

Infection Intelligence Platform



Development of risk assessment models for antimicrobial resistance in urinary tract infections

Scottish Antimicrobial Prescribing Group

14th March 2017

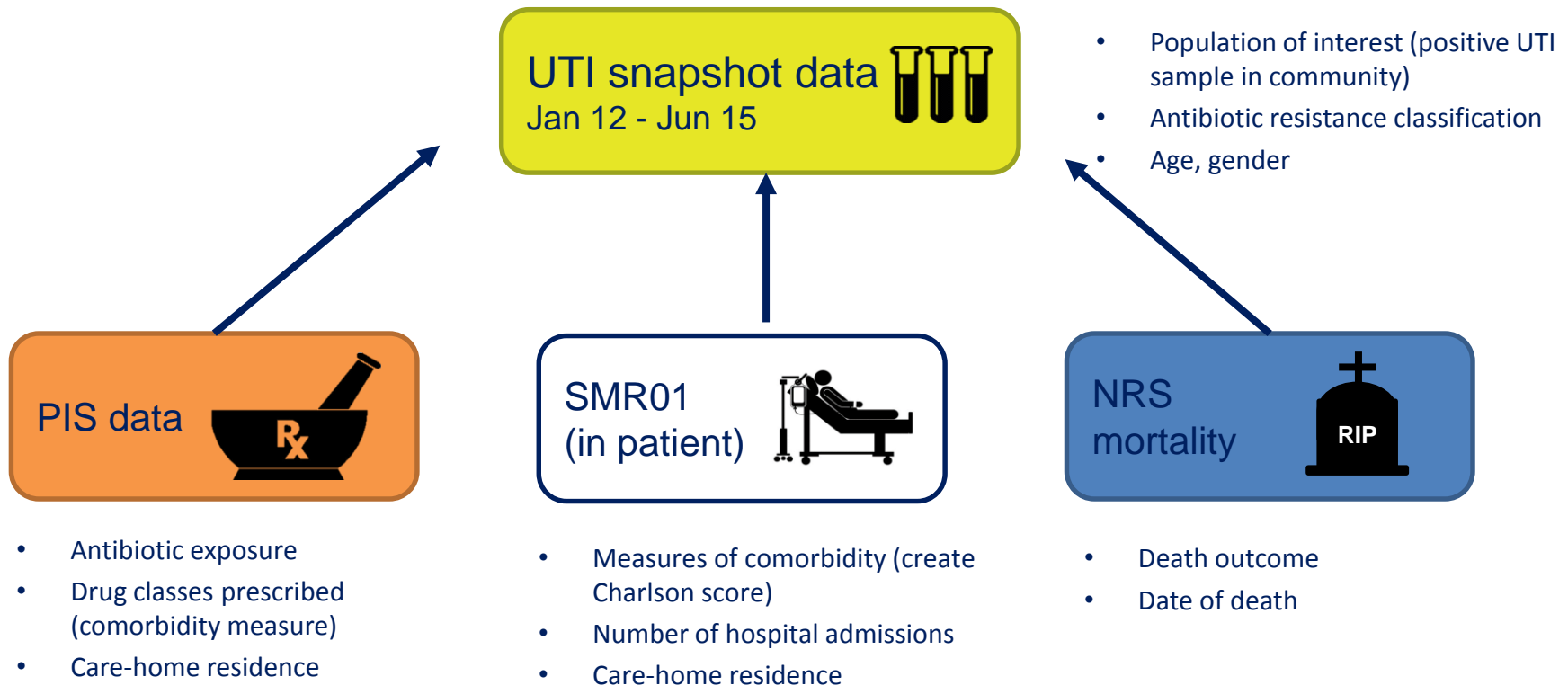
Eilidh Fletcher

Characterisation of risk factors associated with antibiotic resistance in urinary isolates in the community – recap of study and results

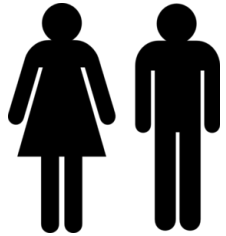
Aim of study

- To investigate risk factors for and outcomes associated with the occurrence of antibiotic resistance in urinary isolates.

