

# 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 QScores
- QCancer Model development
- QCancer Model validation
- QCancer Implementation
- Pilot work with Macmillan and CRUK evaluation

# QResearch Database

[www.qresearch.org](http://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

# QScores –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

# Qscores and national guidance

| Risk score      | Outcome               | NICE guidance   | Implementation                                |
|-----------------|-----------------------|---|---|
| Qrisk.org       | 10 year risk of CVD   | Approved CG68 (2008)<br>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)<br>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.<br>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

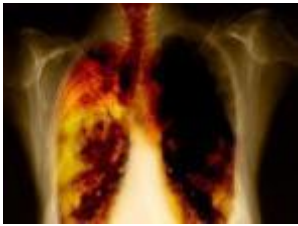
- Accurately predict individual level of risk of multiple cancers for based on multiple risk factors and multiple symptoms
- **Discriminate between patients with and without cancer**
- **Help guide decision on who to investigate or refer and degree of urgency.**
- **Educational tool for sharing information 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

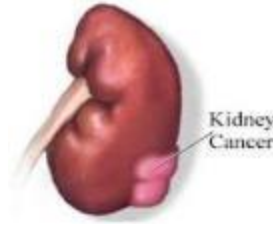
Lung



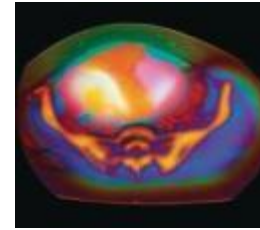
Pancreas



Renal tract



Ovary



Colorectal



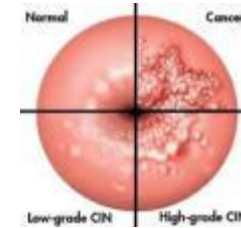
Gastro



Testis



Cervix



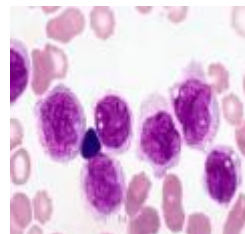
Breast



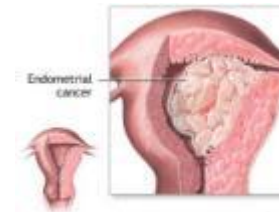
Prostate



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          |
| <b>Total</b>               | <b>10</b> | <b>5</b> | <b>7</b> | <b>9</b> | <b>9</b> | <b>9</b> | <b>4</b> | <b>0</b> | <b>8</b> | <b>7</b> | <b>5</b> | <b>n/a</b> |

# 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         |
| <b>Grand Total</b> | <b>13</b> | <b>8</b> | <b>9</b> | <b>11</b> | <b>14</b> | <b>8</b> | <b>12</b> | <b>4</b> | <b>3</b> | <b>82</b> |

