



Qcancer: symptom based approach to early diagnosis of cancer

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Acknowledgements

- Co-authors
- QResearch database
- EMIS & contributing practices & User Group
- University of Nottingham
- ClinRisk (software)
- Oxford University (independent validation)
- Macmillan Cancer Support (funding implementation)

Overview of talk on QCancer

- QResearch database
- Background on ClinRisk Scores
- QCancer Model development
- QCancer Model validation
- QCancer Implementation
- Pilot work with Macmillan and CRUK evaluation

QResearch Database

www.qresearch.org

- Over 700 general practices across the UK, 14 million patients
- Not-for-profit venture between EMIS & Nottingham University
- EMIS covers 56% of UK GP practices
- Patient level pseudonymised database for research
- Data linkage – deaths, deprivation, cancer, HES
- Available for peer reviewed academic research where outputs made publically available

ClinRisk Scores –new family of Risk Prediction tools

■ Individual assessment

- Who is most at risk of current or preventable disease?
- Who is likely to benefit from interventions?
- What is the balance of risks and benefits for my patient?
- Enable informed consent and shared decisions

■ Population risk stratification

- Identification of rank ordered list of patients for recall or reassurance

■ GP systems integration

- Allow updates tool over time, audit of impact on services and outcomes

■ Availability

- All published, publically available as free open source or professionally supported closed source software

ClinRisk scores and national guidance

Risk score	Outcome	NICE guidance	Implementation
Qrisk.org	10 year risk of CVD	Approved CG68 (2008) QOF & DH vascular screening program	All major GP suppliers
Qdiabetes.org	10 year risk diabetes	Approved PH38 (2012)	EMIS (largest supplier > 55%)
Qfracture.org	10yr risk of fracture	Approved CG146 (2012) QOF 2013	EMIS 2013 + London CCGs
Qthrombosis.org	Risk of VTE	Relevant to CG92	EMIS 2013
Qcancer.org	Current cancer risk	Relevant to current review	Pilot BMJ informatica. Later all suppliers

Early diagnosis of cancer: The problem

- UK has relatively poor track record when compared with other European countries
- Partly due to late diagnosis with estimated 7,500+ lives lost annually
- Later diagnosis due to mixture of
 - late presentation by patient (alack awareness)
 - Late recognition by GP
 - Delays in secondary care

Why symptoms based approach?

- Many patients present with symptoms
- GPs need to decide which patients to investigate and refer
- Decision support tool must mirror setting where decisions made
- Symptoms based approach needed (rather than cancer based)
- **Must account for multiple symptoms**
- **Must have face clinical validity eg adjust for age, sex, smoking, Family history**
- **Need to be able to update to meet changing requirements, populations, recorded data**

QCancer– what it needs to do

- Accurately predict individual level of risk of multiple cancers for based on multiple risk factors and multiple symptoms
- **Discriminate between patients with and without cancer**
- Help guide decision on who to investigate or refer and degree of urgency.
- Educational tool for sharing information with patient. Sometimes will be reassurance.
- Latest combined QCancer combined model published online BJGP 12 Dec 2012
 - Cancer in women
 - Cancer in men

Methods – development algorithm

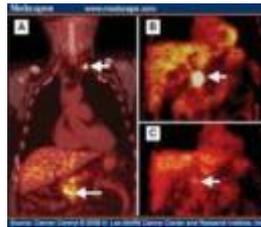
- Representative cohort from QResearch 2.5 million men & women aged 25-89 years
- cancer outcome - all new diagnoses on GP record or linked deaths record in 2 years
- Identify key symptoms
- Identify key risk factors
- Established methods to develop risk prediction algorithm
- Measure of absolute risk of any cancer as well as by cancer type

