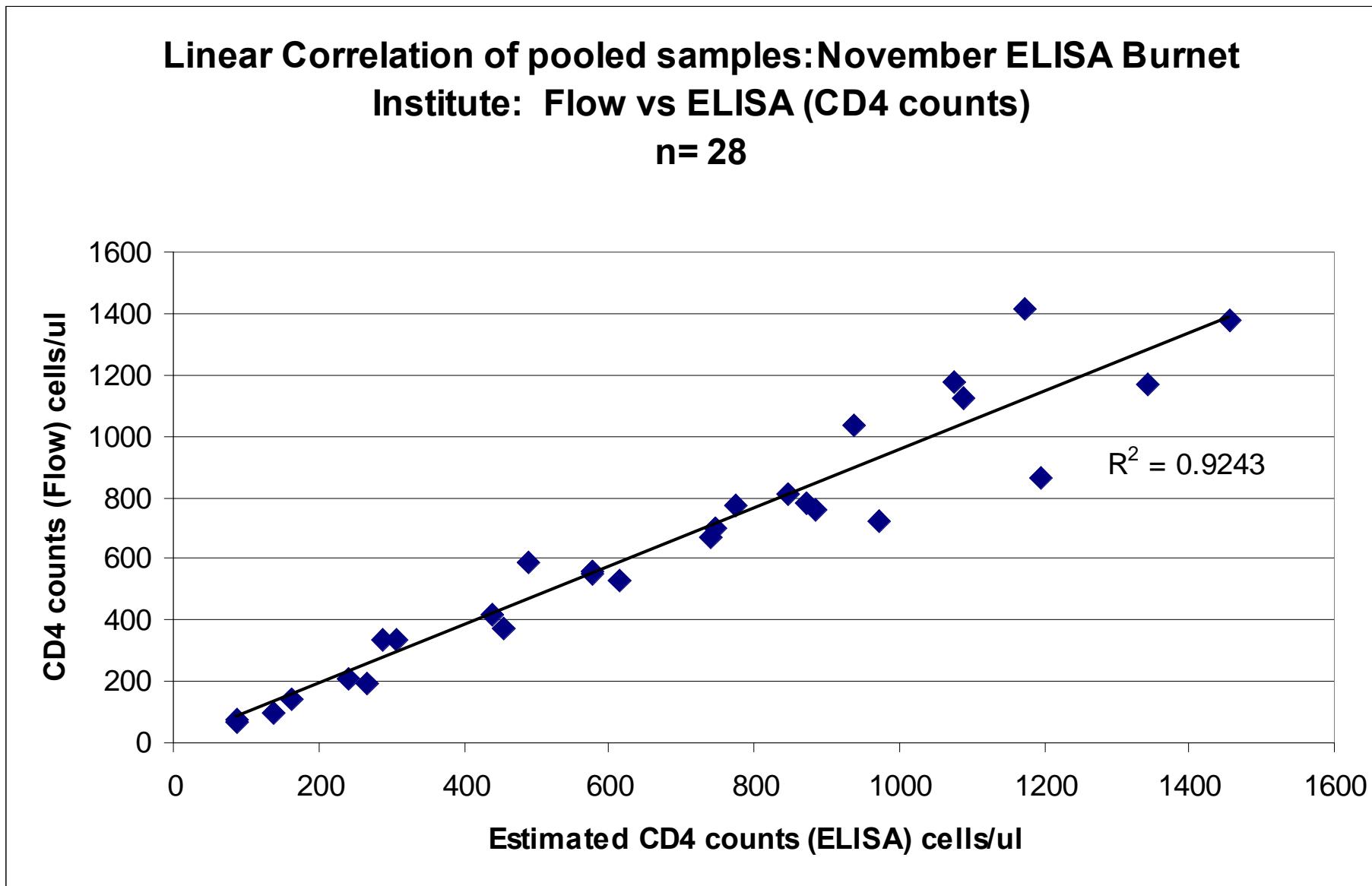
CD64 in sepsis/severe infections

- Sepsis kills around 8 million people each year, mostly neonates and young children plus the elderly – #1 cause of death in hospitalised patients, and major cause of death in HIV patients with Advanced Disease (CD4 <200)
- Urgent need for rapid diagnosis to identify severe bacterial infections requiring antibiotic treatment, while reducing over-treatment / prophylaxis
- Neutrophil CD64 expression (by flow cytometry) is one of the most robust single biomarkers, but utility is severely limited by access to flow cytometry
 - Monocytes show high basal level of CD64, up-regulated by IFN-gamma etc during infection
 - Neutrophils show negligible basal CD64, but high levels during infection in MOST patients, when tested using flow cytometry

Can we adapt “neutrophil CD64” for POC?

- Adaptation of the neutrophil CD64 index test (Leuko64) to point of care using the same approach as CD4 T-cell test
 - But surprising discoveries along the way....
- Measuring NE as an indication of neutrophil numbers (just like CD4), and the total amount of CD64 in **whole blood**
- Ongoing clinical study (lab-based ELISAs) in healthy and ICU controls and sepsis patients (Sepsis-3 criteria), Alfred Hospital, Melbourne; and in neonates (referred to lab for suspicion of sepsis or severe infection), Royal Children's Hospital, Melbourne, and Royal Hobart Hospital, Hobart

CD4 vs CD4 T-cells is linear



CD4 vs CD4 T-cells is linear

Linear Correlation of pooled samples: November ELISA Burnet
Institute: Flow vs ELISA (CD4 counts)
n= 28

1600

CD64 vs Neutrophils (NE)
should be the same (?)

