Imperial College London

# Biosensors and machine learning for improving antimicrobial prescribing

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NIHR invention for innovation (i4i) Clinical Research Fellow

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# Background

NHS
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**Integrated clinical decision support tools for antimicrobial management**

**Personalised antimicrobial selection** ⇨ **Precision dosing** ⇨ **Patient engagement**

**Diagnostics & Surveillance**

**Delivered at point of care**

**Within end-user workflow**

epicimpoc
enhanced, personalized and integrated care for infection management at point of care

# Identified gaps with decision support

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Greater need for flexibility in the face of inter-individual variation

Gaps in:

- Dose optimisation
- Physician engagement with AMS programmes
- Patient engagement
- Ability to integrate with novel diagnostics

Failures in adoption of interventions

Not addressing steps of the physicians decision making pathways

Need for integration with decision making beyond infection management

Rawson, Moore, et al. Clinical Microbiology and Infection. 2017
Rawson, Tivey, et al. Antimicrobial Resistance and Infection Control 2017
Rawson, Charani, et al. BMC Medicine 2016
Rawson, Moore, et al. BMJ open 2016
Rawson, Moore, et al. Journal of Antimicrobial Chemotherapy. 2016
Rawson, Moore, et al. Journal of Antimicrobial Chemotherapy. 2015

# Specialty engagement with AMS

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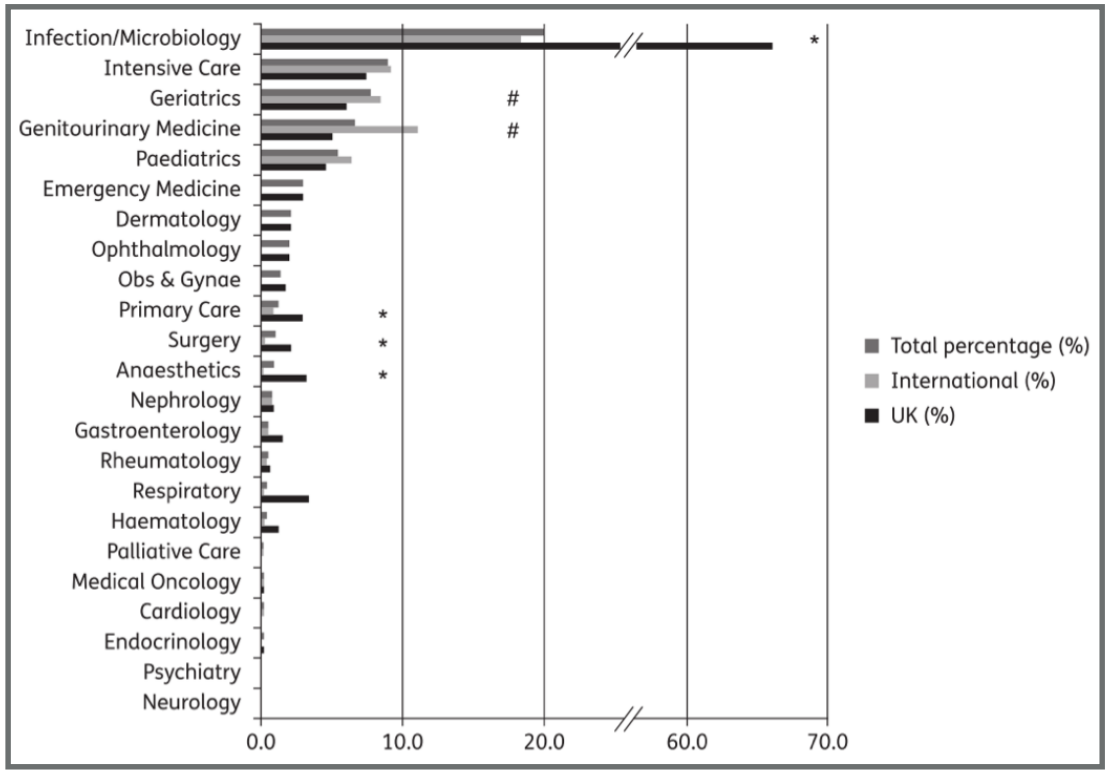