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

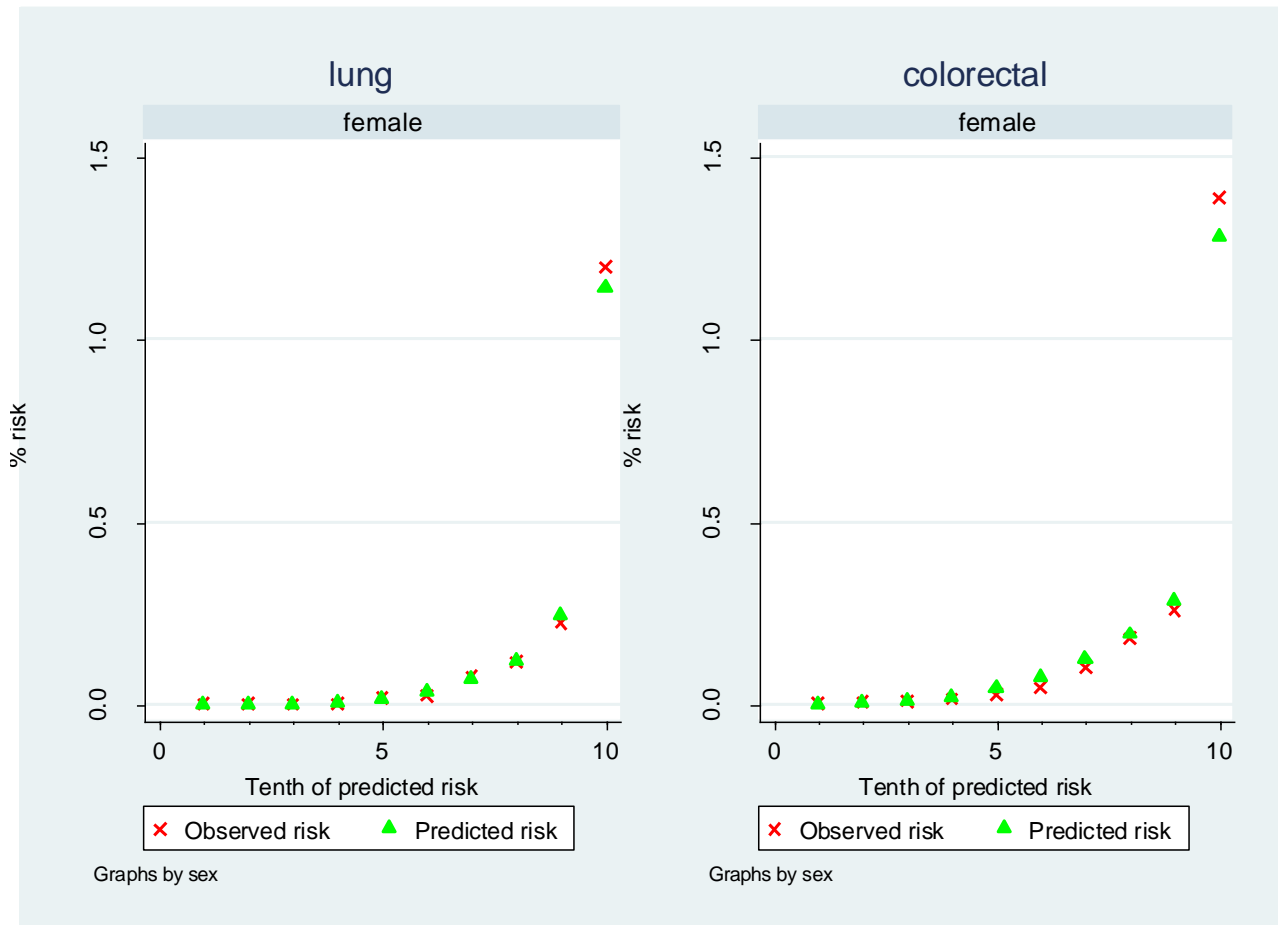
\*reference: Symptoms and risk factors to identify women with suspected cancer in primary care; BJGP; 2013

# Validation Results Men: Discrimination ROC values

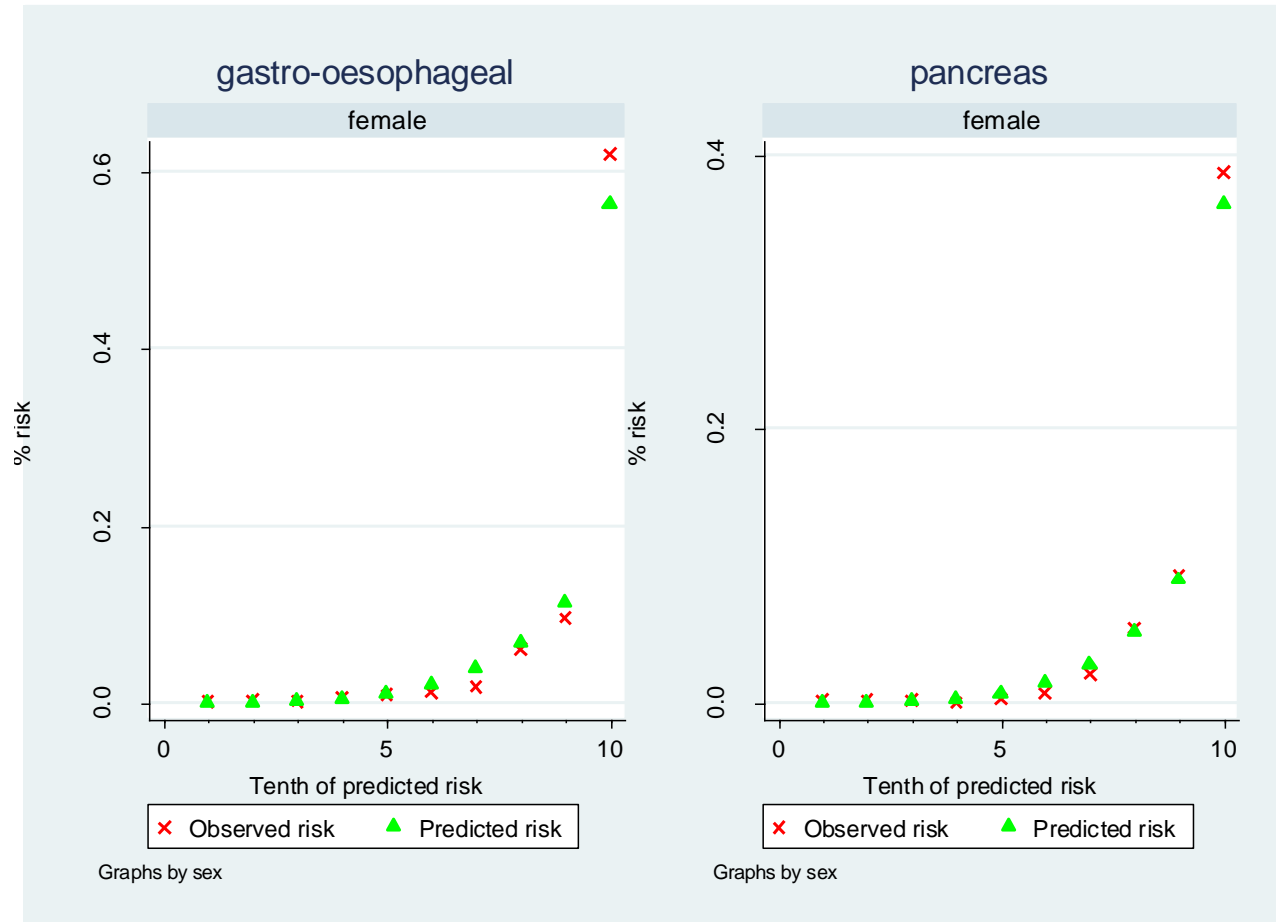
|                   | Combined symptoms model*<br>in separate QResearch cohort | Individual cancer models in separate cohort from QResearch | independent external validation in Vision data |
|-------------------|--|--|--|
| <b>any cancer</b> | 0.89   | n/a  | In progress                             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