QCancer (2013) predicts global cancer risk & risk12 types cancers

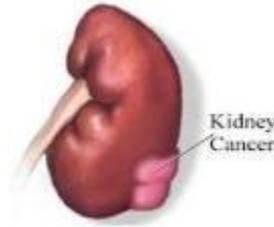
Lung



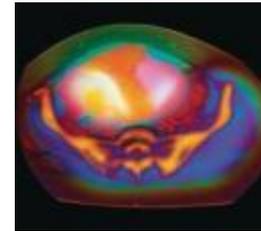
Pancreas



Renal tract



Ovary



Colorectal



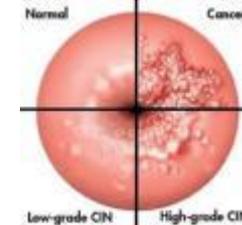
Gastro



Testis



Cervix



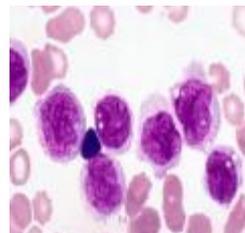
Breast



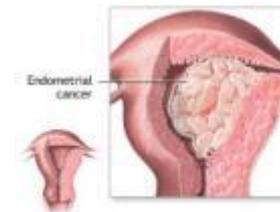
Prostate



Blood



Uterus



- These accounts for 85% cancers
- Plan to extend to rarer cancers when sufficient data

Independent risk factors in model

- Age & sex
- Smoking status
- Deprivation score
- Family history of cancer
- COPD
- Endometrial hyperplasia/polyp
- Chronic pancreatitis
- Type 2 diabetes
- Anaemia (HB < 11g/DL)
- Venous thromboembolism

Key symptoms in model

(identified from studies including NICE guidelines 2005)

- Haemoptysis
- Haematemesis
- Haematuria
- Rectal bleeding
- Haematuria
- Unexplained bruising
- Constipation, cough
- Vaginal bleeding (women)
- Testicular lump (men)
- Loss of appetite
- Unintentional weight loss
- Indigestion +/- heart burn
- Dysphagia
- Abdominal pain or swelling
- Breast lump, pain, skin
- Night sweats
- Neck lump
- Urinary symptoms (men)

QCancer symptoms map women



	blood	breast	cervix	CRC	OG	lung	other	ovary	pancreas	renal	uterine	Total
Abdo distension				+			+	+				3
Abdo pain	+		+	+	+		+	+	+	+	+	9
Anaemia	+		+	+	+	+	+	+		+		8
Appetite loss				+	+	+	+	+	+	+		7
Breast lump		+					+					2
Breast pain		+										1
Breast skin/nipple changes		+										1
Bruising	+											1
Change in bowel	+			+				+	+			4
Constipation				+			+					2
Cough						+						1
Dysphagia					+	+	+		+			4
Haematemesis					+		+		+			3
Haematuria	+		+				+	+		+	+	6
Haemoptysis						+						1
Heartburn					+							1
Indigestion					+	+	+	+	+	+		6
IMB			+								+	2
Neck lump	+					+	+					3
Night sweats	+											1
PCB			+									1
PMB	+	+	+				+	+		+	+	7
Rectal bleed				+								1
VTE	+	+	+	+	+	+	+	+	+		+	10
Weight loss	+			+	+	+	+	+	+	+		8
Total	10	5	7	9	9	9	4	0	8	7	5	n/a

QCancer symptoms map men



	blood	CRC	gastro	lung	other	pancreas	prostate	renal	testis	total
Abdo distension	+	+			+					3
Abdo pain	+	+	+	+	+	+	+	+		8
Anaemia	+	+	+	+	+					5
Appetite loss	+	+	+	+	+	+	+			7
Change in bowel		+			+					2
Constipation		+			+	+				3
Cough				+						1
Dysphagia	+		+	+	+	+				5
Frequency							+			1
Haematemesis			+		+	+				3
Haematuria	+				+		+	+		4
Haemoptysis	+			+	+					3
Heartburn			+							1
Impotence							+			1
Indigestion	+		+	+	+	+				5
Neck lump	+		+	+	+					4
Night sweats	+			+				+		3
Nocturia							+			1
Rectal bleed		+					+			2
Retention							+			1
Testicular lump	+						+		+	3
Testicular pain							+		+	2
VTE	+			+	+	+	+		+	6
Weight loss	+	+	+	+	+	+	+	+		8
Grand Total	13	8	9	11	14	8	12	4	3	82