**Scientific conference engagement with AMS - AMR**

## The gap is also reflected in education

**Primary care:**

- Prescribes **74%** of antimicrobials
- Has **2/1368** unique learning points on AMS – AMR in total

Only **40%** of AMS – AMR learning points require demonstration of skill / behaviour


Rawson, Tivey, et al. Antimicrobial Resistance and Infection Control 2017
Rawson, Moore, et al. Journal of Antimicrobial Chemotherapy. 2016
Rawson, Moore, et al. Journal of Antimicrobial Chemotherapy. 2015

# Mapping decision pathways

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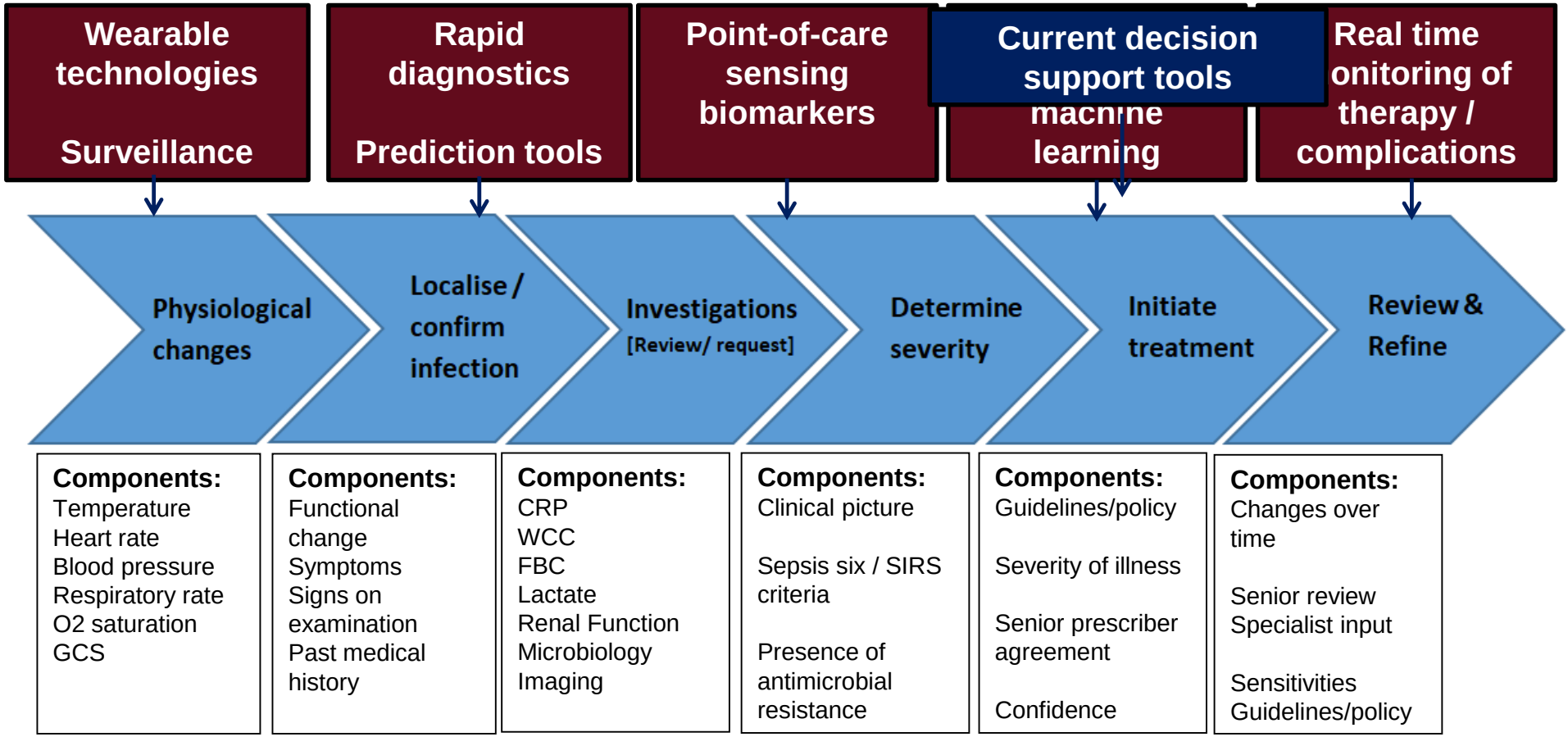