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

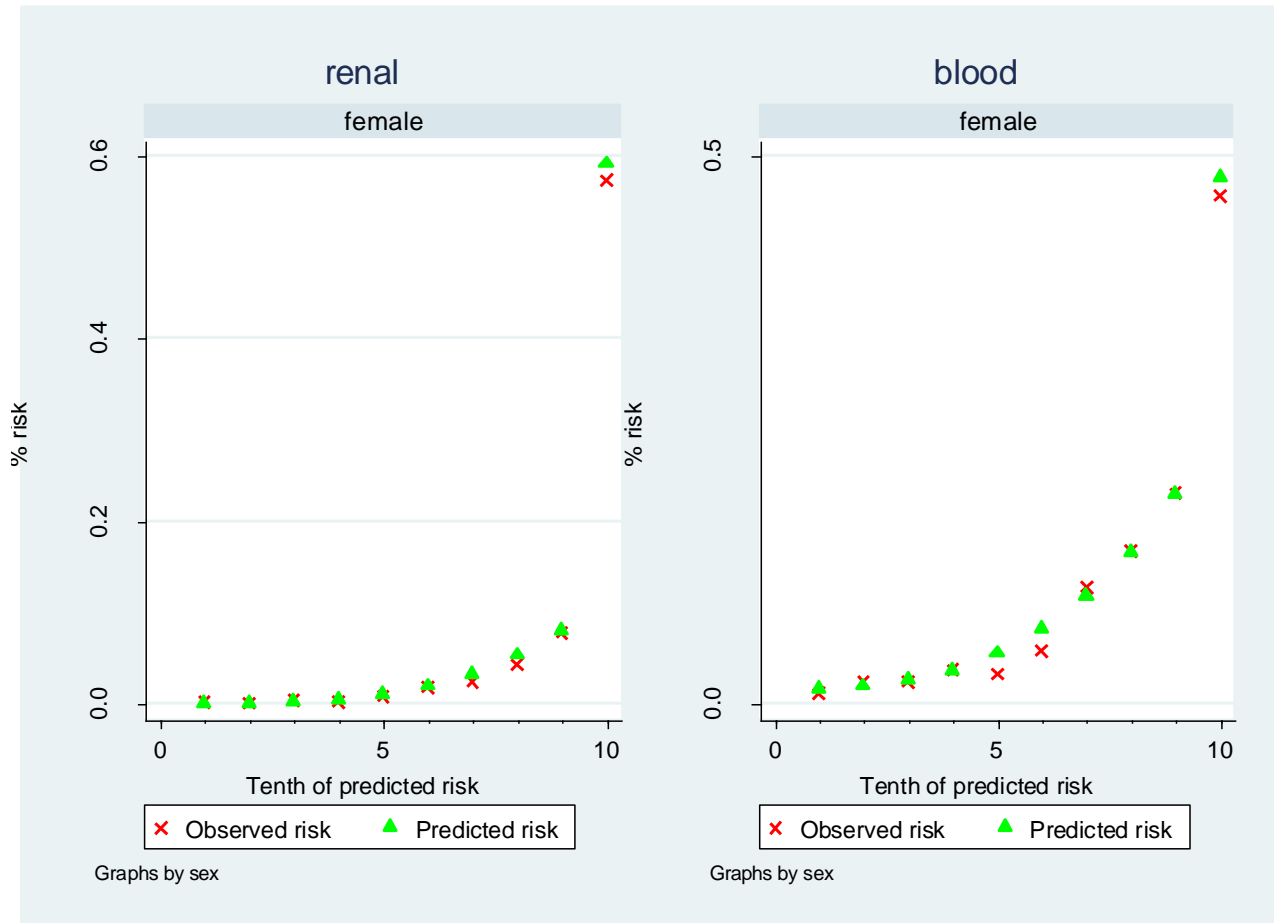
# Validation women calibration mean predicted & observed risk



