PALGA

The nationwide network and registry of histo- and cytopathology in the Netherlands

Introduction of Synoptic Reporting (SR) and experiences with big-data

Carrefour Pathology 2017, Paris

22 November 2017

Paul Seegers, Advisor, national pathology protocols,

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Outline

PALGA

- Introduction

Development of SR in The Netherlands

- What is it and why is it important?
- Implementation of Synoptic Reporting
- What do we gain: big-data !
- Where are we today ?

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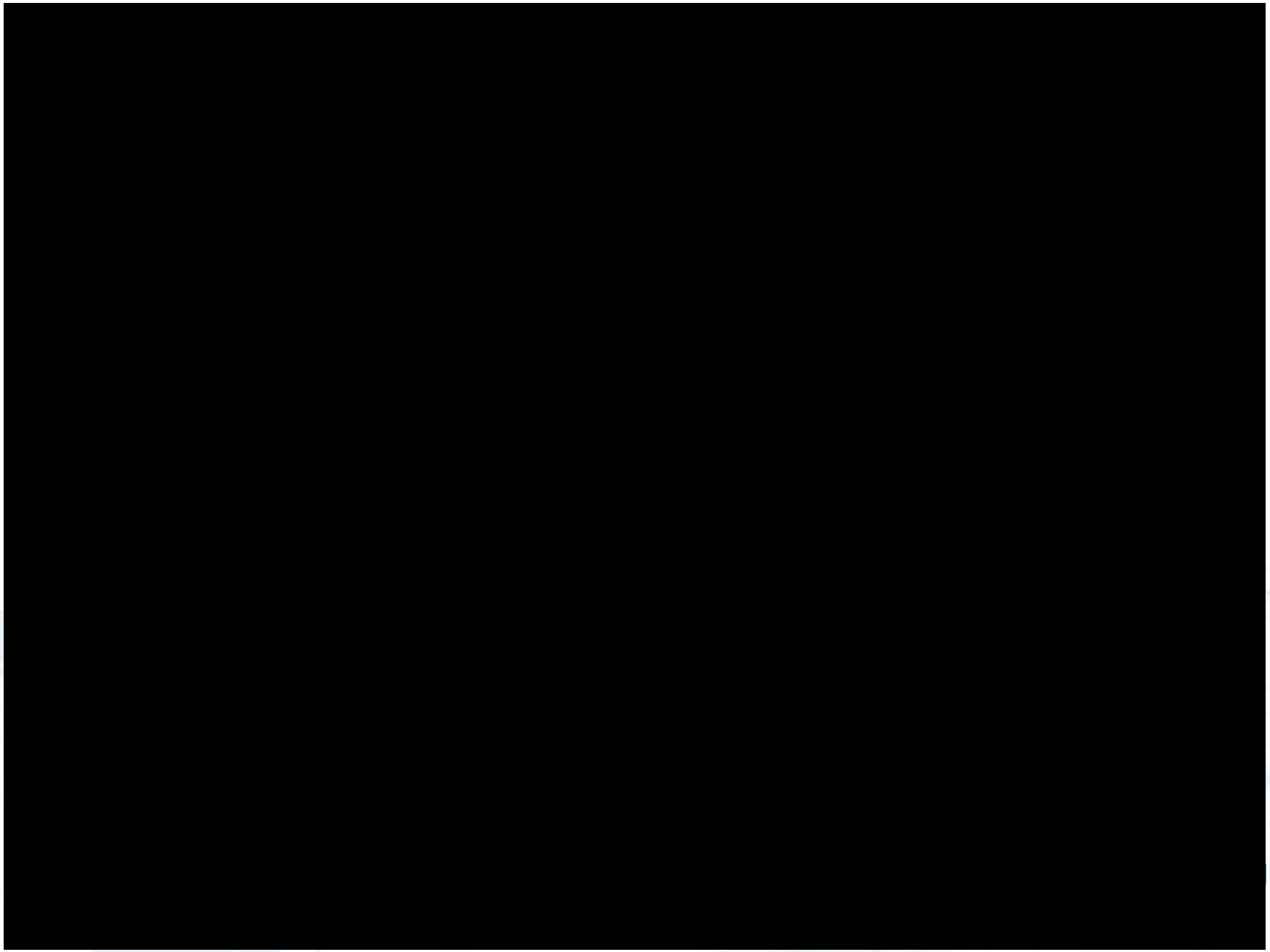
Introduction