Provide better and more **individualised** data at each step of the physicians **decision making pathway** to promote better decisions

Rawson, Charani, et al. BMC Medicine; 2017

# Antibiotic selection

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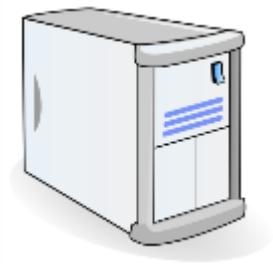
**Presentation with possible infection**



Physician entry

Trust servers

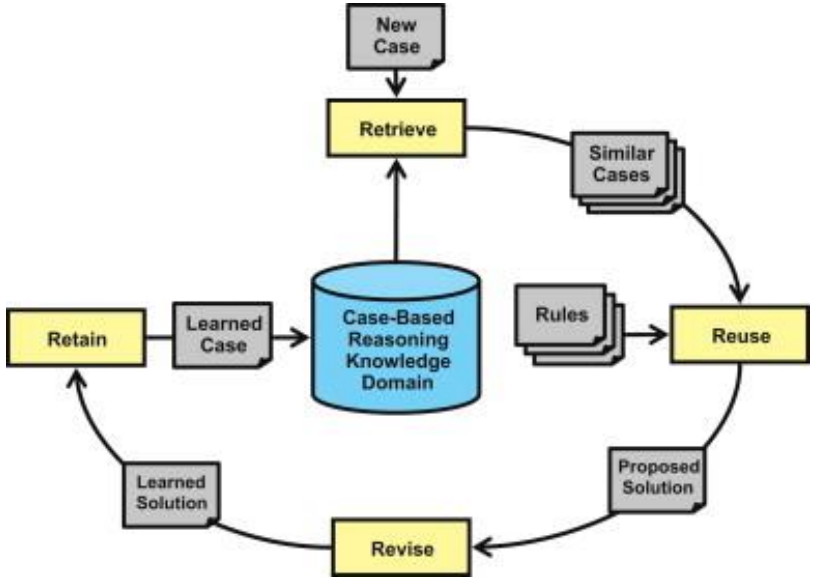
New Case

**45** parameters

Treatment Recommendation

## Case based reasoning (CBR)

To solve a **new problem** by remembering **previous similar situations** and reusing knowledge and data from this scenario




Hernandez, Herrero, Rawson, et al HEALTHINF; 2016
Rawson, Thesis 2017

# Prediction tools

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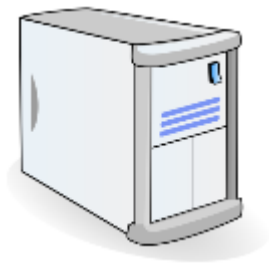
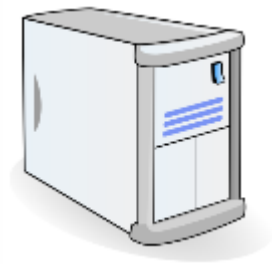
**Presentation with possible infection**



