Aspects of quality in breast pathology

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British breast pathology EQA: performance issues

Ian Ellis Friday 8.30 am

National breast screening pathology audit 2015

Performance for the period 2011-14

Rahul Deb, Ian Ellis, Jacquie Jenkins, Alison Murphy, Sarah E Pinder

- **111,644 core biopsies (or FNAs)**
- **50,142 cancers diagnosed**

GUIDELINES FOR NON-OPERATIVE DIAGNOSTIC PROCEDURES AND REPORTING IN BREAST CANCER SCREENING Non-operative Diagnosis Subgroup of the National Coordinating Group for Breast Screening Pathology NHSBSP Publication No 50 June 2001

https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/448479/nhsbsp50.pdf

B categories for core biopsies

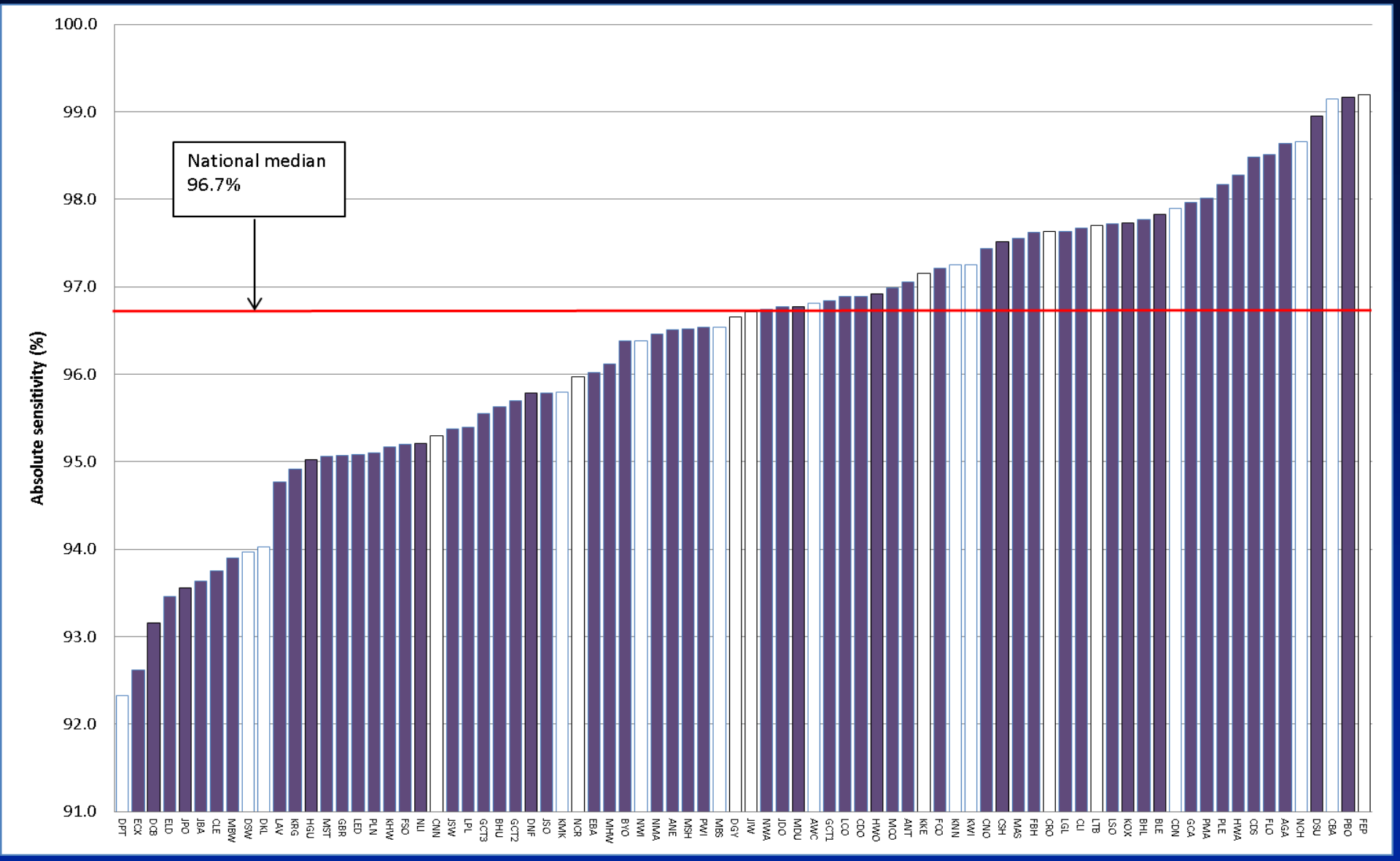
- B1 Normal
- B2 Benign
- B3 Lesion of uncertain malignant potential
- B4 Suspicious of malignancy
- B5b Malignant invasive
- B5a Malignant in situ

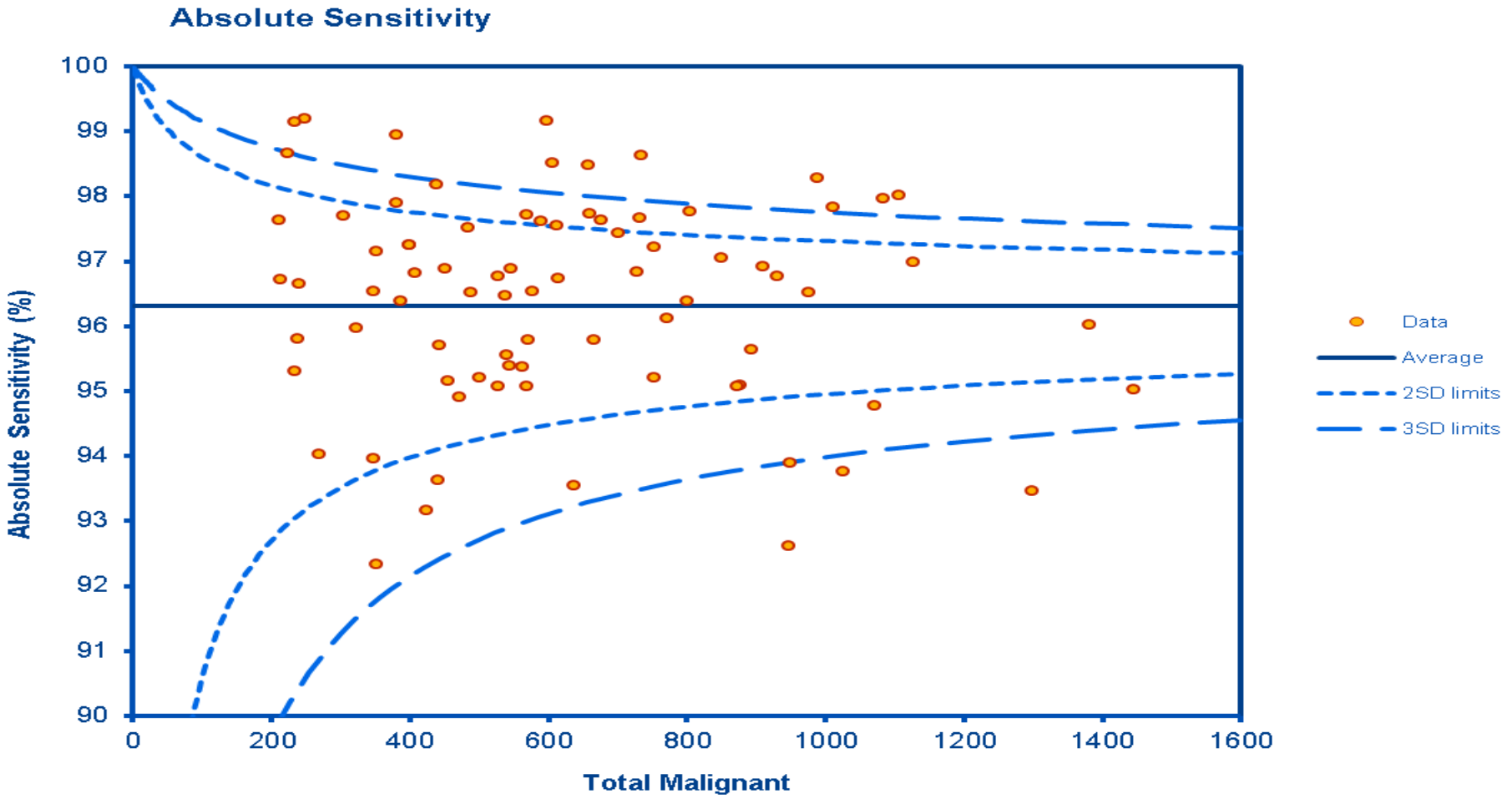
Absolute sensitivity

- **Definition: The number of carcinomas diagnosed as such (B5) expressed as a percentage of the total number of carcinomas sampled**
- **Past standard: >70% (minimum), >80% (achievable)**
- **Proposed standard: >92% (minimum), >95% (preferred)**
- **Current median: 96.7%**