Introduction

- Nationwide network and registry pathology
- Founded in 1971 with a few laboratories
- Since 1991 national coverage (> 65 laboratories)
- Central anonymized databases
- Decentral servers in all pathology laboratories (48 laboratories per 1/1/17)
- > 71 million pathology reports from 12 million individuals
- > 2 million new entries per year
- 403 national and international publications based PALGA data(per 31/12/16)
- 25 National pathology protocols for Synoptic Reporting
- Government funding

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What is Synoptic Reporting

REPORTING LEVEL	LEVEL 1	LEVEL 2	LEVEL 3	LEVEL 4	LEVEL 5	LEVEL 6
	Basic	Most common		Cutting edge		
DESCRIPTION	Narrative No CAP content Single text field data	Narrative No CAP content Single text field data	Level 2+ Synoptic-like structured format	Level 3+ Electronic reporting tools using drop-down menus	Level 4+ Standardized reporting language Data elements stored in discrete data fields	Level 5+ Common data and messaging standards with ckeys, SNOMED CT or other encoding

Srigley J, J.Surg. Oncol 2009

- Complete
- Up to date (guidelines, WHO classifications)
- Complies with ICCR minimal dataset
- Increasing quality
- Scientific research / Benchmarking / Population screening

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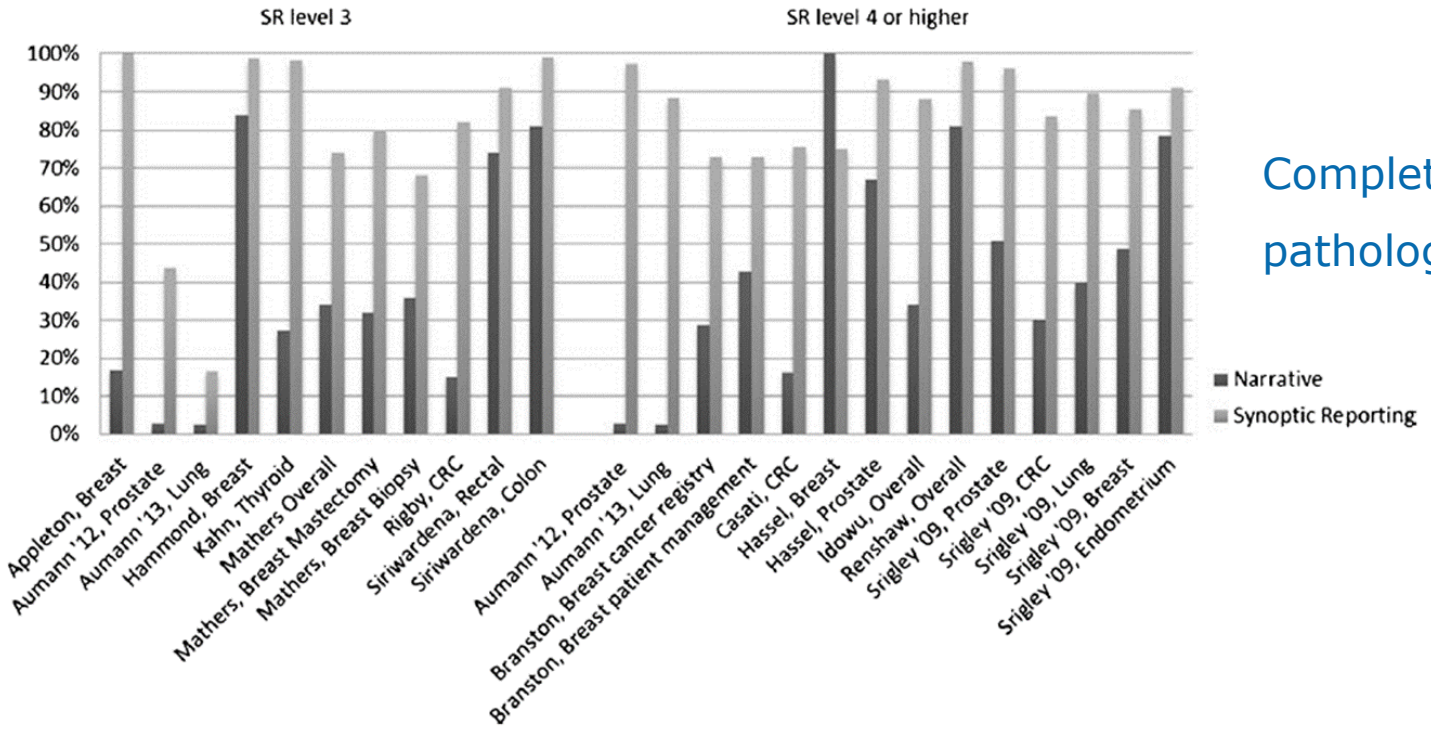
What is Synoptic Reporting and why is it important ?