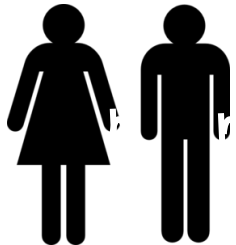
Data sources and linkage



Results: risk factors for resistance



Variable		Resistant infection compared to susceptible infection			Multi-drug resistant infection compared to susceptible infection		
		Adjusted odds ratio	95% CI	p-value	Adjusted odds ratio	95% CI	p-value
Gender	Female	1	-	-	1	-	-
	Male	1.3	1.3-1.4	<0.001	1.2	1.1-1.3	<0.001



Age group	16-24	1	-	-	1	-	-
	25-34	1.1	1.0-1.3	0.075	1.1	0.9-1.3	0.165
	35-44	1.0	0.9-1.1	0.978	1.3	1.1-1.5	0.002
	45-54	1.0	0.9-1.1	0.987	1.4	1.2-1.6	<0.001
	55-64	1.0	0.9-1.1	0.360	1.4	1.2-1.6	<0.001
	65-74	1.0	0.9-1.1	0.915	1.4	1.2-1.6	<0.001
	75-84	1.1	1.0-1.2	0.079	1.5	1.3-1.7	<0.001
	85+	1.2	1.1-1.4	0.001	1.3	1.0-2.1	<0.001



Charlson index (5-year lookback)	0	1	-	-	1	-	-
	1-2	1.1	1.1-1.2	0.001	1.1	1.0-1.2	0.007
	3-4	1.3	1.2-1.5	<0.001	1.3	1.1-1.5	<0.001
	5+	1.4	1.2-1.6	<0.001	1.3	1.1-1.6	0.001
	Unknown	0.9	0.9-1.1	0.393	0.9	0.8-0.95	0.001

Results: risk factors for resistance



Variable	Resistant infection compared to susceptible infection			Multi-drug resistant infection compared to susceptible infection		
	Adjusted odds ratio	95% CI	p-value	Adjusted odds ratio	95% CI	p-value
Care home residence in previous 12 months	No	1	-	1	-	-
	Yes	2.2	1.9-2.5	3.5	3.1-4.0	<0.001



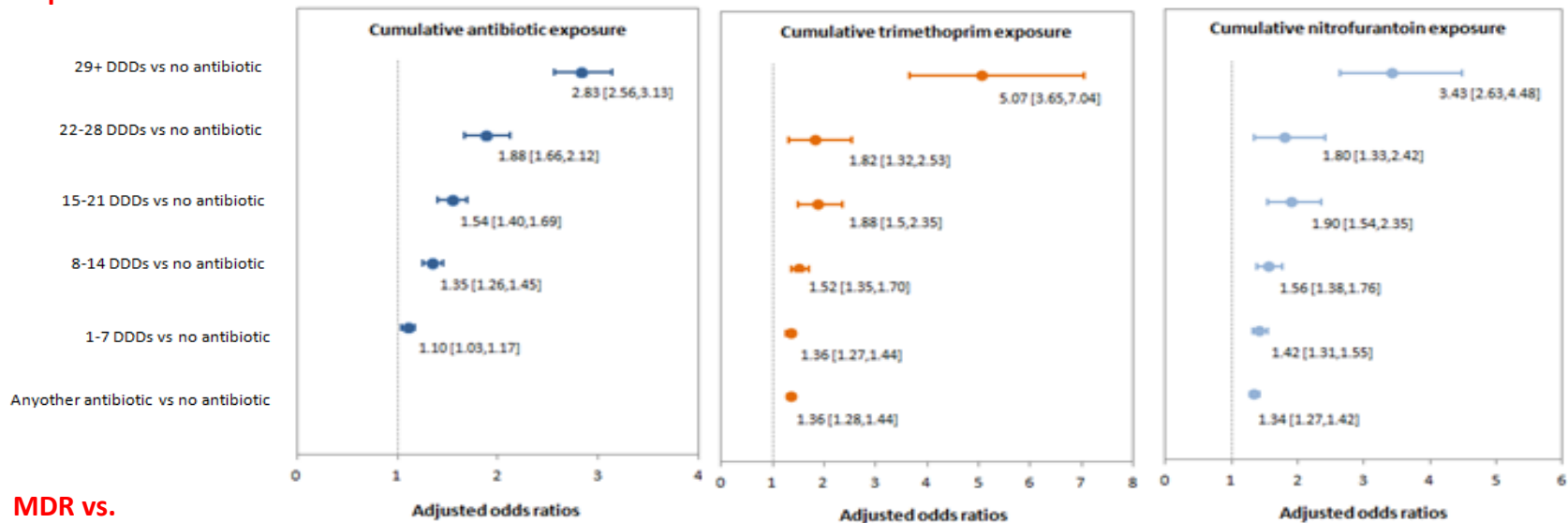
Drug classes prescribed in previous 12 months	0-4	1	-	-	1	-	-
	Adjusted odds ratio	95% CI	p-value	Adjusted odds ratio	95% CI	p-value	
5-9	1.1	1.1-1.2	<0.001	1.1	1.0-1.2	0.035	
10-14	1.3	1.2-1.4	<0.001	1.4	1.3-1.5	<0.001	
15-19	1.5	1.3-1.6	<0.001	1.8	1.6-2.0	<0.001	
20+	1.7	1.4-2.0	<0.001	2.2	1.8-2.6	<0.001	



