Informatics to support clinical decision making
Plan

1. NHS Scotland Infection Intelligence Platform (IIP)
2. Clinical decision support
3. CDI: risk factors to decision support
4. Resistant UTI: risk factors to decision support
5. Key points

Declaration: SARHAI Strategy Group and SIRN (SHAIPi) funding
Plan

1. **NHS Scotland Infection Intelligence Platform (IIP)**
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UK Five Year Antimicrobial Resistance Strategy
2013 to 2018

i. improve the knowledge and understanding of AMR through better information, intelligence, supporting data and developing more effective early warning systems to improve health security,

ii. conserve and steward the effectiveness of existing treatments through improving infection prevention and control and development of resources to facilitate optimal use of antibiotics in both humans and animals,

iii. stimulate the development of new antibiotics, diagnostics and novel therapies by promoting innovation and investment in the development of new drugs and ensuring that new therapeutics reach the market quickly.
Scottish Antimicrobial Prescribing Group (SAPG)

The Scottish Antimicrobial Prescribing Group (SAPG) is a national clinical multi-disciplinary forum formed in March 2008 at the request of the Scottish Government Health Department with representation from key stakeholders including all mainland Health Boards. The forum is hosted by the Scottish Medicines Consortium and its primary objective is to co-ordinate and deliver a national framework for antimicrobial stewardship to enhance the quality of antimicrobial prescribing and management in Scotland. Antimicrobial stewardship means ‘making the best use of antimicrobials to manage infection so as to ensure optimal outcomes and minimal harm to patients and the wider society’.

Scottish Management of Antimicrobial resistance Action Plan 2014 - 18 (ScotMARAP 2)

HEAT targets and quality indicators
Information but not very intelligent

Most patient level with CHI attached
The Scottish Infection Intelligence Platform (IIP)

Improving patient outcomes and reducing harm from infection through innovative data integration to support clinicians within the NHS in Scotland

Key datasets:
- ECOSS-microbiology
- HMUD-medication use in hospital
- PIS-primary care prescribing
- SMR-hospital activity and deaths
- SSIRS-surgical site infections

Marion Bennie, Charis Marwick, William Malcolm, Dilip Nathwani, Jean Sneddon
The Scottish Infection Intelligence Platform (IIP)

- Scottish Antimicrobial Resistance and Healthcare Associated Infection (SARHAI) Strategy Group
- Technical IT platform for linkage and analysis
- Streamlined data governance
- Clinical engagement – SAPG
- Enhanced statistical skills of data analysts
- Generating evidence for policy and practice
  - Evaluating antimicrobial stewardship interventions
  - Risk factors and risk prediction for infection outcomes
  - Surveillance for infection prevention and control
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"If you want a second opinion, I'll ask my computer."
Aim: inform prescribing decision at point of care

- Patient microbiology and antibiotic history
- Population epidemiology: pathogens and AMR
- Patient demographic and health data

Automated data processing

Clinical status and suspected infection

PREScribing (OR NOT) DECISION

Clinician discretion
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1446 cases and 7964 matched controls

Patient-level anonymised data linkage

Any antibiotics, “4C” antibiotics, fluoroquinolones

Incident, cumulative, temporal exposure in prior 6 months

Comorbidity, care home, hospital admissions, PPI
Adjusted OR for CA-CDI with incident exposure 6m
Adjusted OR for CA-CDI with cumulative exposure 6m