C

200
0

0

200

400

600

800

1000

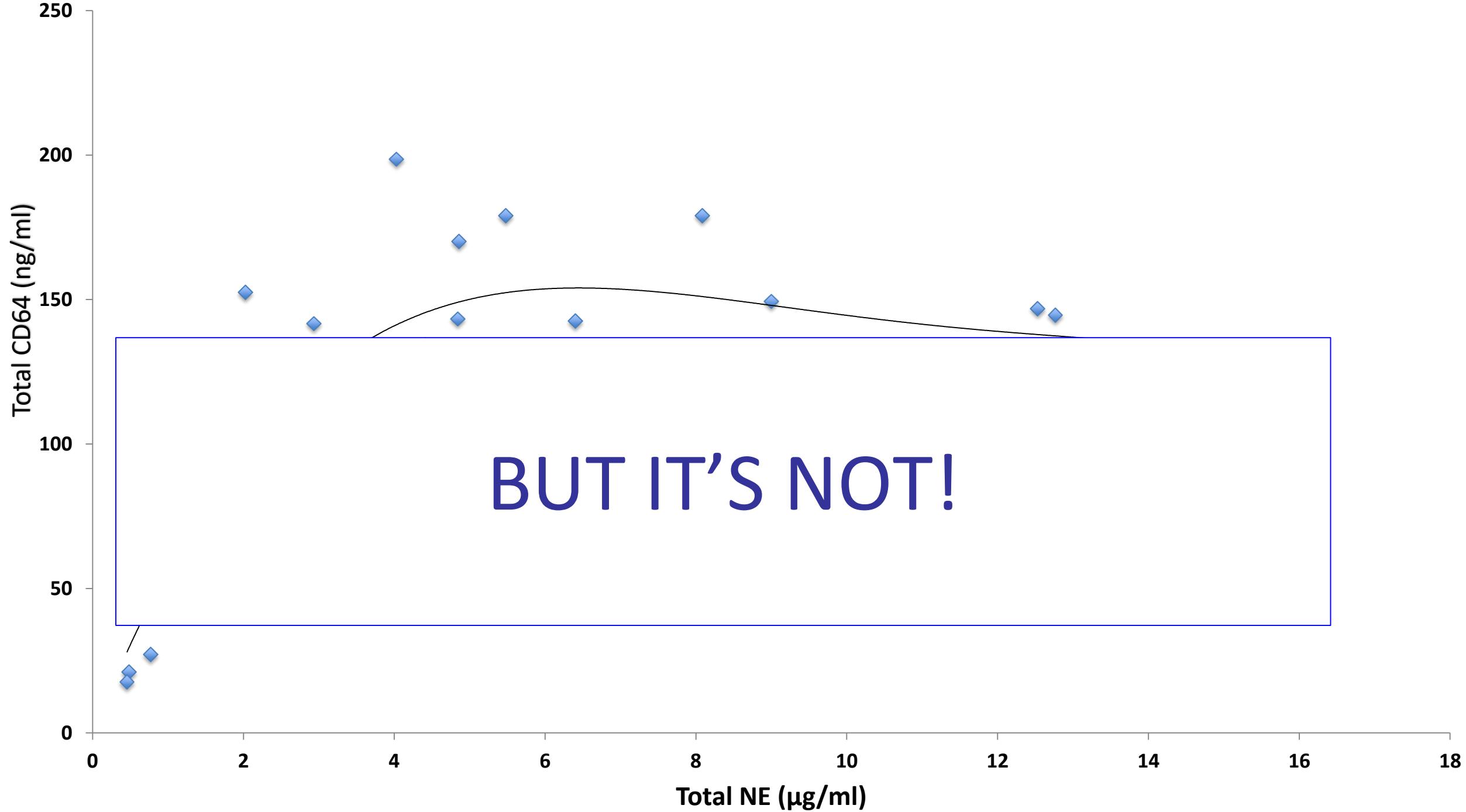