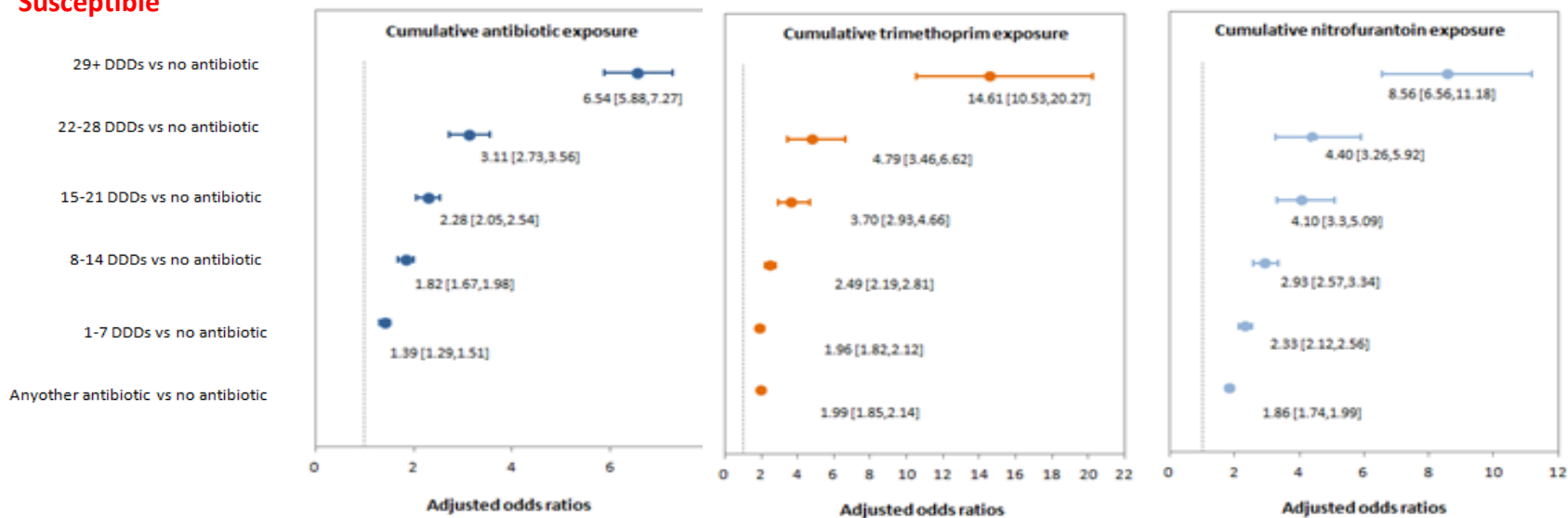
Number of hospital stays in previous 12 months	0	1	-	-	1	-	-
	Adjusted odds ratio	95% CI	p-value	Adjusted odds ratio	95% CI	p-value	
1	1.1	1.0-1.2	0.017	1.2	1.1-1.3	<0.001	
2	1.2	1.1-1.3	0.001	1.4	1.2-1.5	<0.001	
3	1.2	1.1-1.4	0.008	1.8	1.5-2.1	<0.001	
4+	1.3	1.1-1.5	0.002	1.9	1.6-2.2	<0.001	

Results: cumulative antibiotic exposure

Resistant vs. Susceptible



MDR vs. Susceptible



How can these results be used applied in ‘the real world’?

SPARRA Risk Calculator

Health and Social Care



[Calculator Home](#)

Calculating Risk of Emergency Admission

This risk calculator calculates risk for all 3 cohorts of SPARRA Version 3, Long Term Conditions (LTC), Young Emergency Department (YED), and Frail Elderly (FE). The rationale for 3 cohorts is that patients of different ages, lifestyles and chronic conditions possess different risk factors which contribute to their overall risk score.