Complete sensitivity

- **Definition: The number of carcinomas that were not definitely negative (not B1 or B2) on core expressed as a percentage of the total number of carcinomas**
- **Past standard: >80% (minimum), >90% (achievable)**
- **Proposed standard: >99% (minimum), >99.5% (preferred)**
- **Current median: 99.8%**


National median
96.7%
Absolute sensitivity (%)
100.0
99.0
98.0
97.0
96.0
95.0
94.0
93.0
92.0
91.0
DPT ECX DCB ELD JPO JBA CLE MBW DSW DKL LAV KRG HGU MST GBR LED PLN KHW FSO NLI CNN JSW LPL GCT3 BHU GCT2 DNF JSO KNK NCR EBA MHW BYO NWI NMA ANE MSH PWI MBS DGY JIW NWA JDO MDU AWC GCT1 LCO CDO HWO MCO ANT KKE FCO KNN KWI CNO CSH MAS FBH CRO LGL CLI LTB LSO KOX BHL BLE CDN GCA PMA PLE HWA CDS FLO AGA NCH DSU CBA PBO FEP



Source: EMQARC

Control charts

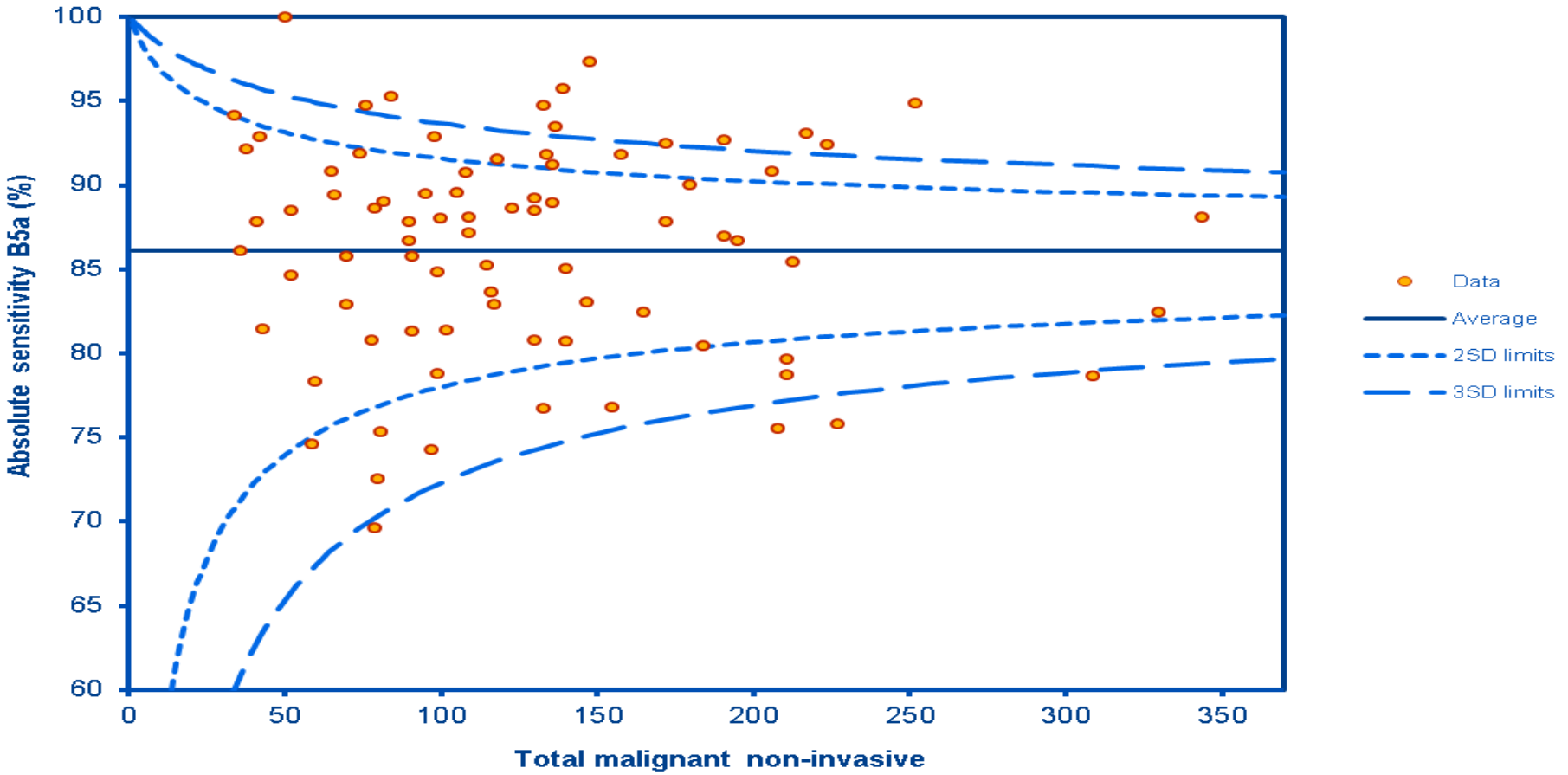
- x axis – feature of interest
- y axis – number of cases
- Upper and lower control limit lines:
- +/- 2 standard deviations (95%)
- +/- 3 standard deviations (99.8%)
- Confidence intervals narrow as number of cases increases
- Outlier does not necessarily mean poor performance

Absolute sensitivity

High outlier: not a problem

Low outlier:

- Look at complete sensitivity
- If complete sensitivity is not low may be undercalling B5 and overusing B3 and B4, or insufficient tissue for diagnosis
- If complete sensitivity is low then core may be missing the cancer – examine B1 and B2 rates from cancers



Source: EMQARC

Complete sensitivity

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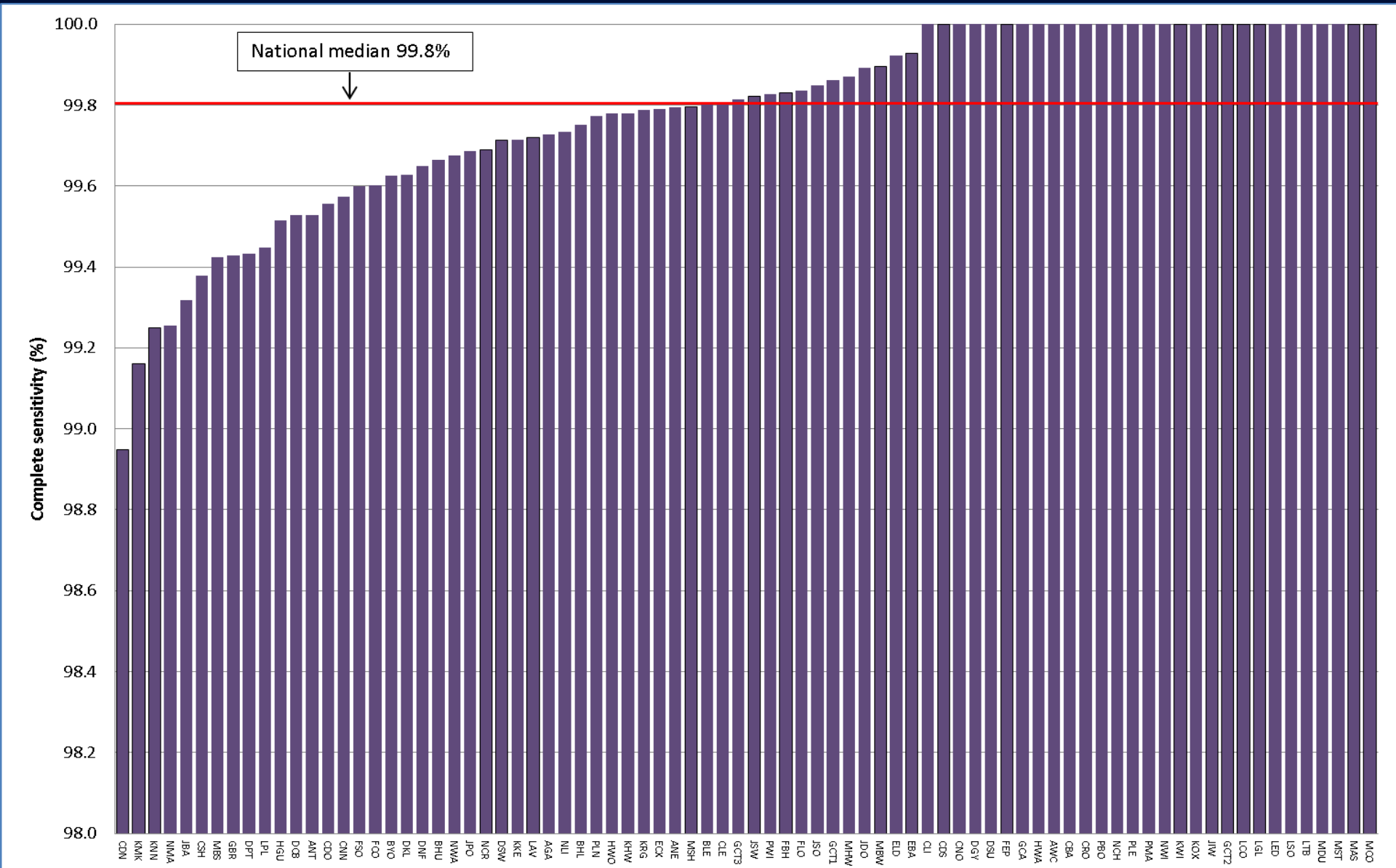