<table>
<thead>
<tr>
<th>Cumulative antimicrobial exposure</th>
<th>Cases n (%)</th>
<th>Controls n (%)</th>
<th>Adjusted OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>no antimicrobials</td>
<td>597 (41.4)</td>
<td>6133 (77.0)</td>
<td>1</td>
</tr>
<tr>
<td>1-7 DDDs</td>
<td>198 (13.7)</td>
<td>659 (8.3)</td>
<td>2.31 (1.88–2.85)</td>
</tr>
<tr>
<td>8-14 DDDs</td>
<td>166 (11.5)</td>
<td>584 (7.3)</td>
<td>2.13 (1.69–2.68)</td>
</tr>
<tr>
<td>15-28 DDDs</td>
<td>195 (13.5)</td>
<td>334 (4.2)</td>
<td>3.59 (2.81–4.60)</td>
</tr>
<tr>
<td>29+ DDDs</td>
<td>287 (19.9)</td>
<td>252 (3.2)</td>
<td><strong>4.36 (3.40–5.61)</strong></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Cumulative 4C antimicrobial exposure</th>
<th>Cases n (%)</th>
<th>Controls n (%)</th>
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<td>no antimicrobials</td>
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<td>6133 (77.0)</td>
<td>1</td>
</tr>
<tr>
<td>1-7 DDDs</td>
<td>114 (7.9)</td>
<td>184 (2.3)</td>
<td><strong>4.60 (3.41–6.21)</strong></td>
</tr>
<tr>
<td>8-14 DDDs</td>
<td>85 (5.9)</td>
<td>70 (0.9)</td>
<td>7.58 (5.05–11.37)</td>
</tr>
<tr>
<td>15-28 DDDs</td>
<td>66 (4.6)</td>
<td>34 (0.4)</td>
<td><strong>7.23 (4.25–12.28)</strong></td>
</tr>
<tr>
<td>29+ DDDs</td>
<td>47 (3.3)</td>
<td>10 (0.1)</td>
<td><strong>17.86 (7.56–42.17)</strong></td>
</tr>
</tbody>
</table>

*J Antimicrob Chemother 2017; 72: 1193–1201*
## Adjusted OR for CA-CDI by most recent exposure

<table>
<thead>
<tr>
<th>Most recent exposure in the previous 6 months</th>
<th>% exposed controls, n = 7964</th>
<th>% exposed cases, n = 1446</th>
<th>Adjusted OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any antimicrobial</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>no antibiotics</td>
<td>77.0</td>
<td>41.3</td>
<td>1</td>
</tr>
<tr>
<td>≤1 month</td>
<td>6.1</td>
<td>32.0</td>
<td>6.3 (5.16–7.69)</td>
</tr>
<tr>
<td>2–3 months</td>
<td>8.1</td>
<td>17.8</td>
<td>2.2 (1.78–2.72)</td>
</tr>
<tr>
<td>4–6 months</td>
<td>8.7</td>
<td>8.9</td>
<td>1.1 (0.86–1.42)</td>
</tr>
<tr>
<td>4C</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>no antibiotics</td>
<td>77.0</td>
<td>41.3</td>
<td>1</td>
</tr>
<tr>
<td>≤1 month</td>
<td>1.0</td>
<td>10.9</td>
<td>12.45 (8.89–17.44)</td>
</tr>
<tr>
<td>2–3 months</td>
<td>1.2</td>
<td>6.4</td>
<td>5.12 (3.5–7.51)</td>
</tr>
<tr>
<td>4–6 months</td>
<td>1.5</td>
<td>4.4</td>
<td>2.59 (1.74–3.87)</td>
</tr>
</tbody>
</table>

*J Antimicrob Chemother 2017; 72: 1193–1201*
CDI risk tool for clinical decision support

• Aim: calculate individual patient’s CDI risk to inform:
  • Risk/benefit of antibiotic(s) in patient with e.g. RTI symptoms
  • Likelihood of CDI as cause in patient with diarrhoea
• Risk factors incorporated into logistic regression models and machine learning (LASSO, Bayesian model averaging, Random forest) models
• Prediction models developed on 2/3 dataset, tested on 1/3
• Statistical priority = model performance
• Clinical priority = ease of use and clinical interpretation
• Working with GP colleagues to optimise clinical utility
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Potential predictors of CA-CDI

Demographic variables
- SIMD (socioeconomic quintile)
- Resident in care home
- (age, gender, location matched)