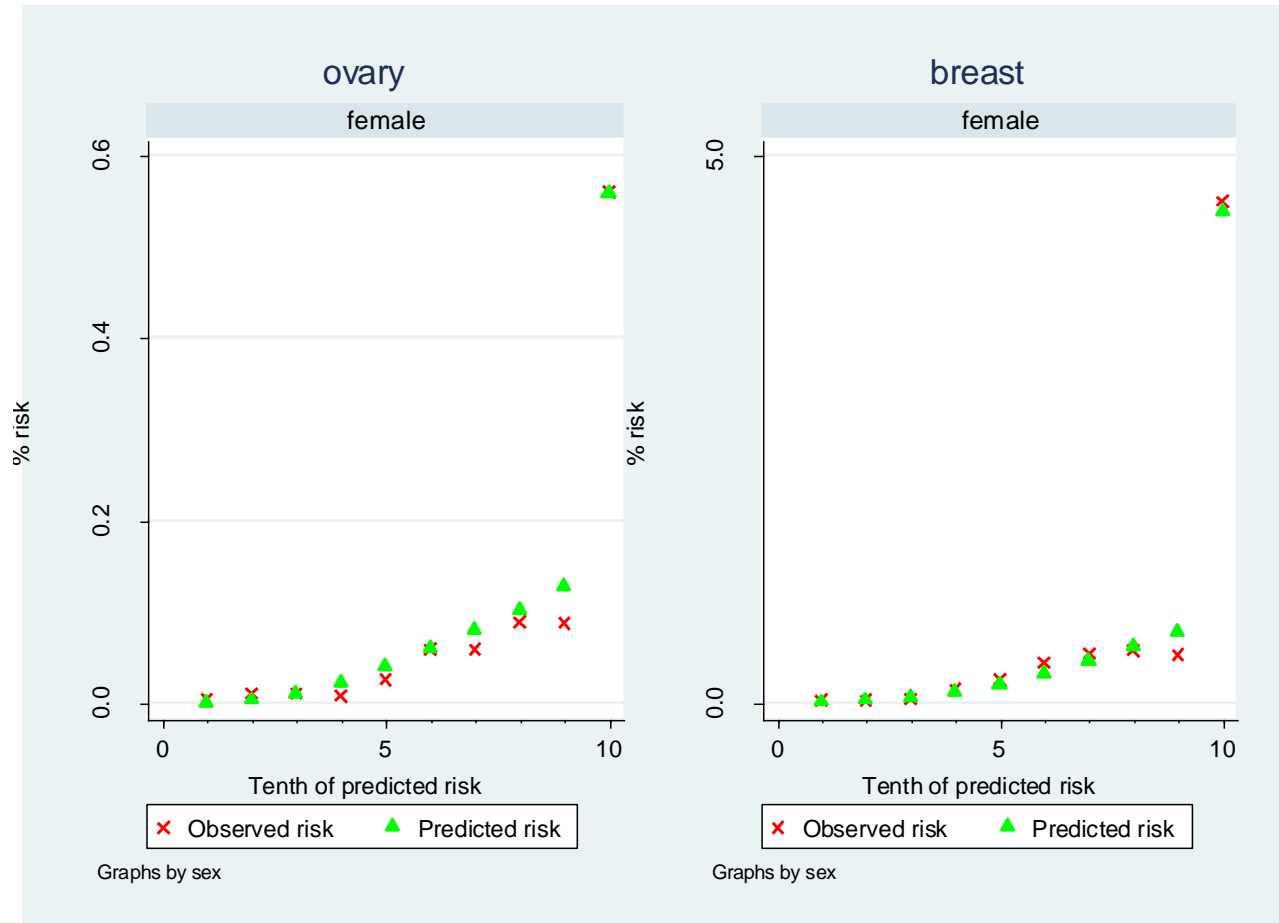
# Validation women calibration mean predicted & observed risk