National median 99.8%
Complete sensitivity (%)
100.0
99.8
99.6
99.4
99.2
99.0
98.8
98.6
98.4
98.2
98.0
CDN KMK KNN NMA JBA CSH MBS GBR DPT LPL HGU DCB ANT CDO CNN FSO FCO BYO DKL DNF BHU NWA JPO NCR DSW KKE LAV AGA NLI BHL PLN HWO KHW KRG ECX ANE MSH BLE CLE GCT3 JSW PWI FBH FLO JSO GCT1 MHW JDO MBW ELD EBA CLI CDS CNO DGY DSU FEP GCA HWA AWC CBA CRO PBO NCH PLE PMA NWI KWI KOX JIW GCT2 LCO LGL LED LSO LTB MDU MST MAS MCO

Positive predictive value of B5

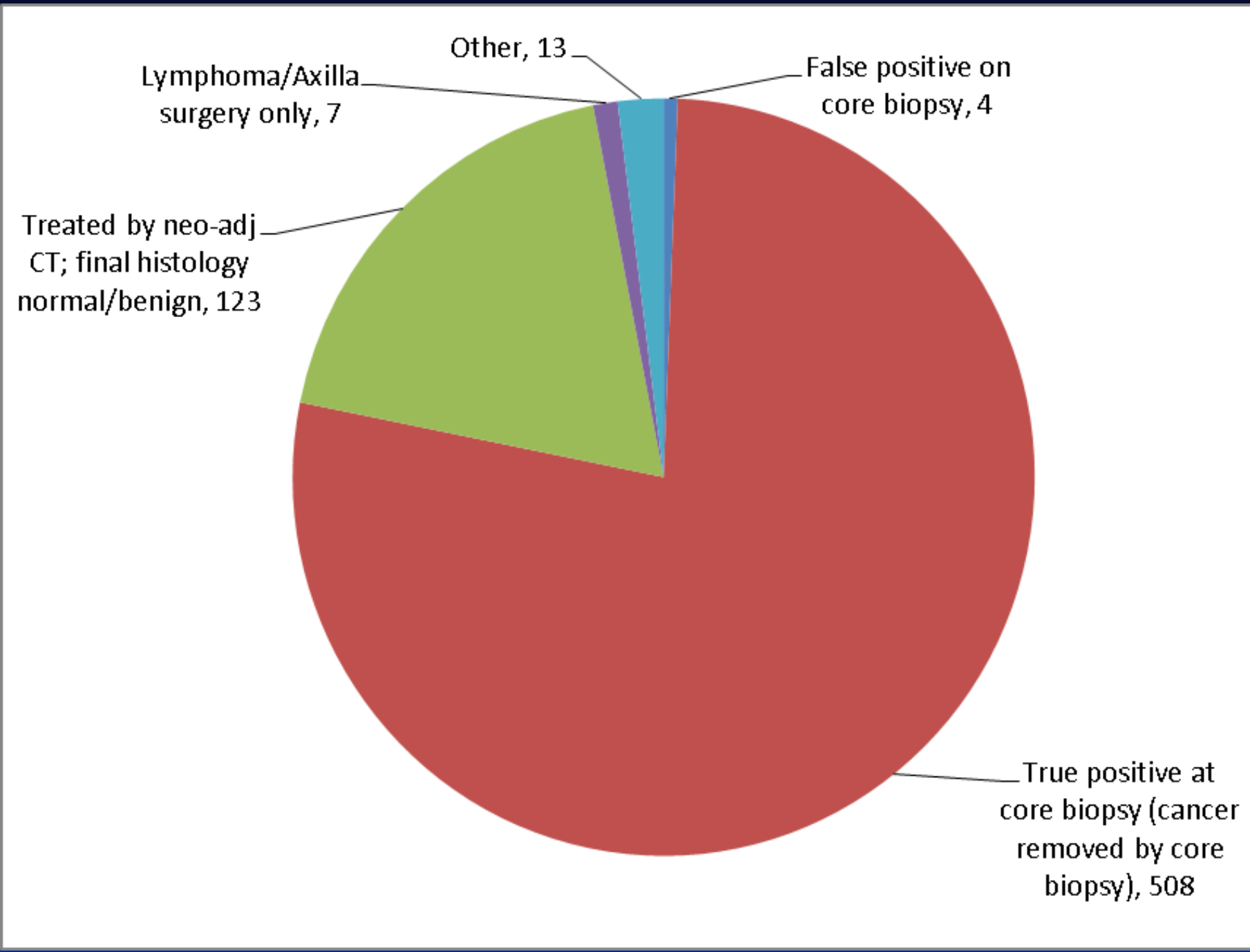
- **Definition: The number of correctly identified cancers (number of B5 results minus the number of false positive results) expressed as a percentage of the total number of positive results (B5)**
- **Past standard: >99% (minimum), >99.5% (achievable)**
- **National median: 100%**
- **Proposed standard: >99.5% (minimum), >99.9% (achievable)**

False positive rate

- Definition: The number of false positives results expressed as a percentage of the total number of carcinomas sampled
- Past standard: <0.5% (minimum), <0.1% (achievable)
- National median: 0%
- Proposed standard: <0.2% (minimum), <0.1% (preferred)
- 4 true false positive core biopsies in 2011-14 (0.004 %)

Investigation of potential false-positive result (B5 Core, benign excision)

- Review core biopsy diagnosis
- Review surgical specimen
- Preoperative systemic treatment – look for fibrosis, macrophages etc
- Identify core site in excision
- If there is doubt about the origin of either specimen – DNA testing
- MDT review