1200

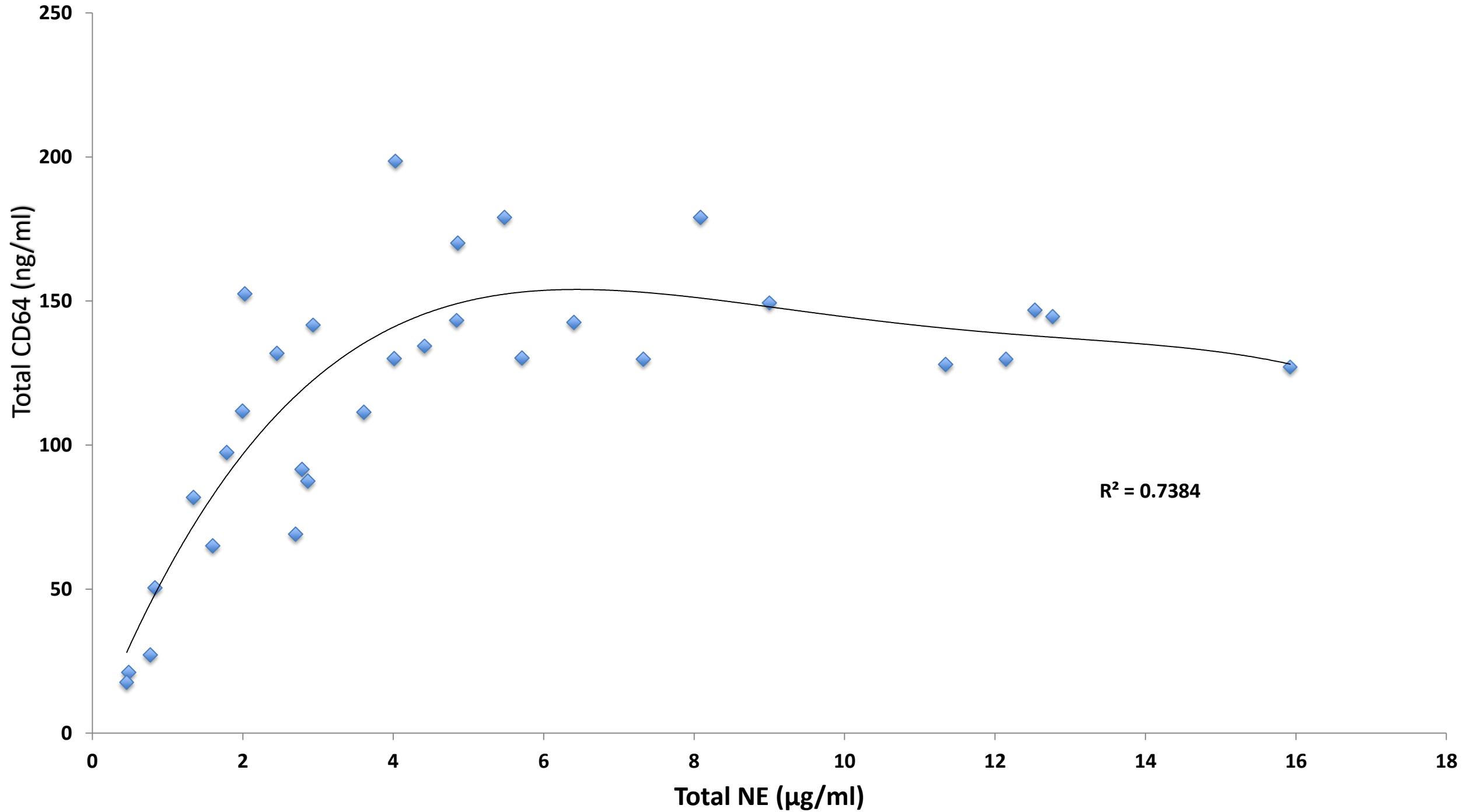
1400