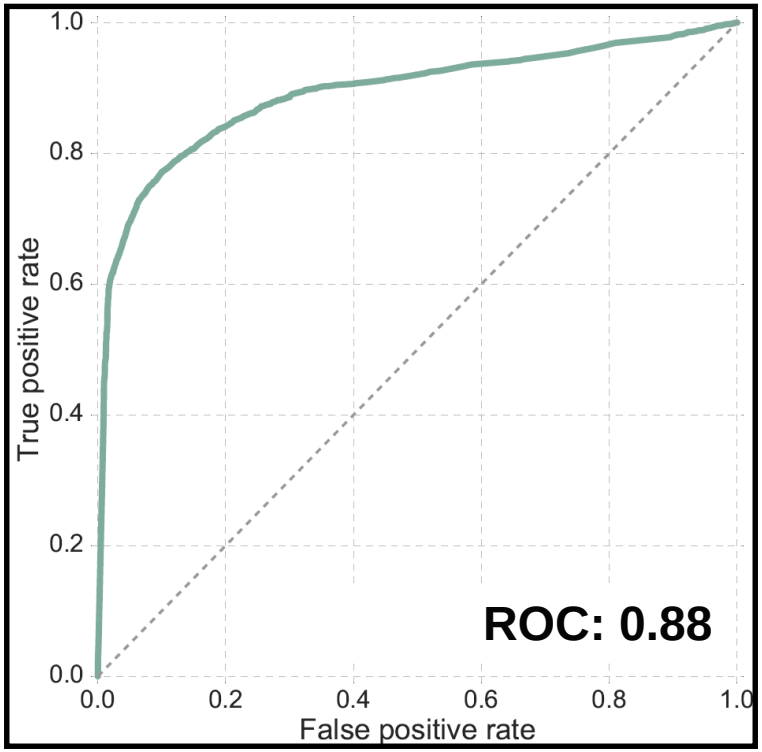


Microbiology

Pathology

Supervised machine learning

Likelihood estimate




**Support Vector Machine (SVM) for predicting culture positivity in advance of microbiology**



Hernandez, Herrero, Rawson, et al BMC Med Dec Mak; 2017

# Challenges to consider

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- Curation of system
- Moving away from guideline based prescribing
- Can only support decision making
- Understanding how data will be interpreted
- Embedding tools into end-users workflow
- Ensuring systems are agnostic to different healthcare systems
- Preparing for integration with new diagnostic tools

Hernandez, Herrero, Rawson, et al BMC Med Dec Mak; 2017

# Dose optimisation

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## As important as antimicrobial selection

Wide pharmacokinetic variation

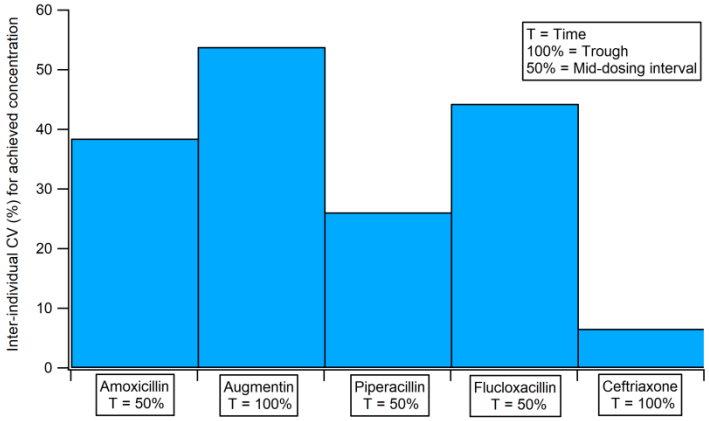
Wide variation in outcomes of therapy

A problem in wide range of antibiotics and clinical areas

## Vancomycin therapy and obesity

| | | |
|---|---|---|
| Obese AUC:MIC ratio | mean (SD) | 320 (74) |
| Obese meeting AUC:MIC target | n=(%) | 1 (17) |
| Overweight AUC:MIC ratio | mean (SD) | 479 (108) |
| Overweight meeting target | n=(%) | 6 (75) |
| Normal AUC:MIC ratio | mean (SD) | 524 (174) |
| Normal weight meeting target | n=(%) | 12 (75)* |

## Beta-lactam variation




Rawson, Thesis; 2017

Rawson, Charani, et al. Journal of Infection; 2016

# Dosing is a dynamic process

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## Inter-individual variability