Health care variables
- Number of hospital admission in the previous year
- Number of emergency hospital admission in the previous year
- Days of hospital stay in the previous year
- Total number of dispensed items last year
- Total number of different dispensed items last year
- PPI in the community last 6 month (y/n)
- H2 antagonist in the community last 6 month (y/n)

Comorbidities
- Congestive heart failure, cardiomyopathy
- Atherosclerosis, aortic aneurysm, vascular disease
- Stroke
- Dementia
- Bronchitis, pneumoconiosis
- Gout, lupus, rheumatoid arthritis
- Gastro ulcers
- Liver problems
- Diabetes
- Diabetes with complications
- Hemiplegia, paraplegia
- Renal problems
- Cancer
- Alcohol-related liver failure
- Metastatic cancer
- Inflammatory bowel disease
- Inflammatory bowel disease

<table>
<thead>
<tr>
<th>Reduced logistic regression model</th>
<th>Adjusted OR</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. different antibiotics last 3m</td>
<td>2.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PPI exposure last 3m</td>
<td>1.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>H2 exposure last 3m</td>
<td>1.6</td>
<td>0.02</td>
</tr>
<tr>
<td>Respiratory disease</td>
<td>1.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Renal problems</td>
<td>5.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Cancer</td>
<td>2.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Inflammatory bowel disease</td>
<td>2.7</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
CDI risk model: performance (example)

Sensitivity 68.9%
Specificity 75.6%

AUC 0.791
CDI risk tool next steps

- Finalise model for implementation
- Build into risk score
- Test in clinical practice
- Clinical priority = ease of use and clinical interpretation
- Working with GP colleagues to optimise clinical utility
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Effect of antibiotic prescribing in primary care on antimicrobial resistance in individual patients: systematic review and meta-analysis

<table>
<thead>
<tr>
<th>0-6 months</th>
<th>0-12 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Steinke 23</td>
<td>Any antibiotic* 19</td>
</tr>
<tr>
<td>Donnan 17</td>
<td>Trimethoprim NR</td>
</tr>
<tr>
<td>Hillier 19</td>
<td>Amoxicillin 28</td>
</tr>
<tr>
<td>Metlay 26</td>
<td>ST 28</td>
</tr>
</tbody>
</table>

Pooled odds ratio
Test for heterogeneity: $I^2=89.2\%$, $P=0.000$

<table>
<thead>
<tr>
<th>0-12 months</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Donnan 17</td>
<td>Trimethoprim NR</td>
</tr>
<tr>
<td>Donnan 17</td>
<td>Any antibiotic* NR</td>
</tr>
<tr>
<td>Hillier 19</td>
<td>Amoxicillin 19</td>
</tr>
<tr>
<td>Hay 18</td>
<td>Any antibiotic* 38</td>
</tr>
<tr>
<td>Hillier 19</td>
<td>Trimethoprim 19</td>
</tr>
</tbody>
</table>

Pooled odds ratio
Test for heterogeneity: $I^2=71.9\%$, $P=0.007$

* Any antibiotic other than trimethoprim. ST=sulfamethoxazole-trimethoprim. NR=not reported

Costelloe et al
BMJ 2010
Risk factors for resistance and MDR in community urine isolates: population-level analysis using the NHS Scotland Infection Intelligence Platform

William Malcolm¹*, Eilidh Fletcher², Kimberley Kavanagh³, Ashutosh Deshpande⁴, Camilla Wiuff⁵, Charis Marwick⁵ and Marion Bennie²,⁶

- 40,984 urine isolates
- Patient-level anonymised data linkage
- Exposure to any antibiotics, trimethoprim, nitrofurantoin
- Number different antibiotics and cumulative exposure
- Age, gender, comorbidity, care home, hospital admissions
Urine data and AMR definition

– Health Protection Scotland “Surveillance of Antimicrobial Resistance in Urinary Isolates in Scotland” data (UTI Snapshot)
– All Scottish NHS boards; first 400 positives per quarter
– 2012-2015, adults, most resistant if >1 sample