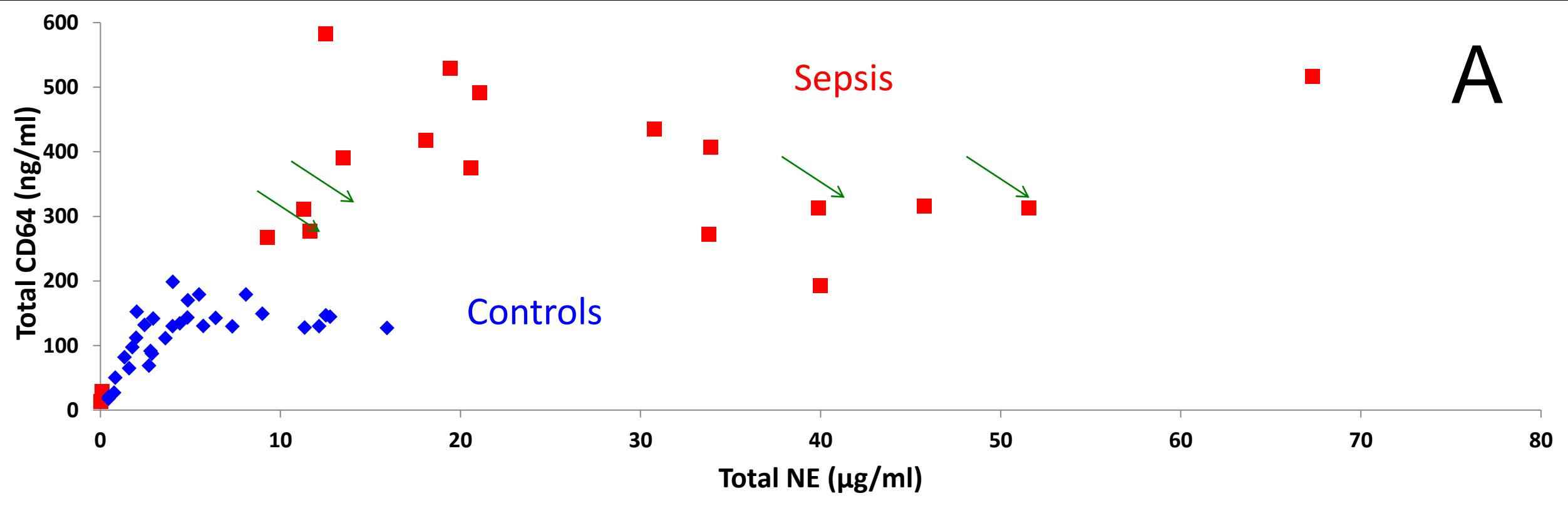
1600

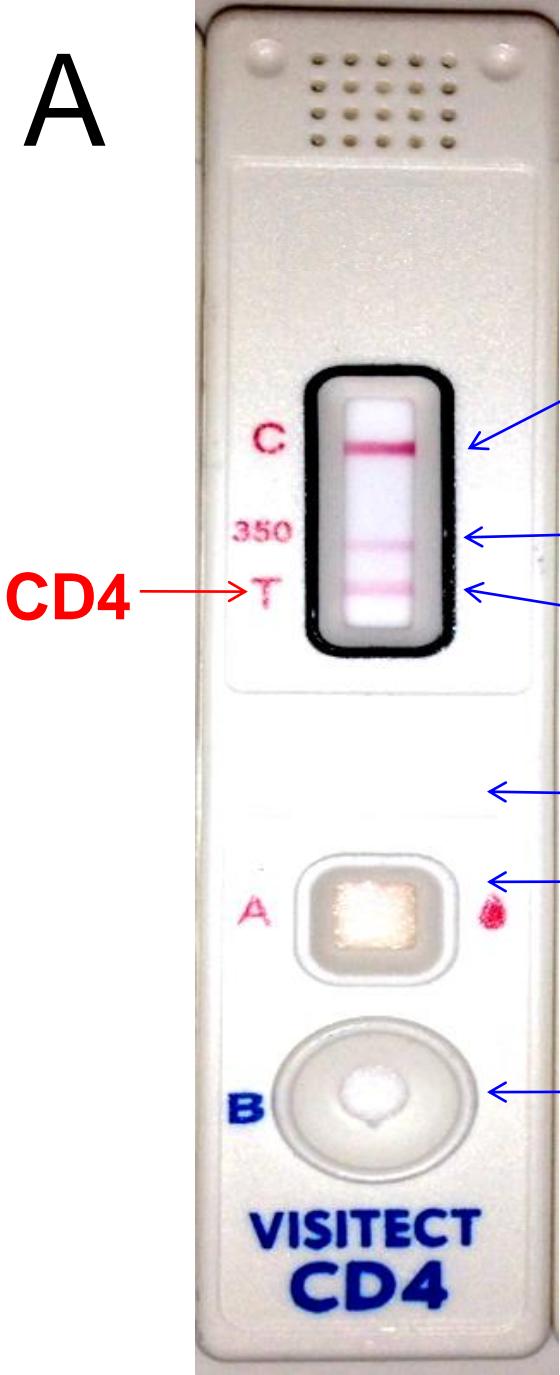