Methods - validation is crucial

- Essential to demonstrate the tools work and identify right people in an efficient manner
- Tested performance
 - ✓ separate sample of QResearch practices
 - ✓ external dataset (Vision practices) at Oxford University
- Measures of discrimination - identifying those who do and don't have cancer
- Measures of calibration - closeness of predicted risk to observed risk
- Measure performance – positive predictive value, negative predictive value, sensitivity, specificity at different thresholds

Gold standard validation

- **Independent** – not involving original study authors
- **External** - test on cohort of patients not involved in original derivation
- **Essential** step to check model
 - Identifies right patients
 - Works in other settings – transportability
- **Different from evaluation**
- **QCancer validation by Oxford University (Collins & Altman)**
 - [Collins GS, Altman DG. Identifying patients with undetected gastro-oesophageal cancer in primary care: External validation of QCancer® \(Gastro-Oesophageal\). European journal of cancer, 2012](#)
 - [Collins GS, Altman DG. Identifying women with undetected ovarian cancer: independent and external validation of QCancer\(\(R\)\) \(Ovarian\) prediction model. European journal of cancer care 2012 doi: 10.1111/ecc.12015.](#)
 - [Collins GS, Altman DG. Identifying patients with undetected colorectal cancer: an independent validation of QCancer \(Colorectal\). Br J Cancer 2012](#)
 - [Collins GS, Altman DG. Identifying patients with undetected renal tract cancer in primary care: An independent and external validation of QCancer \(renal\) prediction model. Cancer Epidemiology; 2012](#)

Validation Results Women: Discrimination ROC values

	Combined symptoms model* in separate QResearch cohort	Individual cancer models in separate cohort from QResearch	independent external validation in Vision data
any cancer	0.85	n/a	In progress
lung	0.91	0.92	In press
colorectal	0.89	0.89	0.92
gastro	0.90	0.89	0.93
pancreas	0.87	0.84	In press
ovary	0.84	0.84	0.86
renal	0.90	0.91	0.92
breast	0.88	n/a	In progress
blood	0.79	n/a	In progress
uterus	0.91	n/a	In progress
cervix	0.73	n/a	In progress
other	0.82	n/a	In progress

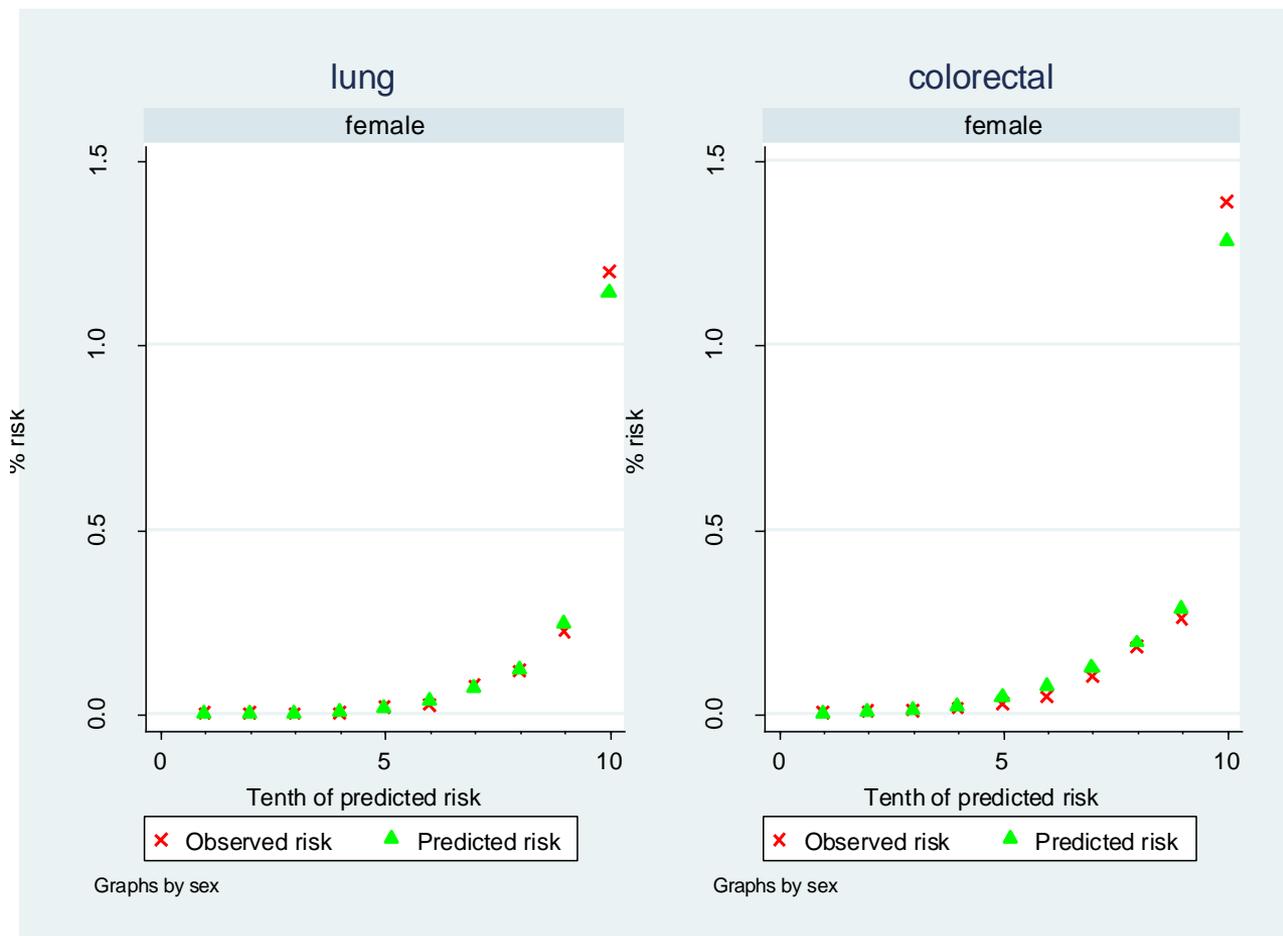
*reference: Symptoms and risk factors to identify women with suspected cancer in primary care; BJGP; 2013