Resistance definitions (Health Protection Scotland)
• **Susceptible**: fully susceptible
• **Resistant**: resistant to any antimicrobial tested
• **Multi-drug resistant**: resistant to >2 categories
### Risk factors

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Resistant OR (95%CI)</th>
<th>Multidrug Resistant OR (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Male vs female gender</strong></td>
<td>1.36 (1.27–1.44)</td>
<td>1.17 (1.09–1.26)</td>
</tr>
<tr>
<td><strong>85+ vs 16-24 years old</strong></td>
<td>1.21 (1.07–1.37)</td>
<td>1.81 (1.56–2.10)</td>
</tr>
<tr>
<td><strong>Charlson comorbidity index 5+ vs 0</strong></td>
<td>1.36 (1.16–1.59)</td>
<td>1.31 (1.11–1.56)</td>
</tr>
<tr>
<td><strong>4+ hospital admissions vs none</strong></td>
<td>1.25 (1.08–1.45)</td>
<td>1.82 (1.56–2.13)</td>
</tr>
<tr>
<td><strong>Care home residence vs not</strong></td>
<td>2.16 (1.90–2.45)</td>
<td>3.36 (2.95–3.83)</td>
</tr>
<tr>
<td><strong>4+ different antibiotics vs none</strong></td>
<td>2.79 (2.36–3.31)</td>
<td>6.81 (5.73–8.11)</td>
</tr>
</tbody>
</table>

#### Notes
- 40,984 isolates
  - 28% fully susceptible
  - 45% resistant
  - **27% MDR**
- 73% *E. coli*
Cumulative exposure

Resistant vs. susceptible

MDR vs. susceptible

J Antimicrob Chemother
doi:10.1093/jac/dkx363
UTI AMR risk assessment for decision support

- Aim: calculate individual patient’s risk of resistant urinary isolate
  - Guide antibiotic choice in patient with UTI symptoms
- Risk factors incorporated into backwards step-wise logistic regression models
- Predict non-susceptibility to nitrofurantoin, trimethoprim or both
- Statistical priority = model performance
- Clinical priority = ease of use and clinical interpretation
- Working with GP colleagues to optimise clinical utility
## UTI AMR risk models: ideal versus realistic

<table>
<thead>
<tr>
<th>Covariate examples</th>
<th>Ideal model</th>
<th>Realistic model</th>
</tr>
</thead>
</table>
| Comorbidity        | -Charlson comorbidity index  
                      -Weighted score (0-18)  
                      -Five year lookback through electronic discharge data (SMR01)                                                                        | -Count of comorbidities included in Charlson (e.g. MI)  
                      -“Patient has/had X?”  
                      -Any available source and patient reported                                                                                           |
| Trimethoprim exposure | -DDD of trimethoprim in previous 6 months: 0, 1-7, 8-14, 15-21, 22-28, 29+                                                                  | -Number of trimethoprim prescriptions in previous 6 months                                                                                   |
UTI AMR risk model: performance

- AUROC 0.68 to 0.77 = “fair”
- Sensitivity and specificity 64-70%
- Realistic model performs as well as ideal
- Model optimisation and conversion to score
- App development
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Key points

1. Need to use routine data for antimicrobial stewardship
2. Infection Intelligence Platform (IIP) key asset for NHS Scotland
3. Wealth of patient-level linkable data in Scotland allows individualised risk modelling
4. Translating risk models into clinical decision support is challenging and needs clinical collaboration
5. Individualised prescribing decisions will benefit individual patients and population through antimicrobial stewardship
Acknowledgements

- Scottish Antimicrobial Resistance and Healthcare Associated Infection (SARHAI) Strategy Group
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- SAPG, Gail Haddock, Carol Philip, Jacqueline Sneddon, Ashutosh Deshpande, Camilla Wiuff, Peter Davey, Scott Bryson
- c.z.marwick@dundee.ac.uk