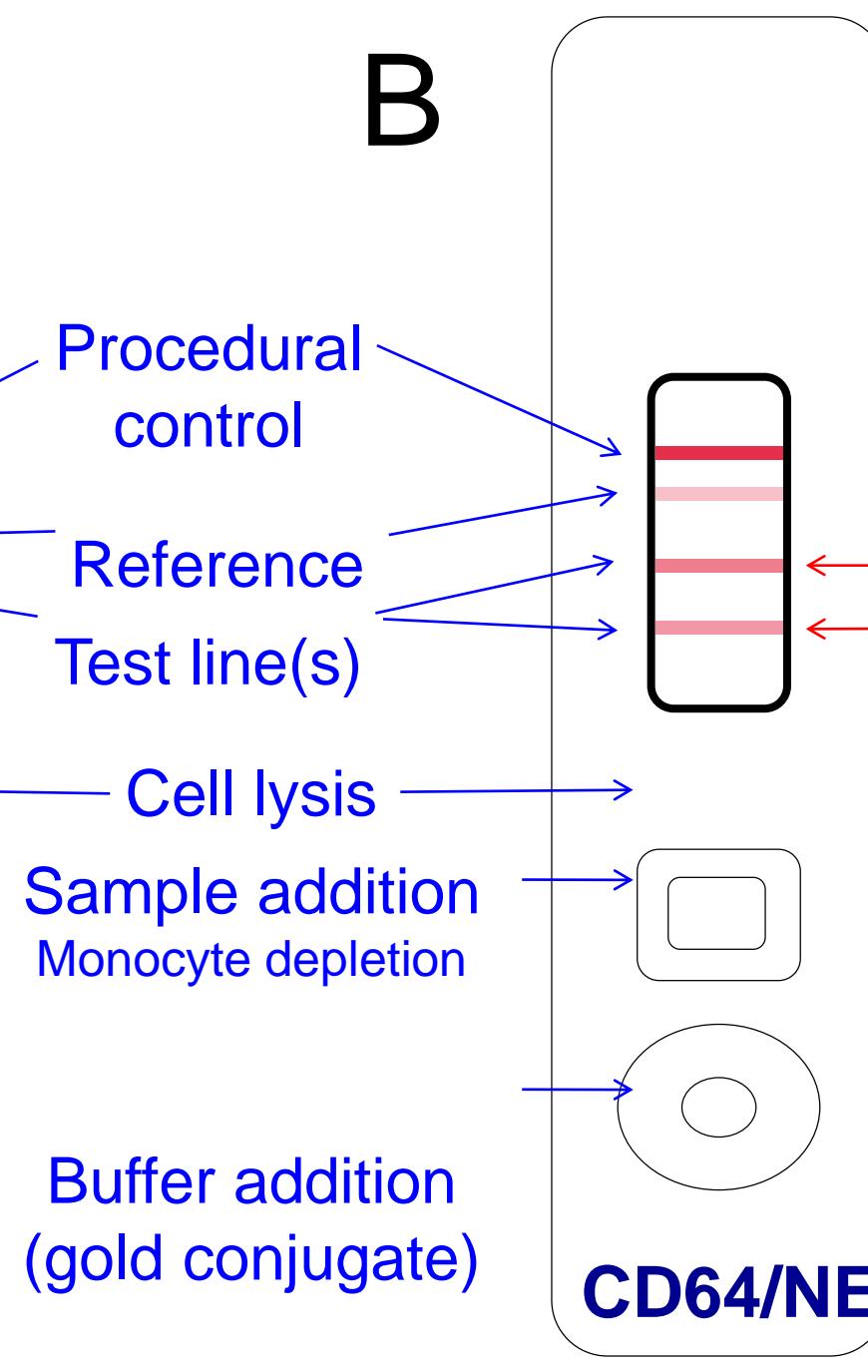
Estimated CD4 counts (ELISA) cells/ul