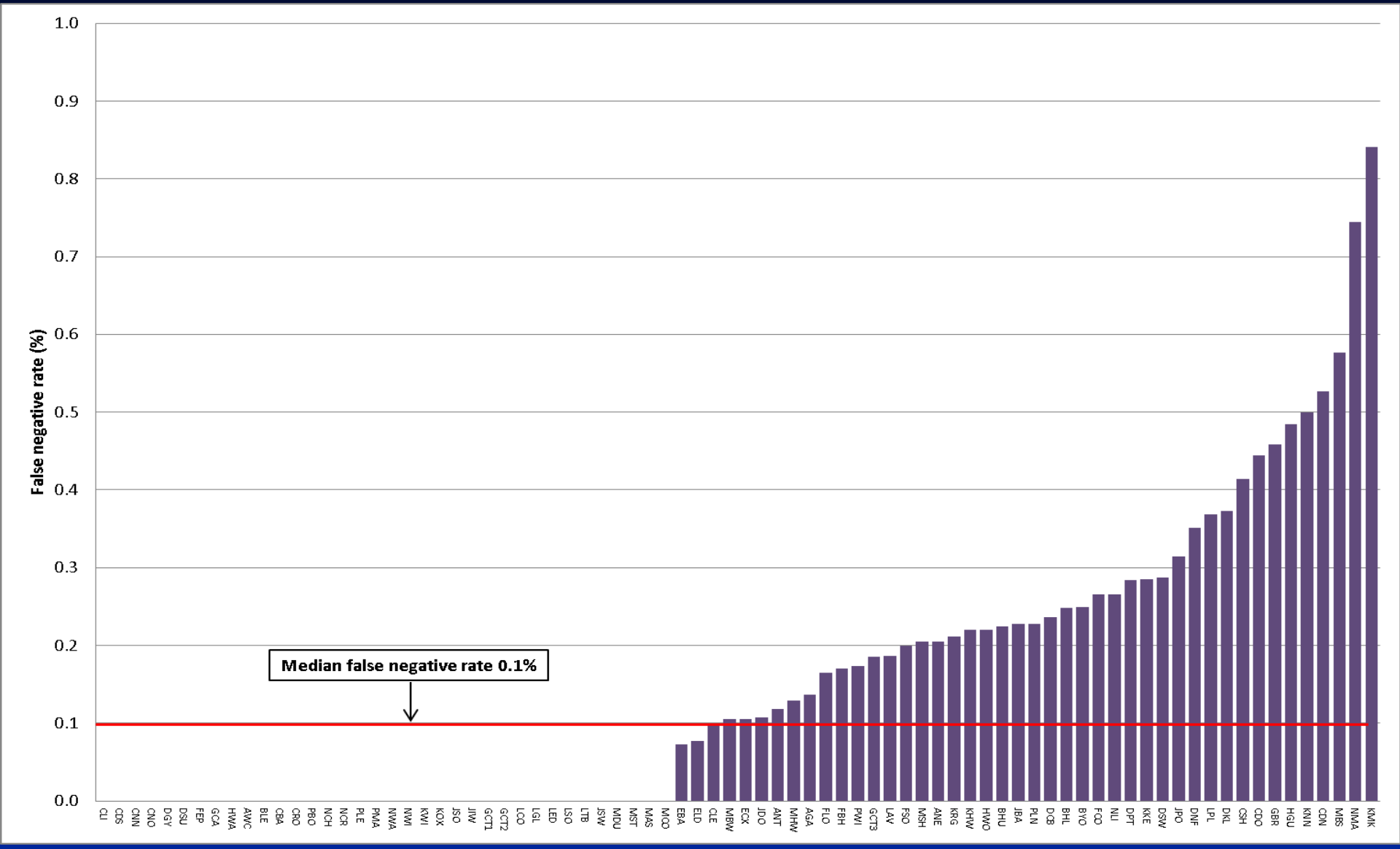

Other, 13
Lymphoma/Axilla surgery only, 7
False positive on core biopsy, 4
Treated by neo-adj CT; final histology normal/benign, 123
True positive at core biopsy (cancer removed by core biopsy), 508

REPORTING, RECORDING AND AUDITING B5 CORE BIOPSIES WITH NORMAL/BENIGN SURGERY
NHSBSP Good Practice Guide No 9
November 2007

https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/442171/nhsbsp-gpg9.pdf

False negative rate

- **Definition: The number of false negative results (B2 from cancer) expressed as a percentage of the total number of carcinomas sampled.**
- **Past standard: <15% (minimum), <10% (achievable)**
- **National median: 0.1%**
- **National range: 0% to 0.8%**
- **Proposed standard: <0.5% (minimum), <0.2% (preferred)**


False negative rate (%)
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
Median false negative rate 0.1%
CLI CDS CNN CNO DGY DSU FEP GCA HWA AWC BLE CBA CRO PBO NCH NCR PLE PMA NWA NWI KWI KOX JSO JIW GCT1 GCT2 LCO LGL LED LSO LTB JSW MDU MST MAS MCO EBA ELD CLE MBW ECX JDO AMT MHW AGA FLO FBH PWI GCT3 LAV FSO MSH AME KRG KHW HWO BHU JBA PLN DOB BHL BYO FCO NLI DPT KKE DSW JPO DNF LPL DKL CSH CDO GBR HGU KNN CDN MBS NMA KMK

False negative rate

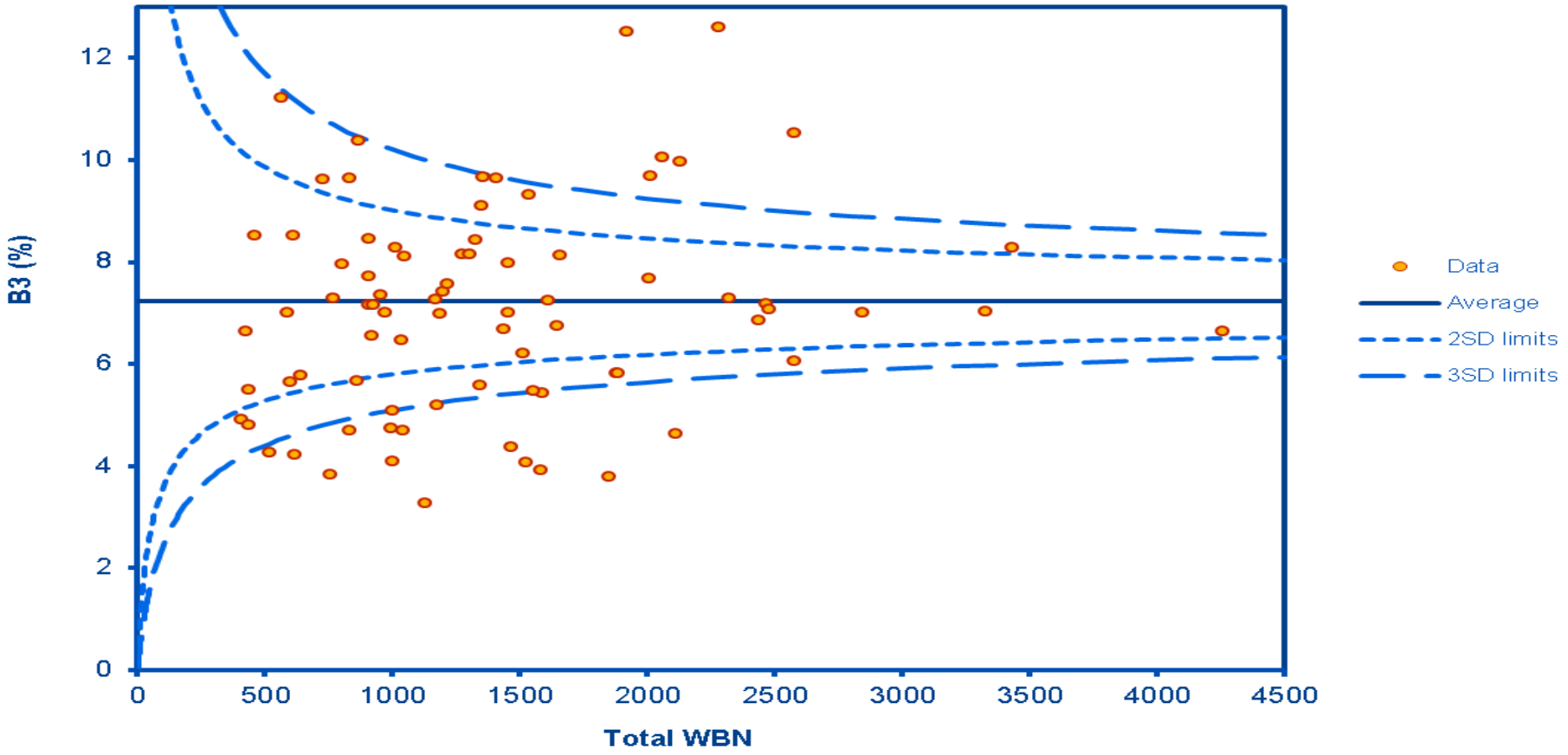
- Nationally, of 48,942 malignancies proven on histology, just 74 cancers (0.2%) were reported B2 non-operatively.
- Lesion missed by core biopsy
- Lesion not identified by pathologist