Unsure of which Cohort to use?

What is the patient's age?

- 75 or over
- 56—74
- 16—55

Submit

Risk assessment tools

Cohorts

- [Frail Elderly](#)
- [Long Term Conditions](#)
- [Young Emergency Department](#)



Breast Cancer Risk Assessment Tool

An interactive tool to help estimate a woman's risk of developing breast cancer

Last modified date: 05/16/2011

Get Started with the Risk Tool

About the Tool

Breast Cancer Risk Factors

Download Source Code

Page Options

Print Page

Quick Links

- [Breast Cancer Home Page](#)
- [Breast Cancer: Prevention, Genetics, Causes](#)
- [Current Clinical Trials: Breast Cancer in Situ: Treatment](#)
- [Current Clinical Trials: Breast Cancer: Prevention](#)
- [Current Clinical Trials: Breast Cancer: Screening](#)
- [Breast Cancer Risk in American Women](#)

Need Help?

Contact us by phone, Web, and e-mail

Risk Tool

(Click a question number for a brief explanation, or [read all explanations](#).)

- Does the woman have a medical history of any breast cancer or of ductal carcinoma in situ (DCIS) or lobular carcinoma in situ (LCIS) or has she received previous radiation therapy to the chest for treatment of Hodgkin lymphoma?
- Does the woman have a mutation in either the *BRCA1* or *BRCA2* gene, or a diagnosis of a genetic syndrome that may be associated with elevated risk of breast cancer?
- What is the woman's age? This tool only calculates risk for women 35 years of age or older.
- What was the woman's age at the time of her first menstrual period?
- What was the woman's age at the time of her first live birth of a child?
- How many of the woman's first-degree relatives - mother, sisters, daughters - have had breast cancer?

ClinRisk Welcome to the QRISK[®]2-2016 risk calculator: <https://qrisk.org>

This calculator is only valid if you do not already have a diagnosis of coronary heart disease (including angina or heart attack) or stroke/transient ischaemic attack.

Reset Information Publications About Copyright Contact Us Algorithm Software

About you

Age (25-84):

Sex: Male Female

Ethnicity:

UK postcode: leave blank if unknown

Postcode:

Clinical information

Smoking status:

Diabetes status:

Angina or heart attack in a 1st degree relative < 60?

Chronic kidney disease (stage 4 or 5)?

Atrial fibrillation?

On blood pressure treatment?

Rheumatoid arthritis?

Leave blank if unknown

Cholesterol/HDL ratio:

Systolic blood pressure (mmHg):

Body mass index

Height (cm):

Weight (kg):

Calculate risk over years.

Welcome to the QRISK[®]2-2016 cardiovascular disease risk calculator

Welcome to the QRISK[®]2-2016 Web Calculator. You can use this calculator to work out your risk of having a heart attack or stroke over the next ten years by answering some simple questions. It is suitable for people who do not already have a diagnosis of heart disease or stroke.

The QRISK[®]2 algorithm has been developed by doctors and academics working in the UK National Health Service and is based on routinely collected data from many thousands of GPs across the country who have freely contributed data for medical research. It is updated annually each April, refitted to the latest data to remain as accurate as possible.

Whilst QRISK2 has been developed for use in the UK, it is being used internationally. For non-UK use, if the postcode field is left blank the score will be calculated using an average value. Users should note, however, that CVD risk is likely to be underestimated in patients from deprived areas and over-estimated for patients from affluent areas. All medical decisions need to be taken by a patient in consultation with their doctor. The authors and the sponsors accept no responsibility for clinical use or misuse of these score.

The science underpinning the QRISK[®]2 equations has been published here:

- [Predicting cardiovascular risk in England and Wales: prospective derivation and validation of QRISK2. BMJ 2008;336:1475-82](#)

Click [here](#) for more information on QRISK[®]2.

ClinRisk Welcome to the QRISK[®]2-2016 risk calculator: <https://qrisk.org>

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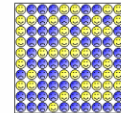
Calculate risk over years.

Your results

Your risk of having a heart attack or stroke within the next 10 years is:

55.3%

In other words, in a crowd of 100 people with the same risk factors as you, 55 are likely to have a heart attack or stroke within the next 10 years.