Validation Results Men: Discrimination ROC values

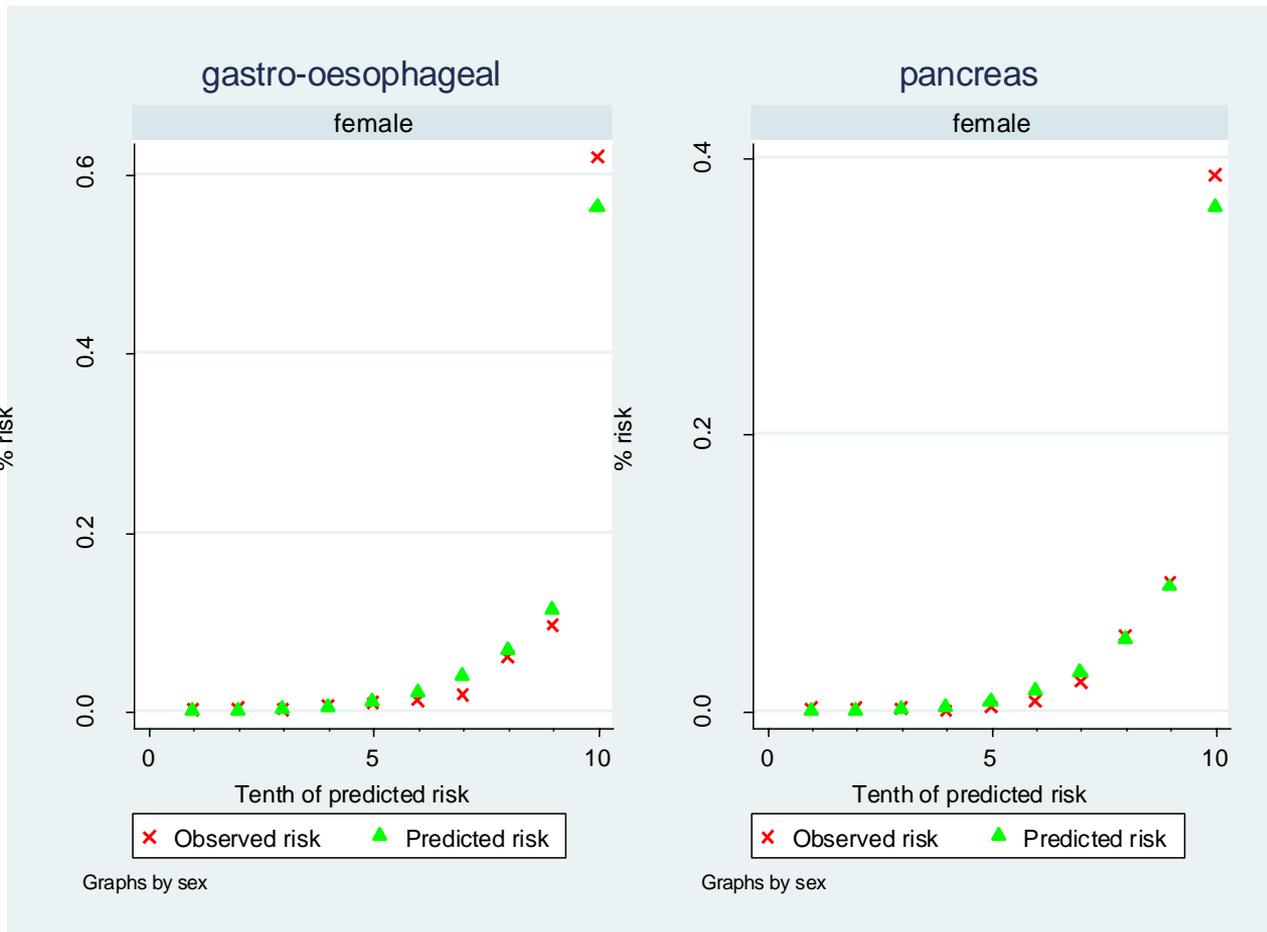
	Combined symptoms model* in separate QResearch cohort	Individual cancer models in separate cohort from QResearch	independent external validation in Vision data
any cancer	0.89	n/a	In progress
lung	0.92	0.92	In press
colorectal	0.90	0.91	0.91
gastro	0.93	0.92	0.94
pancreas	0.89	0.87	In press
renal	0.94	0.95	0.95
prostate	0.90	n/a	In progress
blood	0.83	n/a	In progress
testis	0.82	n/a	In progress
other	0.86	n/a	In progress