B1 from cancer rate

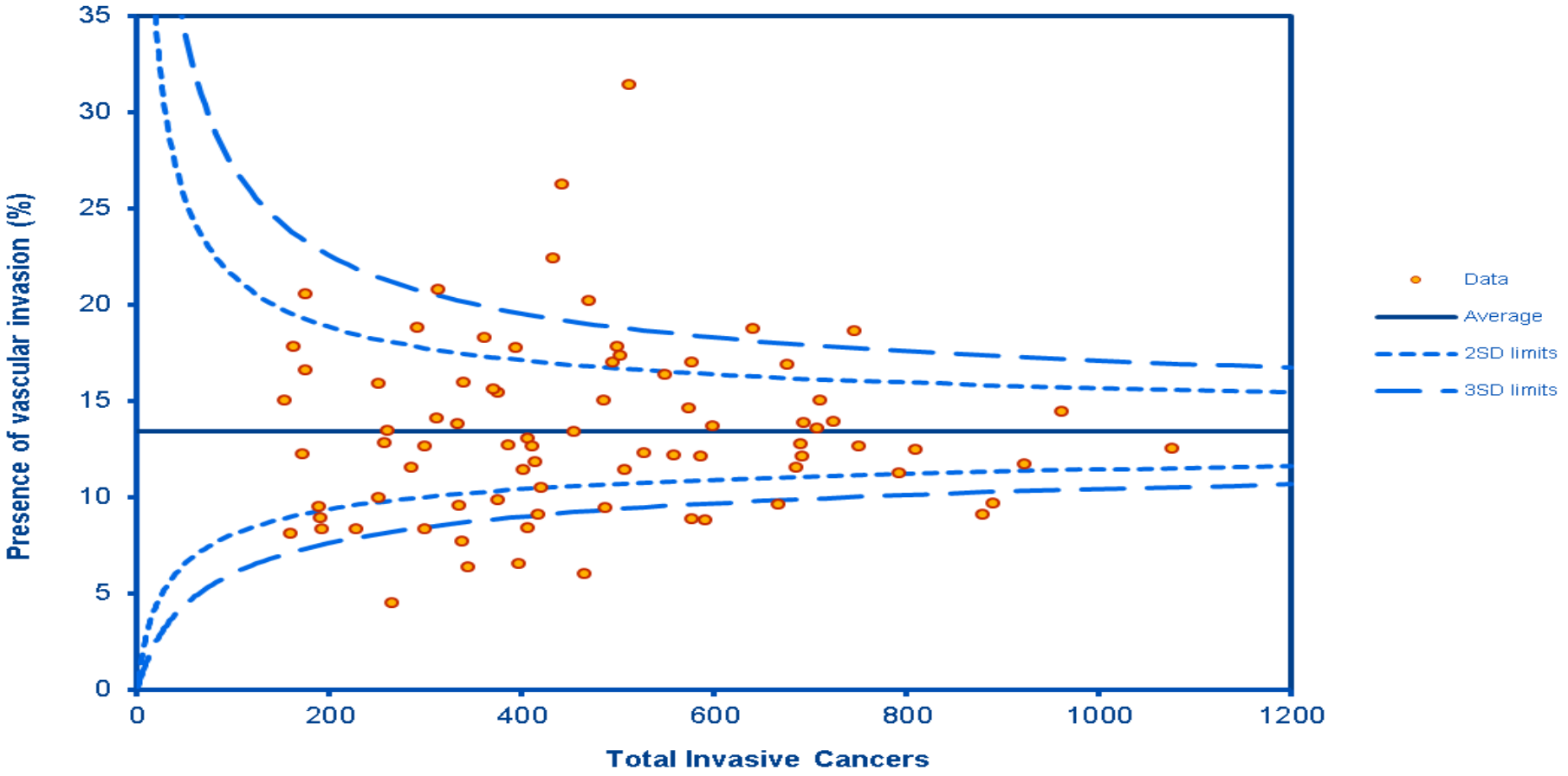
- Definition: The number of cancers categorized as B1
- Past standard: <15% (minimum), <10% (achievable)
- National median: 0%
- Proposed standard: < 0.5% (minimum), < 0.3% (preferred)

B1 from cancer rate

- Almost two thirds of services (n. 56/80) had no cancers reported non-operatively as B1 demonstrating good performance.
- There were no services whose results were significantly high on this indicator.
- Lesion missed by core biopsy
- Lesion not identified by pathologist



Source: EMQARC



Source: EMQARC

Vascular invasion outlier

- Check data
- Look at proportion of possible VI and VI not reported
- Consider looking at data from different time periods especially if numbers small
- Look at fixation
- Review cases with multiple observers

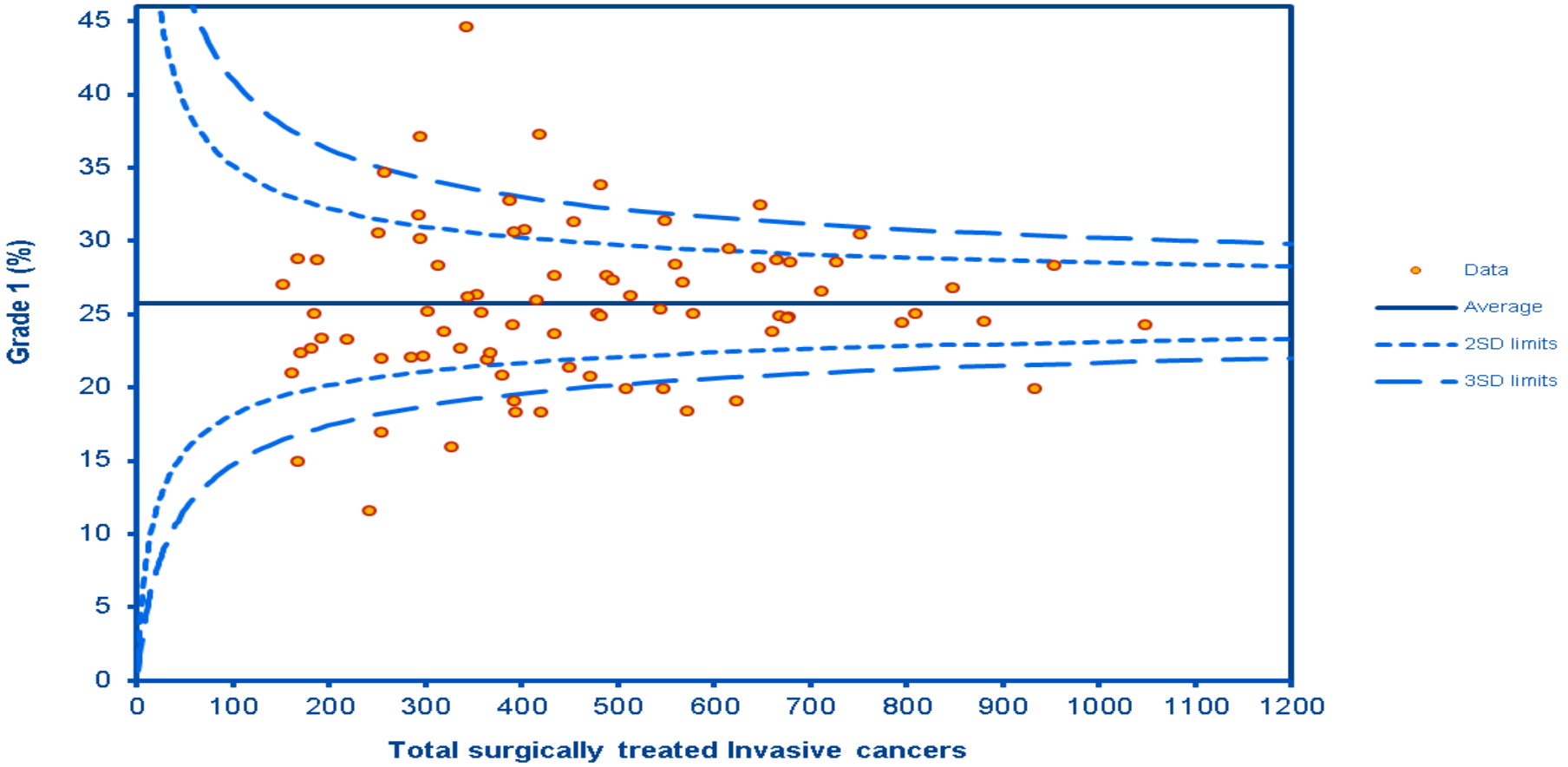
Histological grade

National breast screening pathology audit

- Grade 1 26%
- Grade 2 54%
- Grade 3 20%

Elston and Ellis 1991 (symptomatic)