1







A**B****C**

Thanks

- Mary Garcia, Robyn Lloyd, Suzanne Crowe, Simone van de Waarsenburg, Jocelyn Diaz, Nadine Barnes, Alan Landay (Rush U.), Tom Denny (Duke U.)
- Stanley Luchters, Minh Duc Pham (Burnet), Dr Pachamuthu Balakrishnan (YRG Care, Chennai), Matthew Chersich (WITS, Johannesburg) – CD4 test validation and implementation studies
- Andrew Shepherd, Edward Valente, John Bannister and teams, Omega Diagnostics, UK – Visitect® CD4 commercialisation
- Riya Palchaudhuri, Suzanne Crowe, Clovis Palmer, Mary Garcia, Shuning Zheng, Nobin Khan, Grace Anderson, Serina Cucuzza, Viv Gleeson, Naomi Spotswood (Burnet), Steve McGloughlin, Shirley Vallance, Emma Martin and team (Alfred ICU Melbourne) and lab team at RCH/RHH – CD64/sepsis

Today's speakers

Innovation in point-of-care diagnostics for sepsis and bloodstream infections



Till T. Bachmann
University of Edinburgh, UK



Amrita Sukrity
SpotSense, India



David Anderson
Burnet Institute, Australia



Moderator:
Caroline Purslow
Nesta Challenges, UK

Submit your questions via the
questions window!

We will announce our first
2020 webinars soon.
Stay tuned!



Thank you for joining us

Visit now revive.gardp.org/webinars to find more
webinars about antimicrobial drug R&D