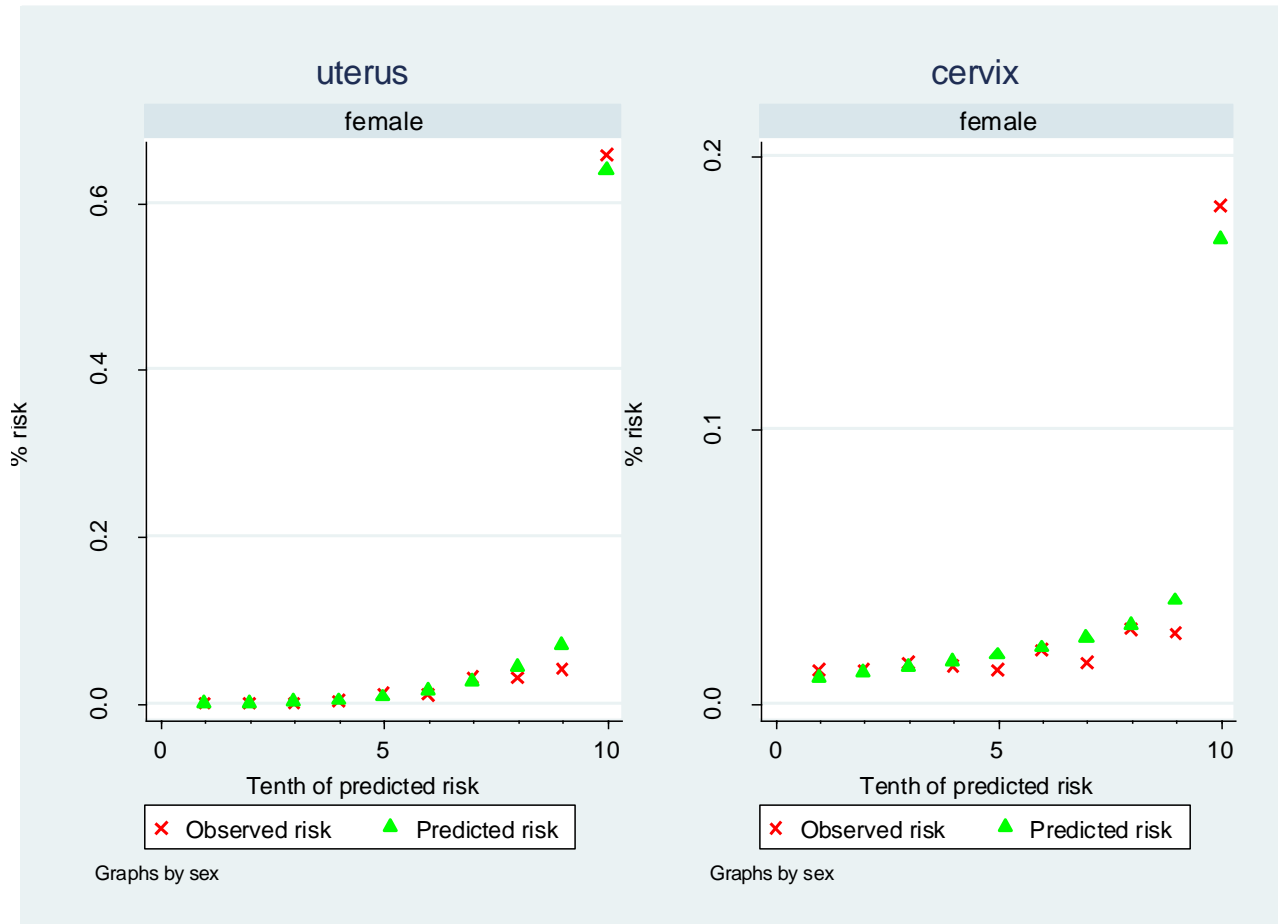
# Validation women calibration mean predicted & observed risk



# 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](http://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](http://www.qcancer.org)

# Using QCancer in practice – v similar to QRISK2

- Standalone tools
  - a. Web calculator
    - [www.qcancer.org/2013/female/php](http://www.qcancer.org/2013/female/php)
    - [www.qcancer.org/2013/male/php](http://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