**Age**

**Race**

**Ethnicity**

**Gender**

**Comorbidities**

**Medications**

## Intra-individual variability

**Hyper-dynamic circulation**

**Altered fluid balance**

**Renal dysfunction**

**Hepatic dysfunction**

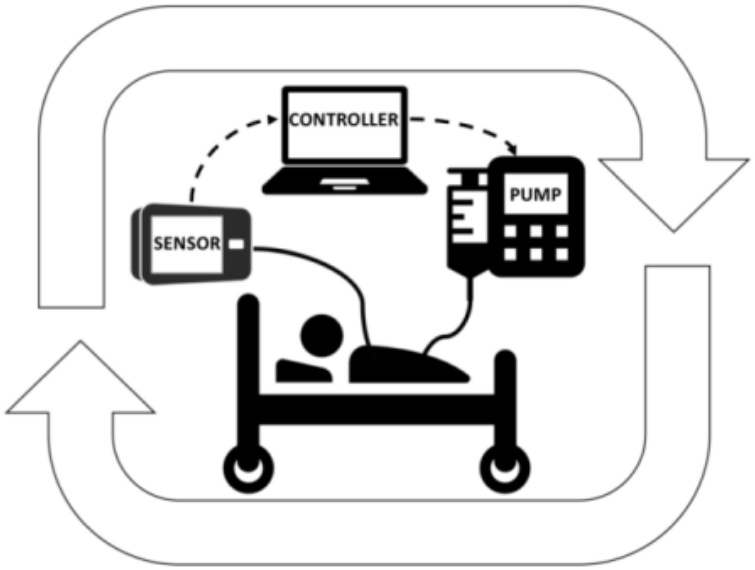
**Augmented renal clearance**

**Organ support**



Rawson, O'Hare, et al. Journal of Antimicrobial Chemotherapy; 2017

# Individualised dosing




**Closed-loop control for precision antimicrobial delivery.**

Already validated in diabetes control through individualised insulin delivery and anaesthesia control intra-operatively

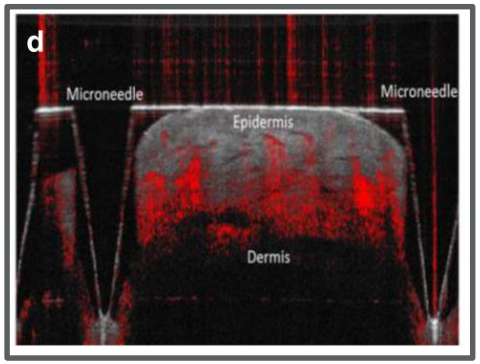
**Improved methods for drug monitoring required**

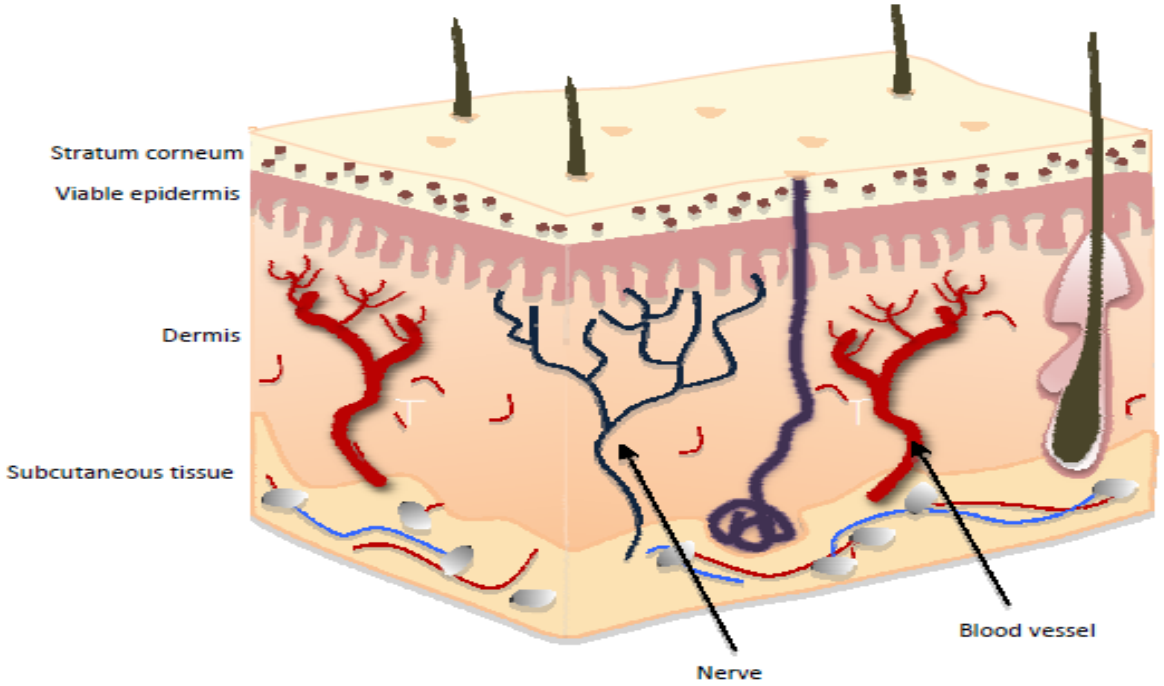
**Minimally invasive**
**Point-of-care**
**Continuous monitoring**
**Broad range of agents**