*reference: Symptoms and risk factors to identify men with suspected cancer in primary care; BJGP; 2013

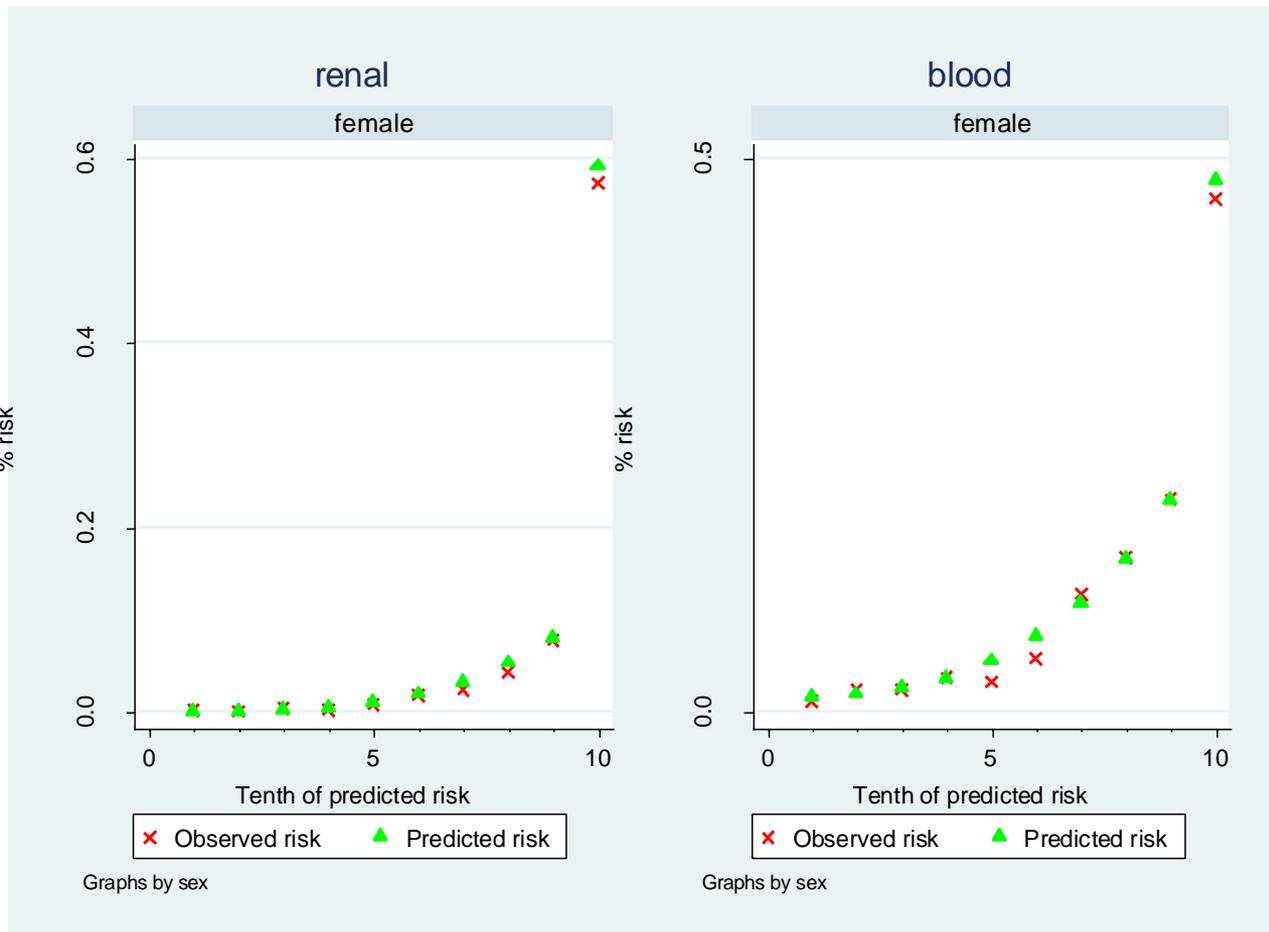