Your score has been calculated using estimated data, as some information was left blank.

Your body mass index was estimated as 28.9 kg/m².

How does your 10-year score compare?

Your score

Your 10-year QRISK[®]2 score: 55.3%

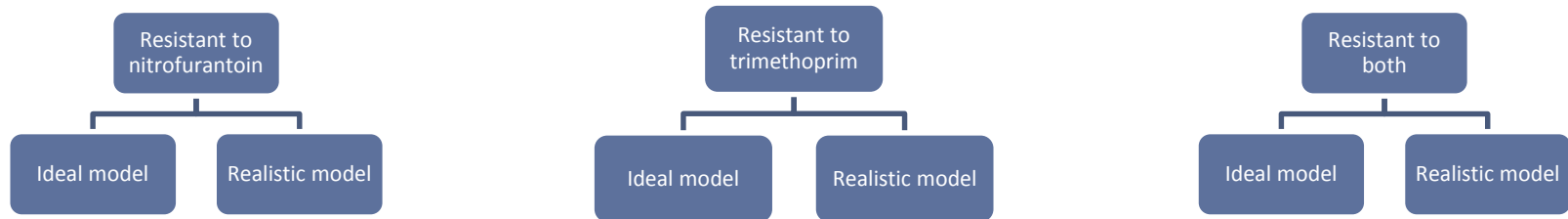
The score of a healthy person with the same age, sex, and ethnicity: 13%

Relative risk: 4.3

Your QRISK[®] Healthy Heart Age: > 84

Risk of resistance models

- Use risk factors identified in previous work to develop models
 - plus additional potential risk factors identified
- Focus on resistance to two individual antibiotics
 - nitrofurantoin and trimethoprim



Outcome – resistant (y/n) to the antibiotic

Data sources and linkage

- HPS UTI Snapshot – Jan2012 to June 2016
- SMR00 Outpatients
- SMR01 Inpatients/daycases
- PIS community prescribing data

Realistic vs. Ideal models

Previous work identified risk factors which are not likely to be available to the clinician at point of care, e.g.:

- Charlson score – weighted score of 18 different diagnoses
- Exposure to antibiotics measure in DDDs

Solution: develop adapted versions of these covariates, e.g.

Covariate (e.g.)	'Ideal' model	'Realistic' model
Measures of co-morbidity	<ul style="list-style-type: none">• Charlson score – measure of co-morbidity• Weighted numerical score (0-18)• 5 year lookback through hospital records	<ul style="list-style-type: none">• individual covariates for each of the 18 diagnoses – e.g. MI, stroke, diabetes• All available data sources used; lookback to 1996• Allows question to be “does the patient have a history of X?”
Exposure to trimethoprim	<ul style="list-style-type: none">• DDDs of trimethoprim in previous 6 months – 0, 1-7, 8-14, 15-21, 22-28, 29+	<ul style="list-style-type: none">• Number of times trimethoprim was prescribed in previous 6 months