Rawson, O'Hare, et al. Journal of Antimicrobial Chemotherapy; 2017

# Minimally invasive sensing



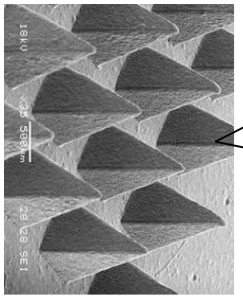



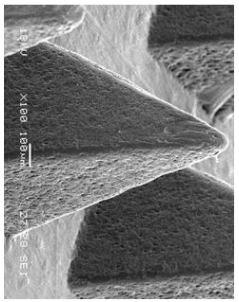

Interstitial Fluid (ISF) is in equilibrium with capillary blood.

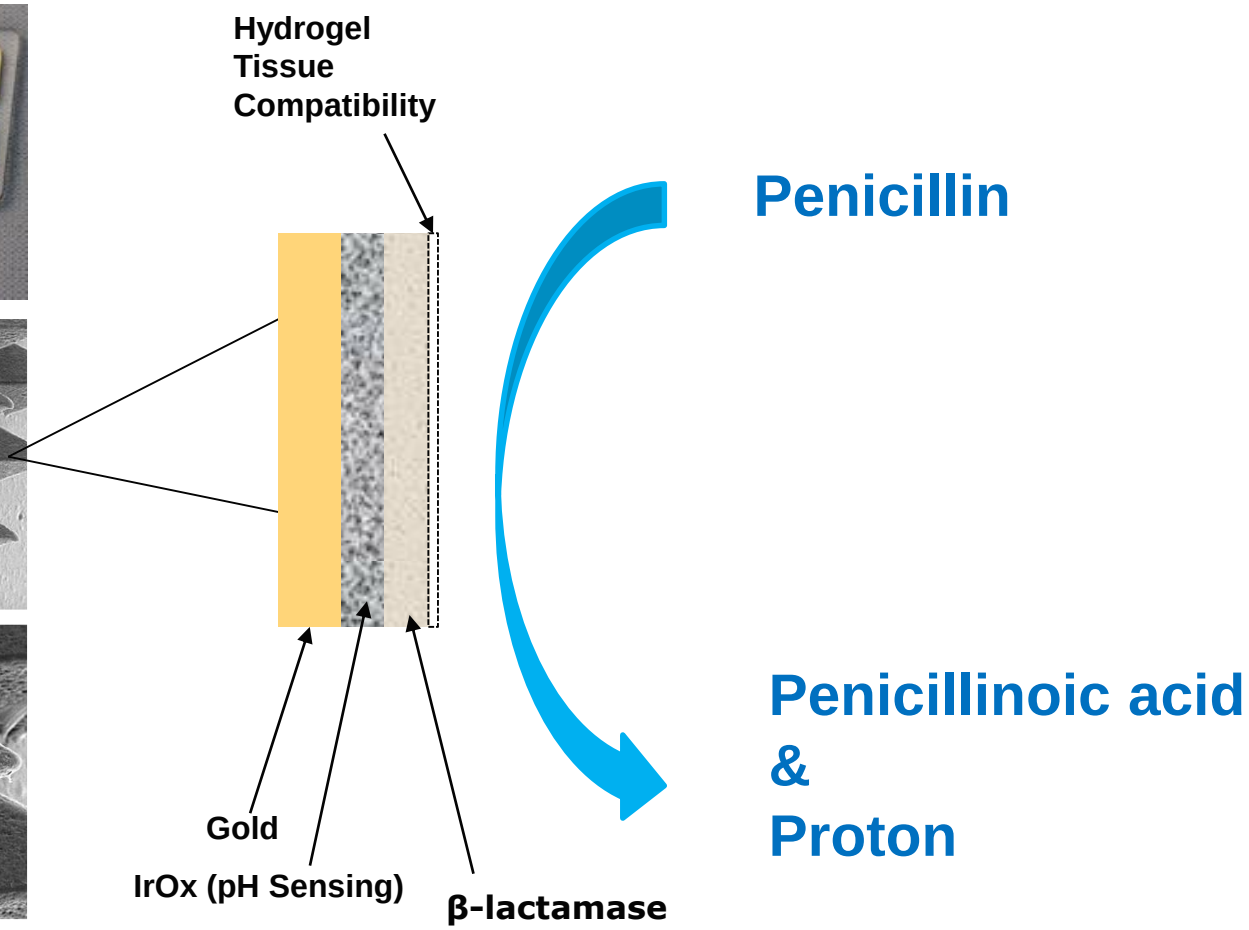
**Composition includes:** Metabolites, drugs, and proteins.