Validation women calibration mean predicted & observed risk



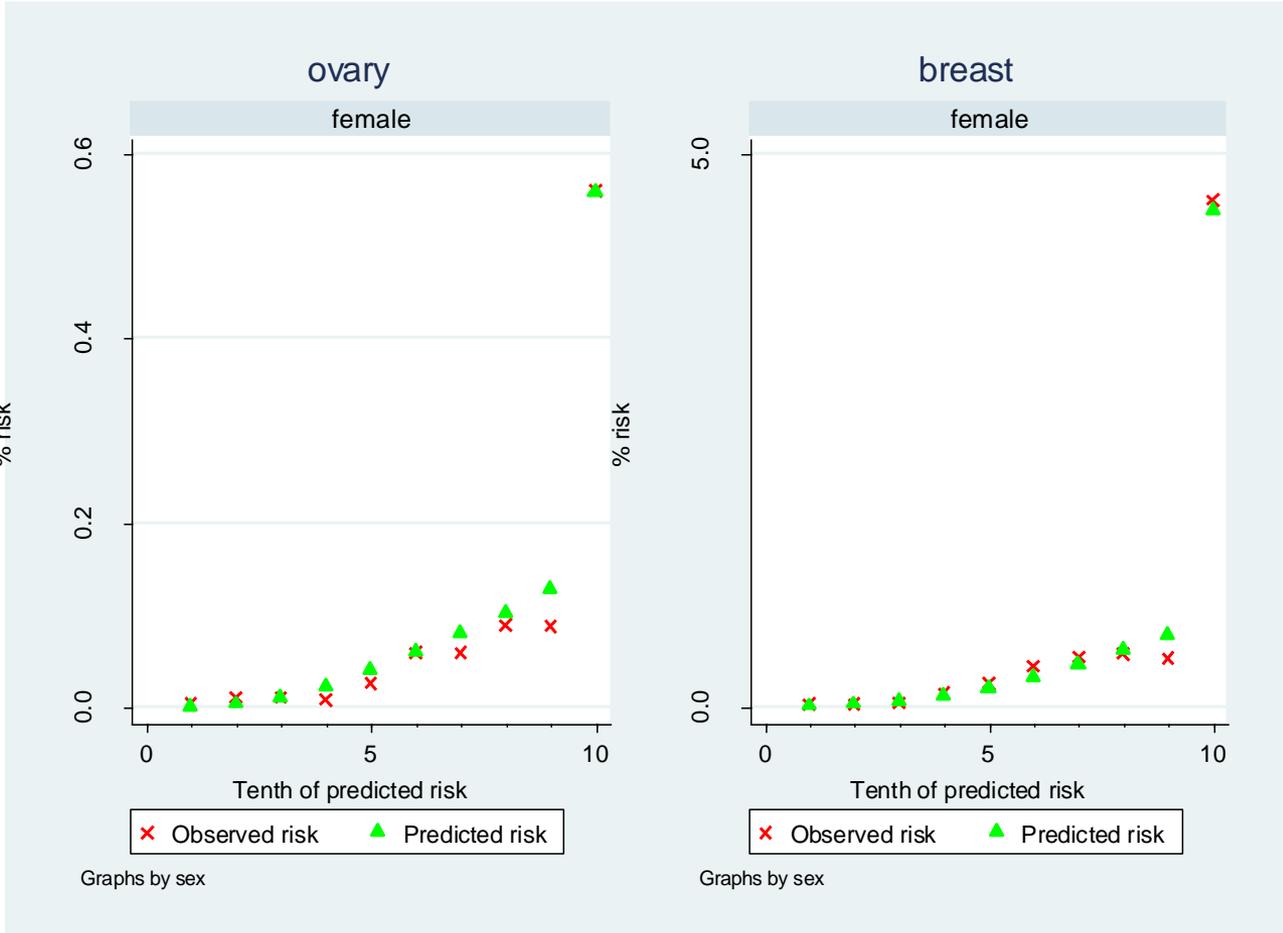
Validation women calibration mean predicted & observed risk