Process

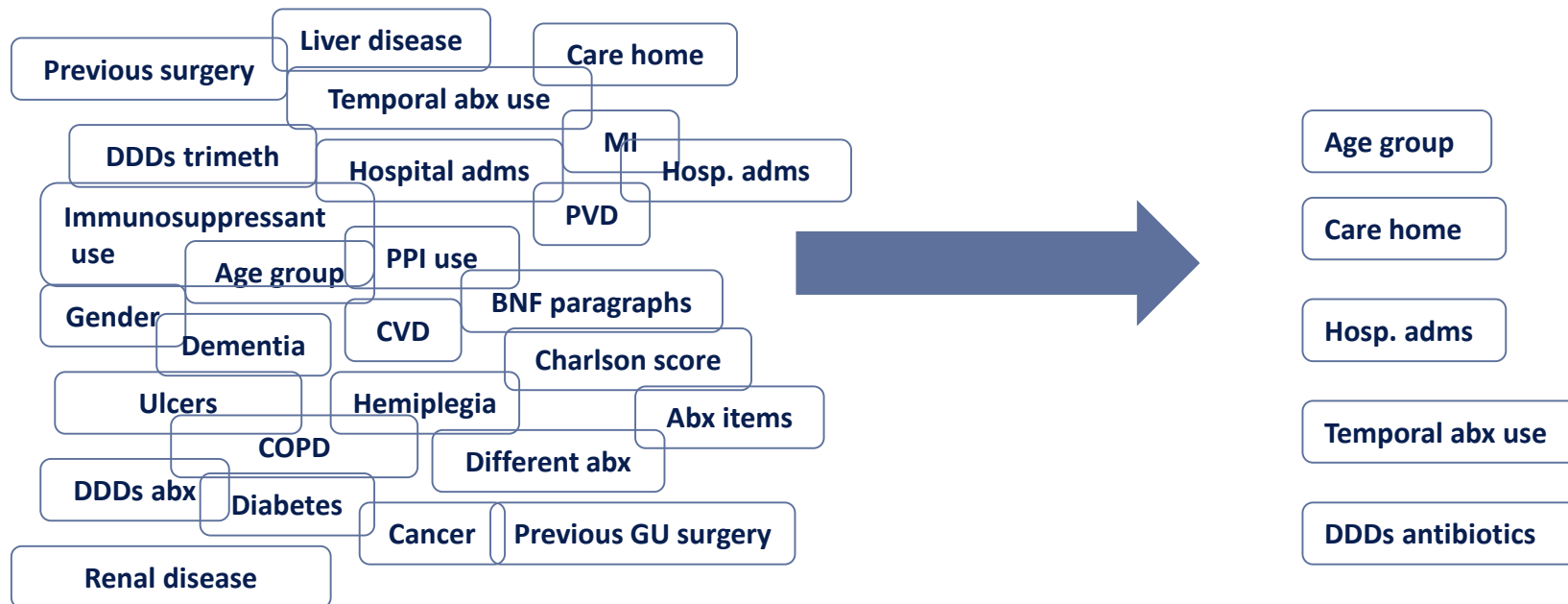
- Data split into training and test datasets (2:1)
- Statistical model (logistic regression) built using training dataset outcome = resistant to antibiotic
- Derived model tested on test dataset – test how well this model predicts high/low risk of resistance

Measures

- AUC: area under ROC curve
- Sensitivity: % of cases correctly identified as resistant
- Specificity: % of cases correctly identified as sensitive

Developing the model

- Backwards stepwise logistic regression
- All variables included where $p < 0.3$ at univariate level
- Basically, start off with a all (lots) of variables in model

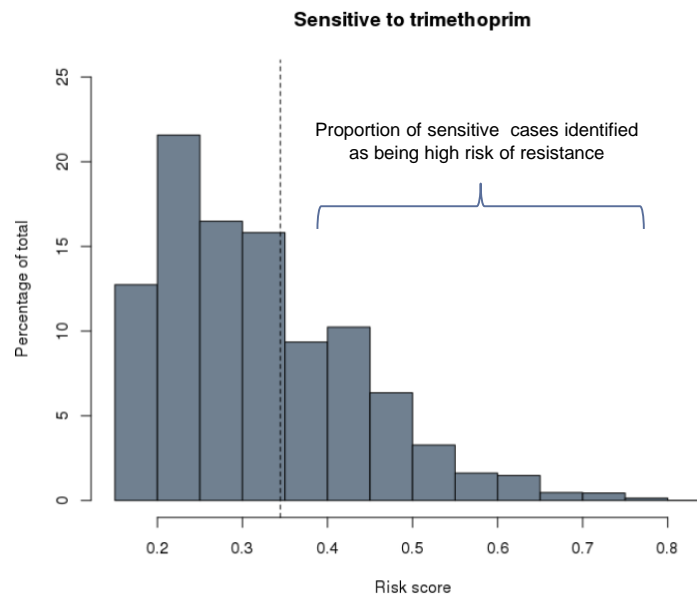
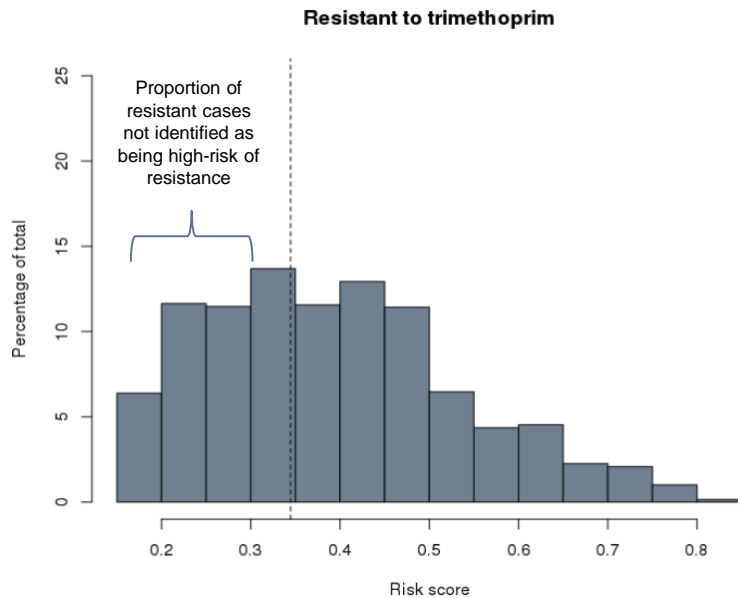