El-Laboudi, et al. Diab Tech & Therap; 2013
Rawson, O'Hare, et al Journal of Antimicrobial Chemotherapy; 2017
Sharma; et al. Sens Biosensing Res; 2017

# Bio-inspired β-lactam sensor



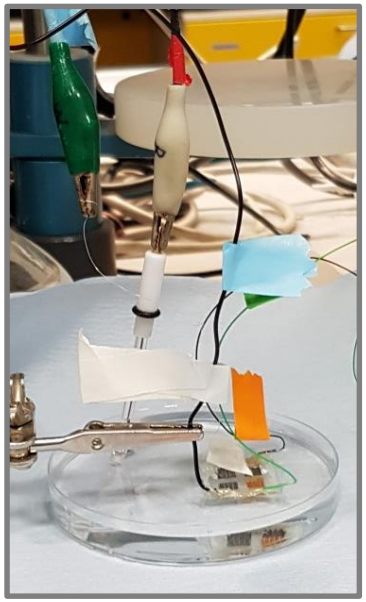


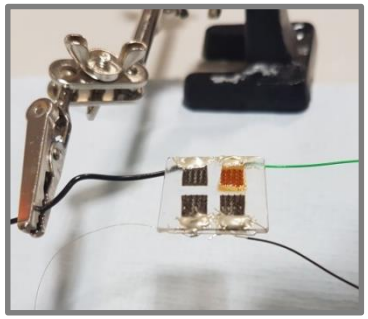


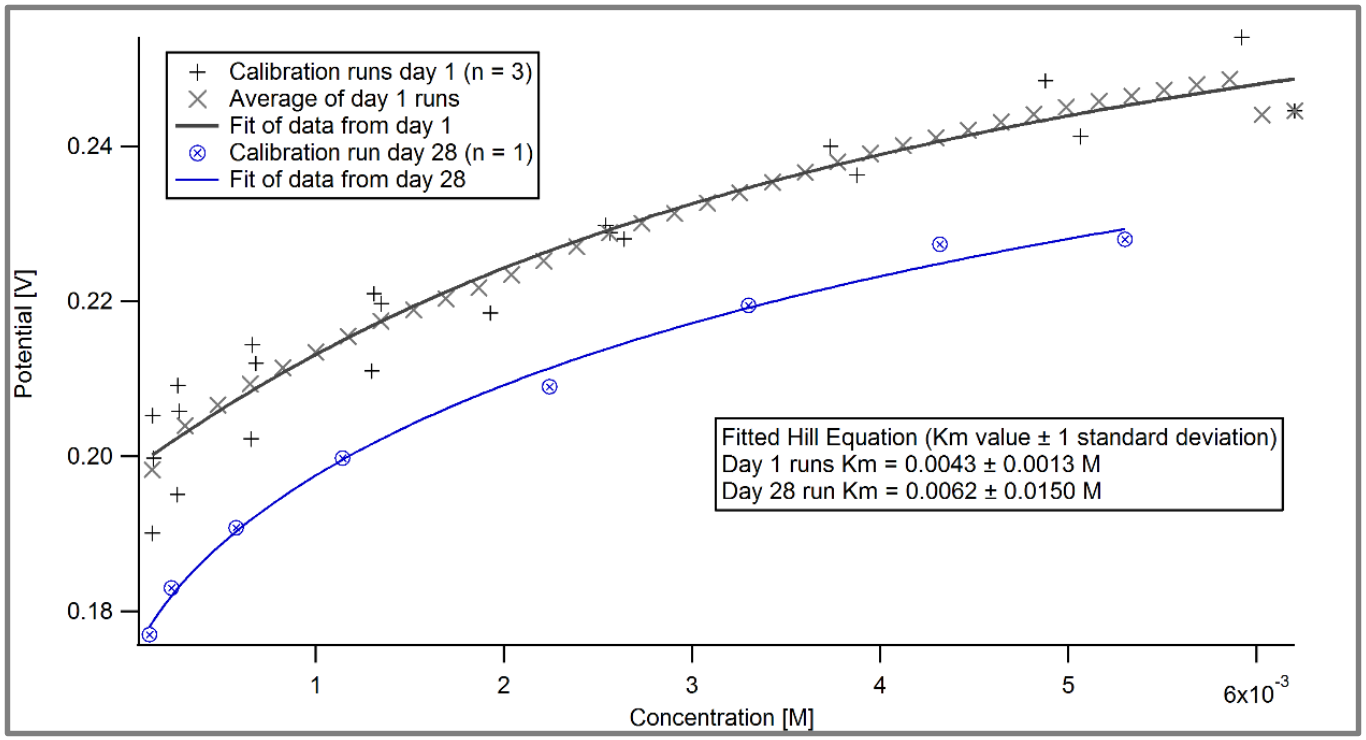



Rawson, Sharma, et al. Electrochemistry Communications; 2017

# Laboratory characterisation



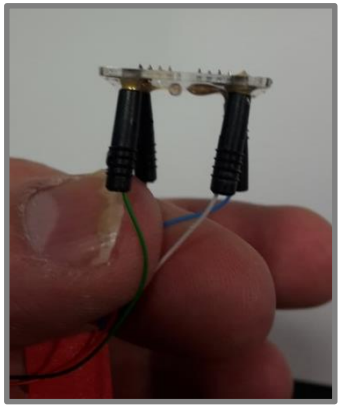


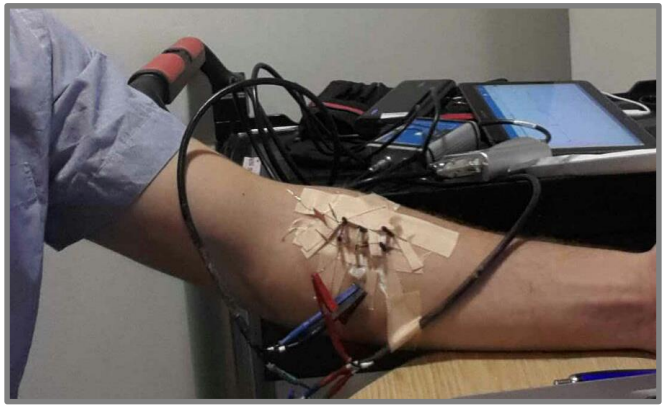



Calibrated in artificial interstitial fluid for penicillin-G, amoxicillin, ceftriaxone, and meropenem.

Rawson, Sharma, et al. Electrochemistry Communications; 2017
Rawson, Thesis; 2017

# Human testing – penicillin V





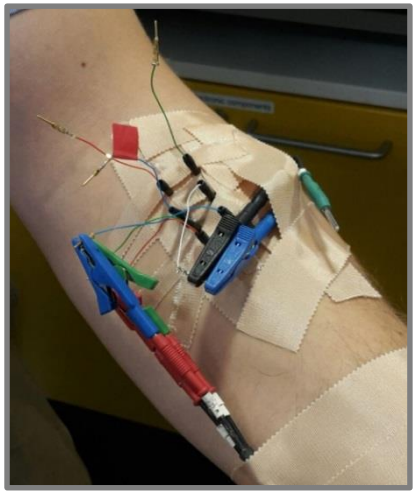



Applied to non-dominant forearm

Semi-portable potentiostat connected

Recording once every second

Worn for 6 hours





Rawson, Thesis; 2017

# In conclusion

Artificial intelligence provides ability to better use data we have available.

Biosensor technology may provide novel way of performing drug monitoring.

Requires understanding of end-user decision making.

Requires better engagement with non-infection specialties.

Need for integration of tools and move away from narrow focus.

# Acknowledgements


NHS
National Institute for Health Research

EMBRACE
Engineering, Physical, Natural Sciences and Medicine Bridging Research in Antimicrobial resistance: Collaboration and Exchange

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MÉRIEUX RESEARCH GRANTS

Imperial Biomedical Research Centre

Imperial College London

epic impoc
enhanced, personalized and integrated care for infection management at point of care

UNIVERSITY OF LIVERPOOL