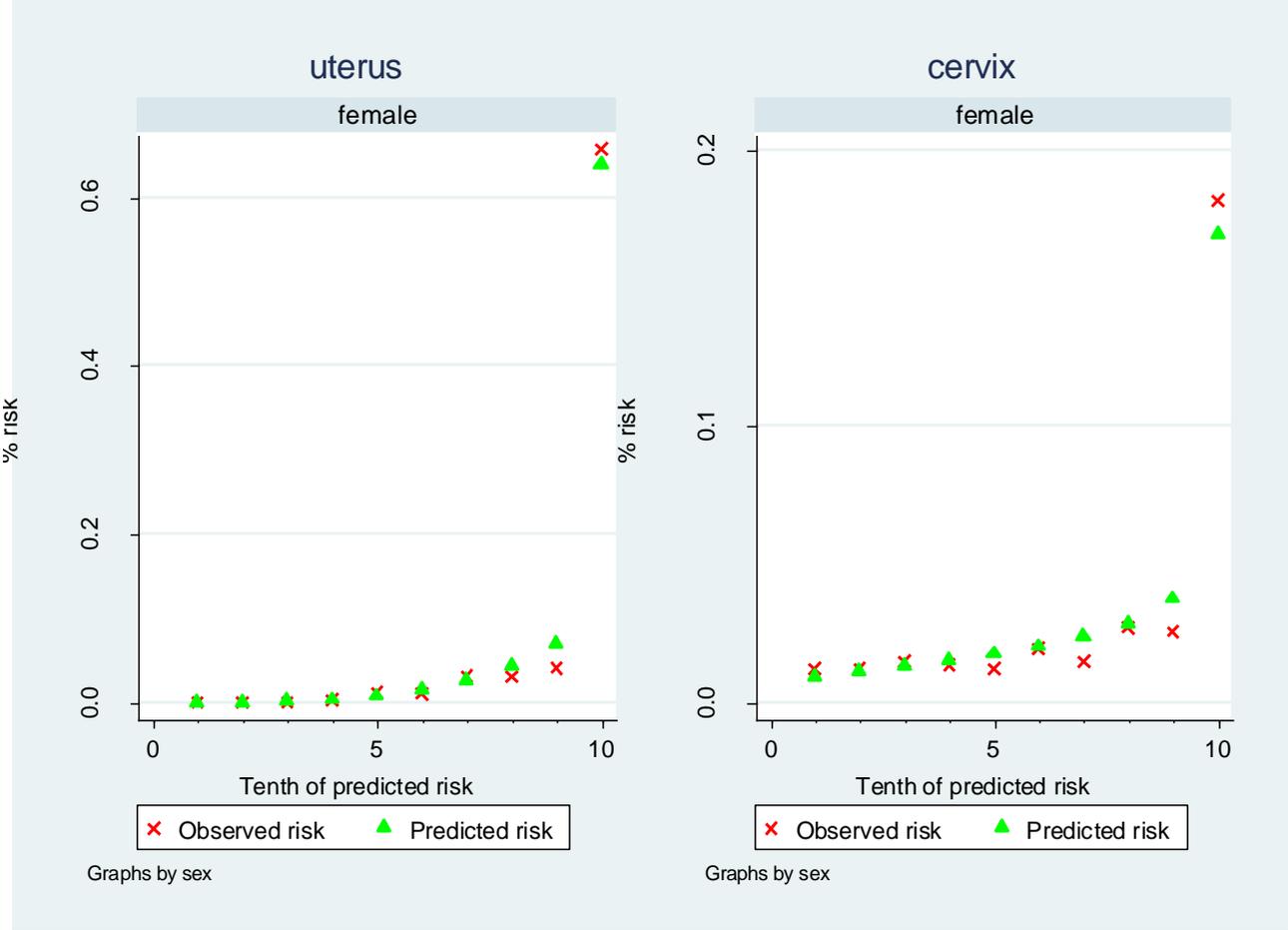
Validation women calibration mean predicted & observed risk