- Grade 1 19%
- Grade 2 34%
- Grade 3 47%



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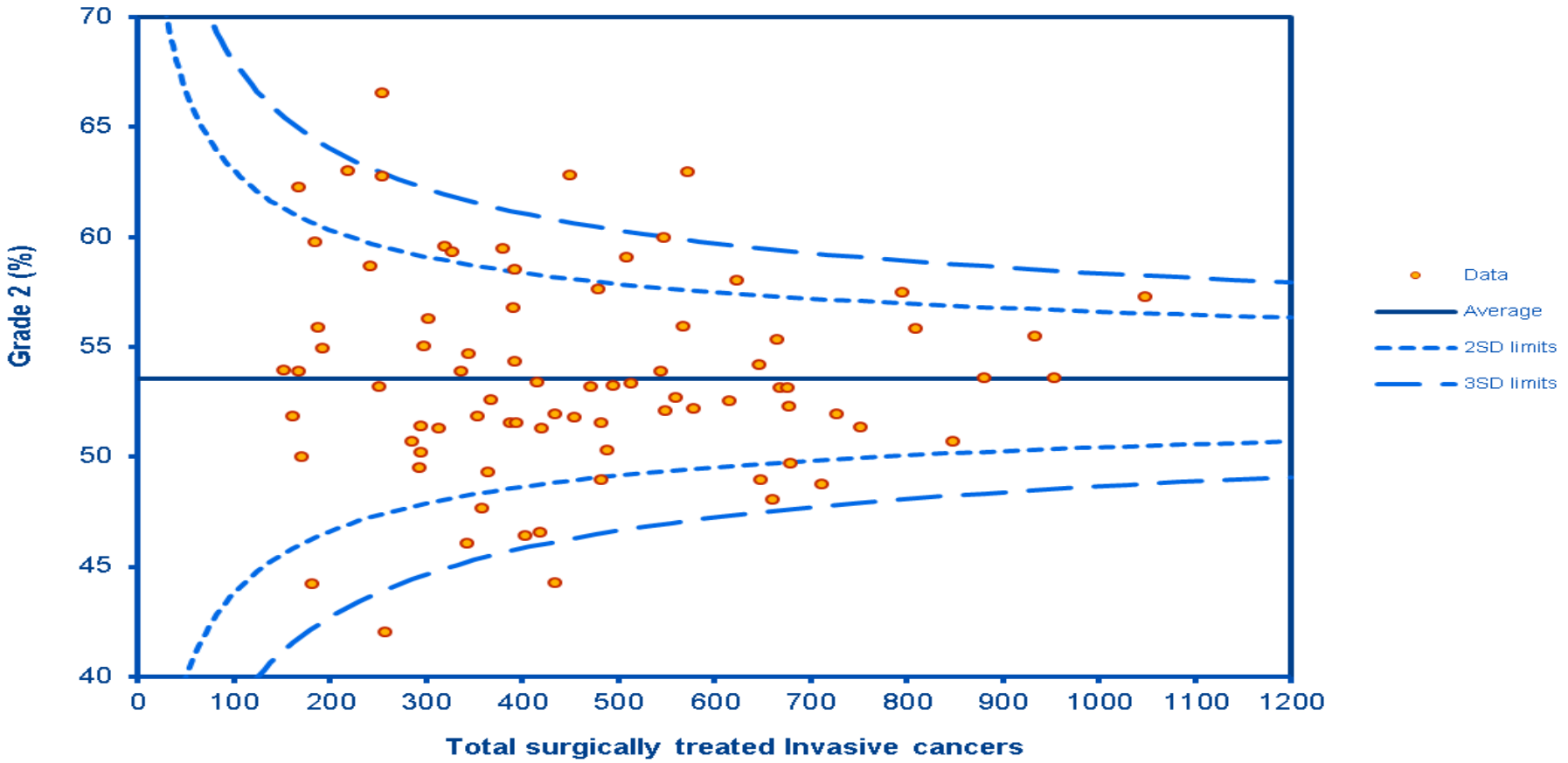

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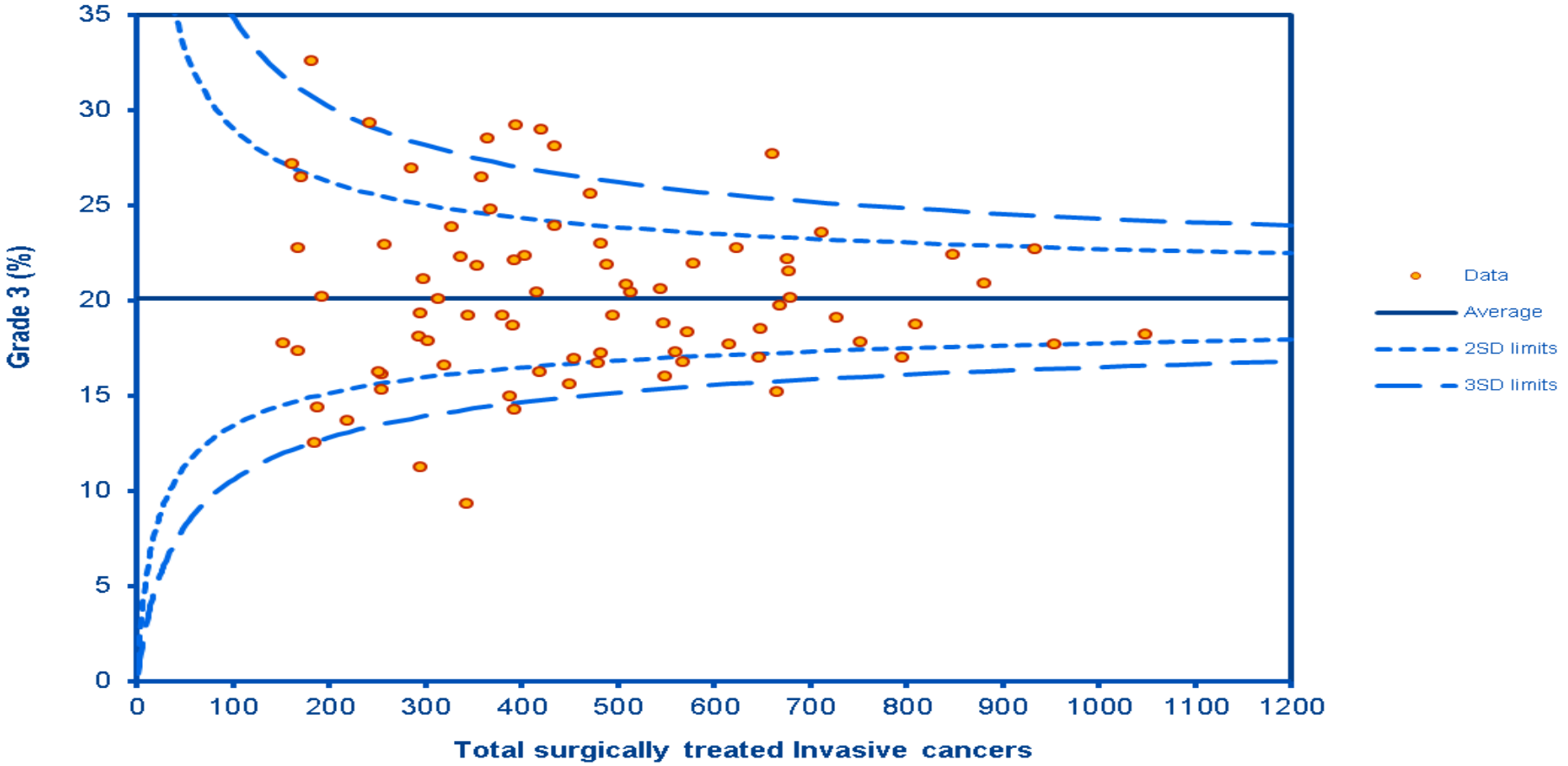
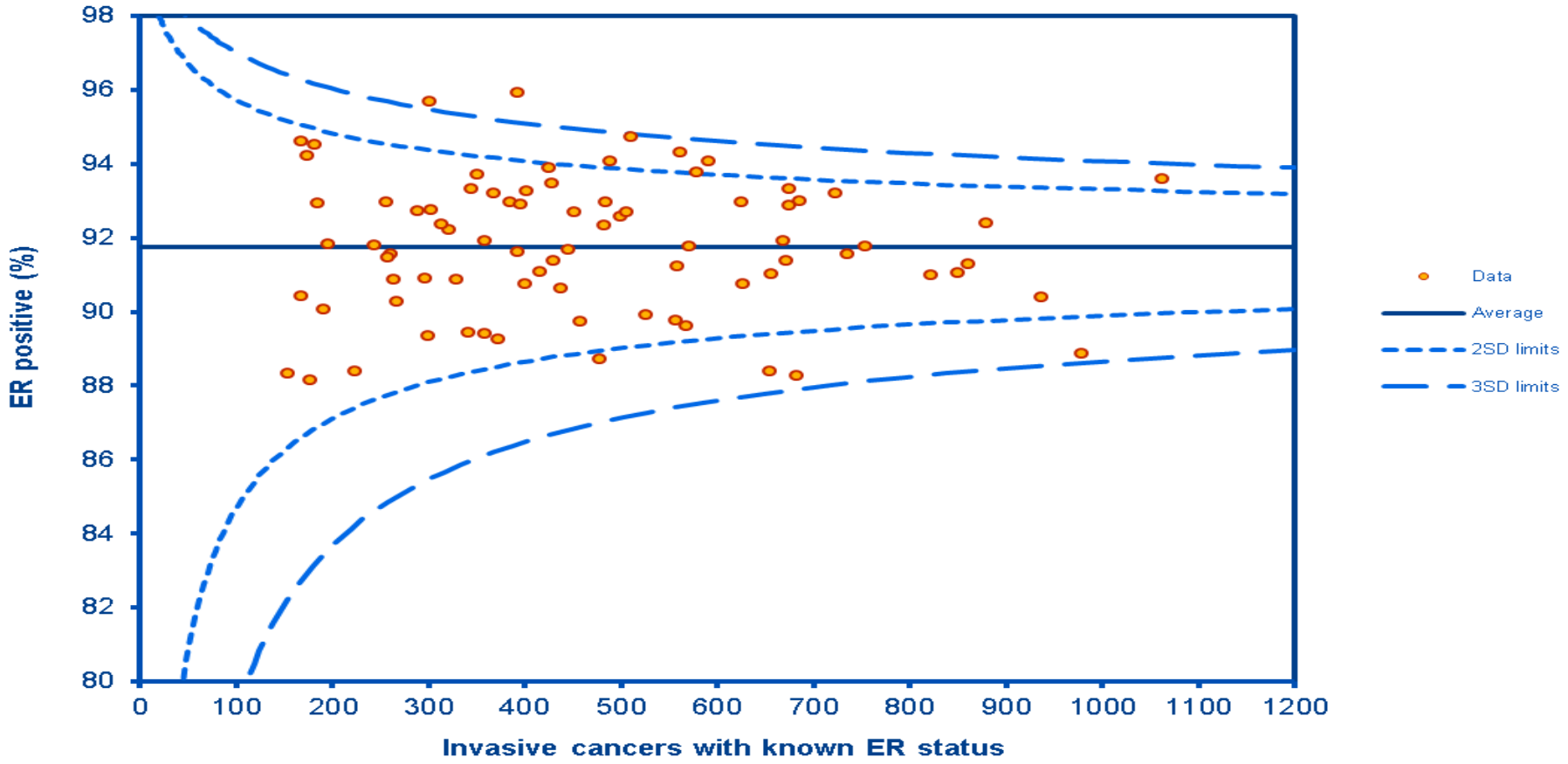