Current 'best fit' Trimethoprim model

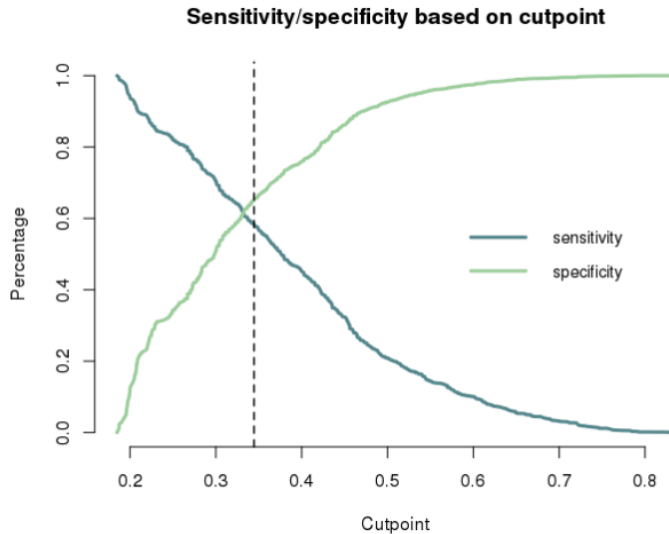
Variables included - *age group, care home residence, previous hospital admissions, total antibiotics prescribed in previous 6 months, time since most recent trimethoprim prescription*

Sensitivity: 58.4%
Specificity: 65.1%
AUC: 0.6815

} Based on optimal cutpoint from model



Model refinement



Cutpoint	Sensitivity (%)	Specificity (%)
0.20	93.61	12.74
0.25	81.97	34.32
0.30	70.50	50.80
0.33	58.38	65.13
0.35	56.81	66.62
0.40	45.24	75.97
0.45	32.31	86.21
0.50	20.88	92.57
0.55	14.41	95.85
0.60	10.05	97.47
0.65	5.51	98.94
0.70	3.25	99.41

Trade-offs

- Addition of 15 extra covariates may improve sensitivity by 2%
- Using number of antibiotics items prescribed in previous 12 months, as opposed to previous 6 months, may improve AUC by 0.03
- Are these improvements worth it?

How is this all translated?

Regression coefficients - and cutoff - scaled and rounded for ease of use in practice

Variable		Coefficient	Scaled (x5)	Scaled (x5) and rounded
Age group	40-49	0.072	0.360	0
	50-59	0.126	0.630	1
	60-69	0.045	0.225	0
	70-79	0.065	0.325	0
	80-89	0.137	0.685	1
	90+	0.146	0.730	1
Care home residence	Yes	1.017	5.085	5
Number of hospital admissions in previous 12 months	1	0.124	0.620	1
	2	0.337	1.685	2
	3	0.390	1.950	2
	4+	0.631	3.155	3
Time since last trimethoprim prescription	<= 1 month	1.144	5.720	6
	2-3 months	0.792	3.960	4
	4-6 months	0.591	2.955	3
	Some other abx in previous 6 mths	0.506	2.530	3

Example1:

Patient aged 40-49 (0), 1 hospital admission (1) and prescribed trimeth 5 months ago (3)

Total risk score = 4

Example2:

Patient aged 70-79 (0), care home resident (5), 3 hospital admission in previous 12 months (2) and trimethoprim last week (6);

Total risk score = 13

Further work

- Investigate 'unknown' missing covariates
- Finalise models with study team
- Develop test calculators

Ultimately.....?

Be available to clinicians via
SAPG Antimicrobial Companion



Thanks to:



- Study team
 - Ashutosh Deshpande
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 - Kim Kavanagh
 - William Malcolm
 - Carol Philip

- Colleagues in HPS and the PHI Indexing Team

Questions/comments/suggestions?