Validation women calibration mean predicted & observed risk



Validation women calibration mean predicted & observed risk



Comparison strategies in women based on top 10% risk

	Risk threshold %	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
lung cancer	0.38	72.1	90.1	1.2	99.9
colorectal	0.35	68.2	90.1	1.4	99.9
gastro-oesoph	0.14	75.0	90.1	0.6	100.0
pancreas	0.12	67.9	90.0	0.4	100.0
ovarian	0.18	61.6	90.0	0.6	100.0
renal	0.10	76.7	90.0	0.6	100.0
breast	0.72	68.1	90.4	4.6	99.8
blood	0.22	44.0	90.0	0.5	99.9
uterine	0.10	83.7	90.1	0.7	100.0
cervical	0.05	54.5	90.0	0.2	100.0
other	0.55	19.4	90.0	0.1	100.0

Comparison strategies in men based on top 10% cancer risk

	% threshold	Sensitivity (%)	specificity (%)	PPV (%)	NPV (%)
lung	0.67	71.5	90.2	1.9	99.9
colorectal	0.45	69.5	90.2	1.8	99.9
gastro-oesoph	0.29	76.6	90.1	1.3	100.0
pancreas	0.10	70.1	90.0	0.4	100.0
renal tract	0.20	82.7	90.1	1.6	100.0
prostate	1.30	59.5	90.2	2.2	99.8
blood	0.27	49.0	90.1	0.6	99.9
testicular	0.02	67.1	90.0	0.2	100.0
other	0.66	27.0	90.0	0.1	100.0

Web calculator www.qcancer.org

- Publically available
- Interactive
- Gives global cancer risk
- Risk of different cancer types
- Visual display of absolute risk to help shared decision making e.g. “of a 100 patients like 7 you. 20 will have cancer”
- www.qcancer.org

Using QCancer in practice – v similar to QRISK2

- Standalone tools

- a. Web calculator

www.qcancer.org/2013/female/php

www.qcancer.org/2013/male/php

- b. Windows desk top calculator

- c. Iphone – simple calculator

- Integrated into clinical system

- a. Within consultation: GP with patients with symptoms

- b. Batch: Run in batch mode to risk stratify entire practice or PCT population

GP systems integration

Batch processing

- Similar to QRISK2 which is in 95% of GP practices– automatic daily calculation of risk for all patients in practice based on existing data.
- Identify patients with symptoms/adverse risk profile without follow up/diagnosis
- Enables systematic recall or further investigation
- Systematic approach - prioritise by level of risk.
- Safety netting