Source: EMQARC

Histological grade: outlier investigation

- Check accuracy of data
- Consider looking at data from different time periods especially if numbers small
- Consider comparing observers EQA grades with the consensus
- Check observers understand system
- Check microscope calibration
- Check fixation (especially if low percentage of grade 3 tumours)
- Consider review of cases with multiple observers



Source: EMQARC

Oestrogen receptor

- Overall positive rate (symptomatic + screening): 82.6% (NEQAS)

Positive rate affected by:

- Fixation (incising surgical specimen and duration)
- Choice antibody and detection system
- Threshold for positivity

Oestrogen receptor positive rate in Nottingham

Positive rate

1999 – 2004:	73% (Hodi J Clin Pathol 2007)
2007	77% (Gill 2012)
Present	83%

Thresholds

- H score 50
- H score 10
- 1%

ER bimodal distribution

88 (26%) H score 0 both core & excision

236 (70%) H score 50+ on both

Hodi et al. J Clin Pathol 2007

Similar results:

Collins Am J Clin Pathol 2005

Nadji Am J Clin Pathol 2005

Oestrogen receptor assessment on core biopsy

- 99% agreement with excision (Hodi 2007)
- 98% agreement with excision (Arnedos 2009)

Repeat on core:

- Negative internal controls
- Unexpected result e.g. negative tubular or classical lobular

Repeat on excision:

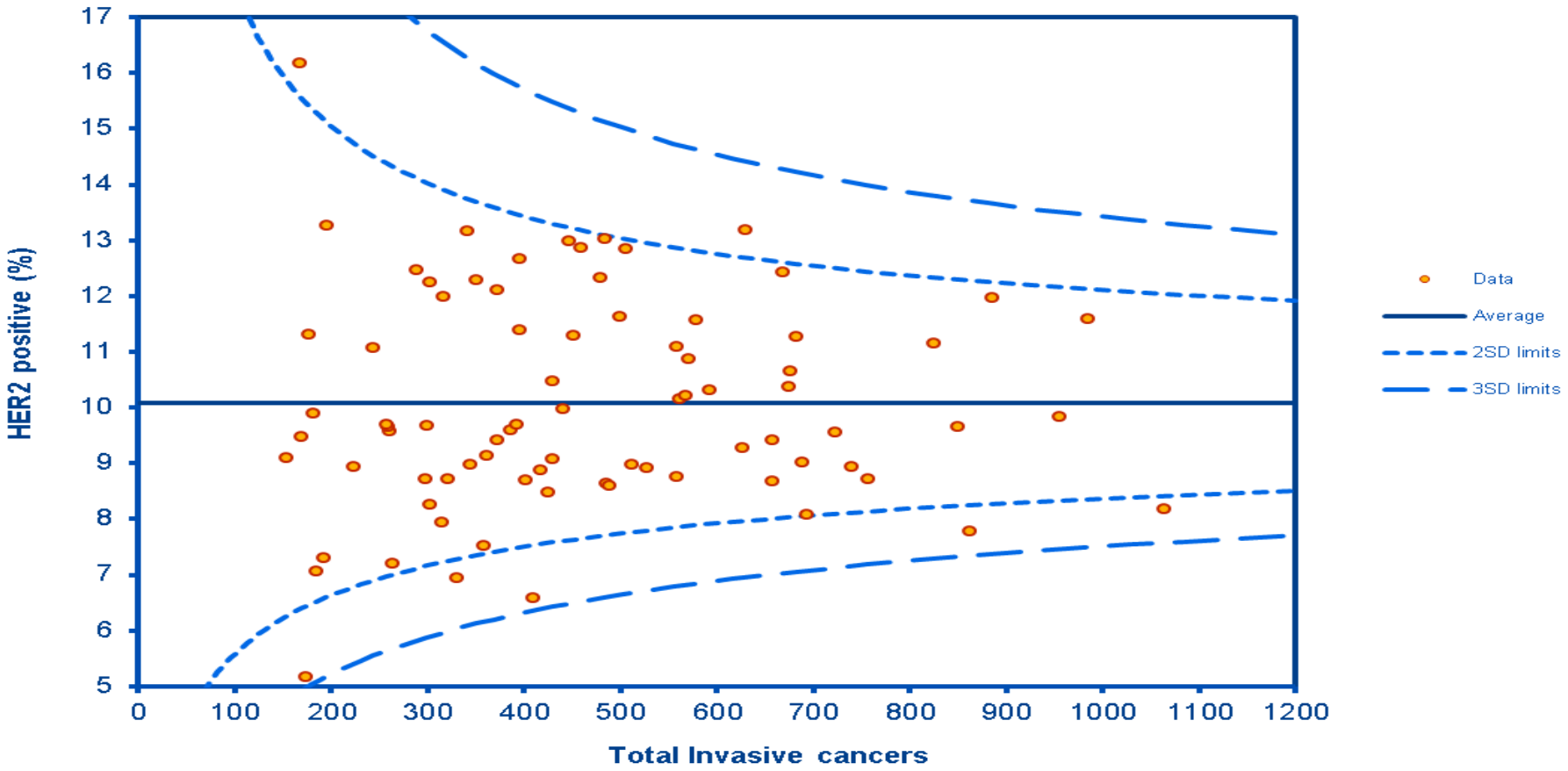
- Weakly positive
- Morphological heterogeneity
- Poor morphology in core e.g. crushing
- Scanty tumour in core

Oestrogen receptor – UK guidelines

- Minimum 300 tumours/year
- Mandatory collecting of data from 2016 (COSD)
- Fixation minimum 6 to 8 hours
- Incise surgical specimens
- Well characterised antibodies
- Well characterised visualisation systems
- NEQAS provides data on Abs etc
- Controls: strong, weak and negative
- Must be part of EQA scheme

Oestrogen receptor – if outlier

- Check data
- Look at other time periods
- Look at positive rate in symptomatic patients
- Review procedures
- Look at NEQAS results
- Look at controls
- Is repeat testing performed when appropriate
- Slide review
- Retesting in separate laboratory
- Ongoing audit



Source: EMQARC

HER2

- Overall positive rate (symptomatic + screening): 14% (NEQAS)

Positive rate affected by:

- Fixation
- Choice antibody and detection system

HER2 assessment on core biopsy

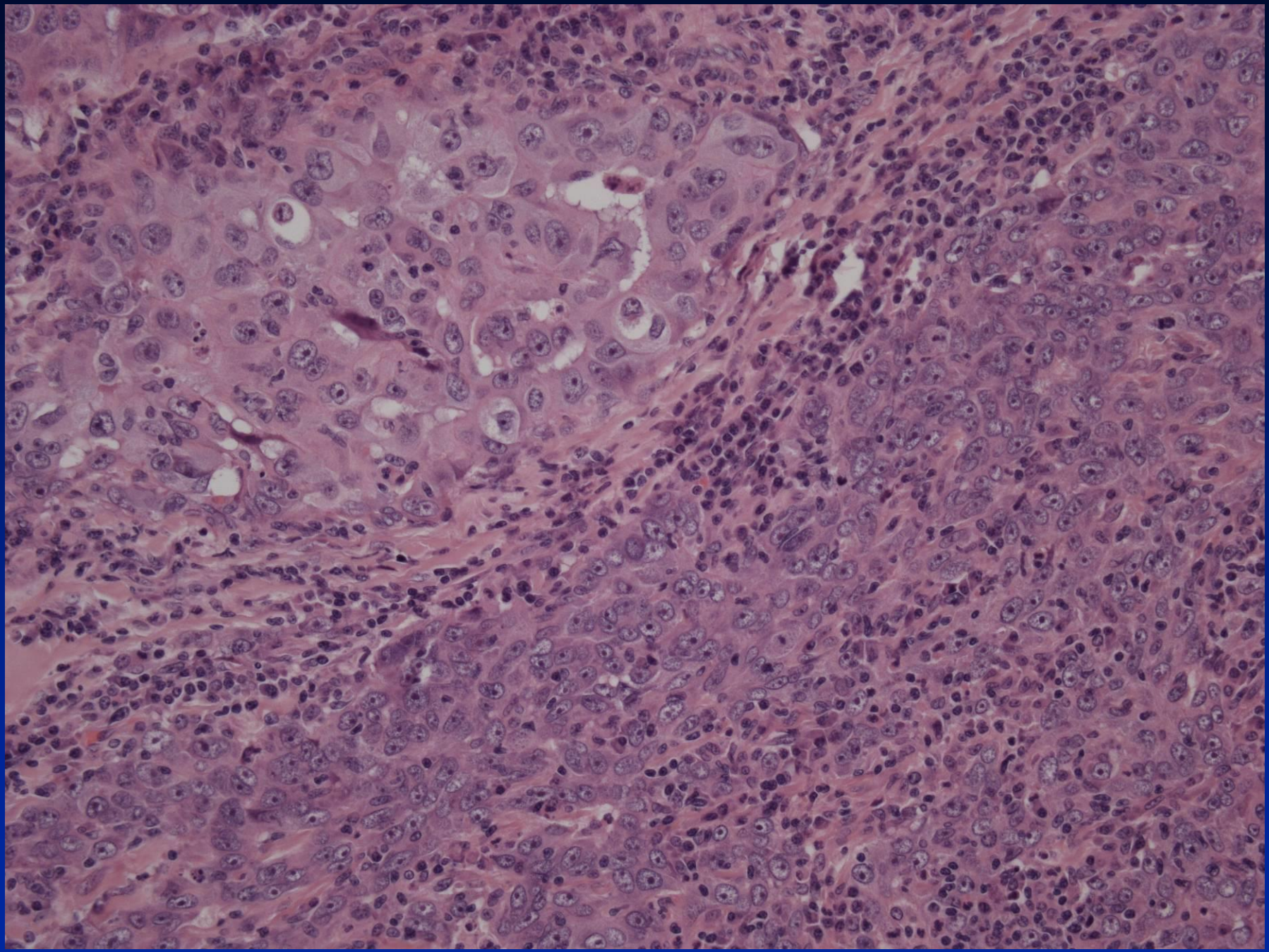
- 98% agreement with excision (Lee 2012)
- 99% agreement with excision (Arnedos 2009)

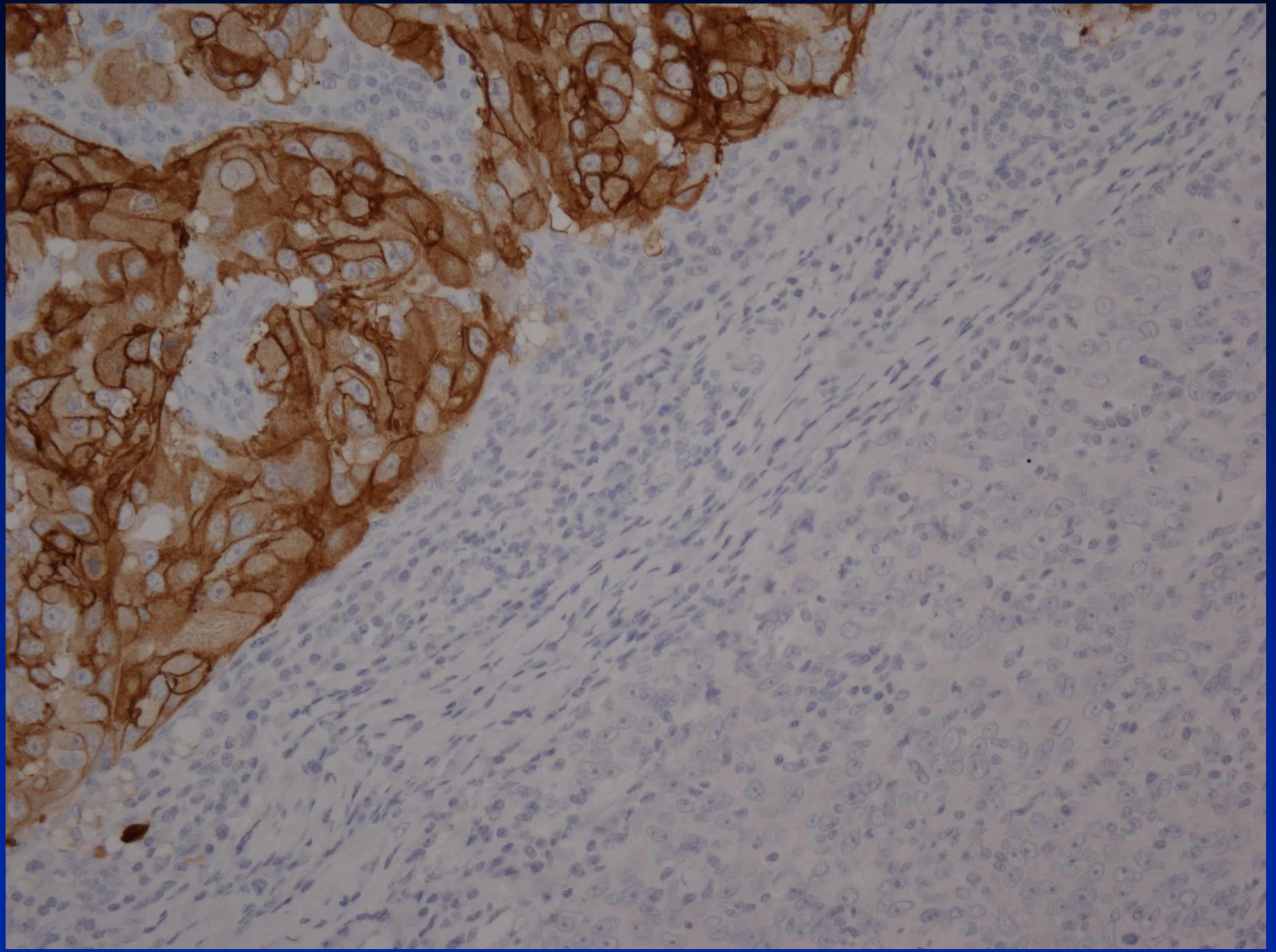
Repeat on core:

- Negative internal controls

Repeat on excision:

- Borderline negative FISH (ratio 1.8 – 1.99)
- Morphological heterogeneity that is not present in the core and the core has been scored as negative
- Poor morphology in core e.g. crushing
- Scanty tumour in core
- Strong HER2 staining < 10% in core





HER2 – UK guidelines

- Minimum 250 tumours/year
- Mandatory collecting of data from 2016 (COSD)
- Fixation minimum 6 to 8 hours???
- Incise surgical specimens
- Well characterised antibodies
- Well characterised visualisation systems
- NEQAS provides data on Abs etc
- Recommend dual ISH probe (HER2 & chr 17)
- Controls: 0, 1+, 2+, 3+
- Must be part of EQA scheme

HER2 – if outlier

- Check data
- Look at other time periods
- Look at positive rate in symptomatic patients
- Review procedures
- Look at NEQAS results
- Look at controls
- Is repeat testing performed when appropriate
- Slide review
- Retesting in separate laboratory
- Ongoing audit