Virchows Arch (2016) 468:639–649
DOI 10.1007/s00428-016-1935-8

REVIEW AND PERSPECTIVES

The effects of implementing synoptic pathology reporting in cancer diagnosis: a systematic review

Caro E. Sluijter[1,2] · Luc R. C. W. van Lonkhuijzen[3] · Henk-Jan van Slooten[2,4] · Iris D. Nagtegaal[1,2] · Lucy I. H. Overbeek[2]



Completeness pathology report

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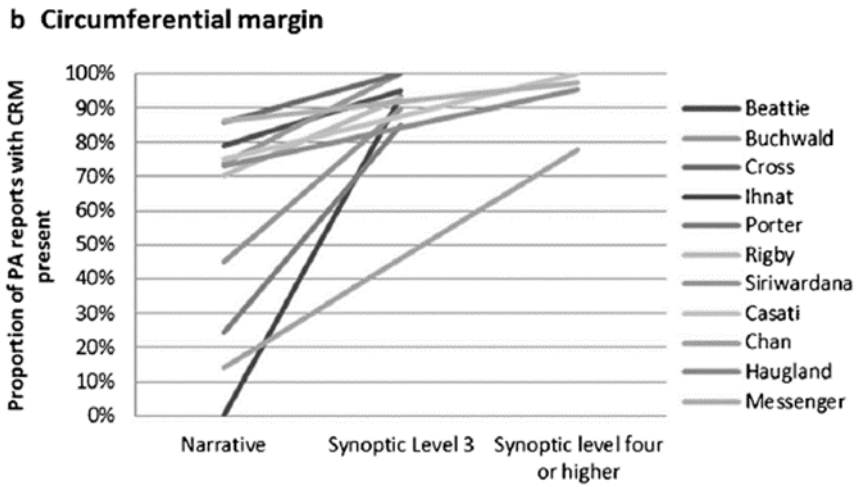
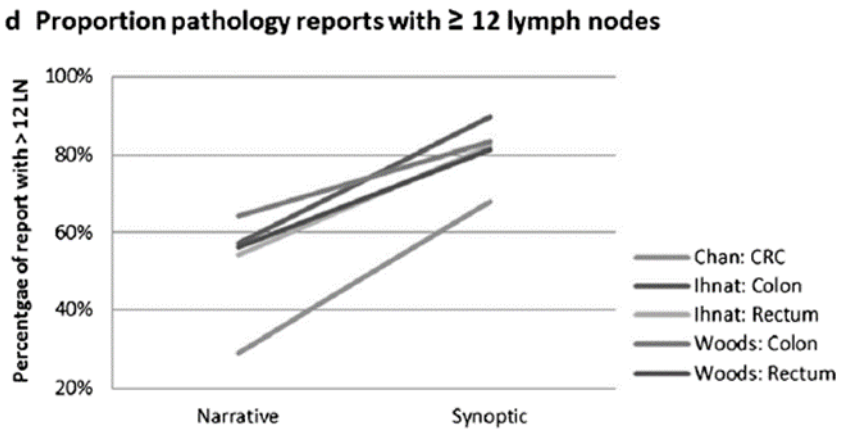
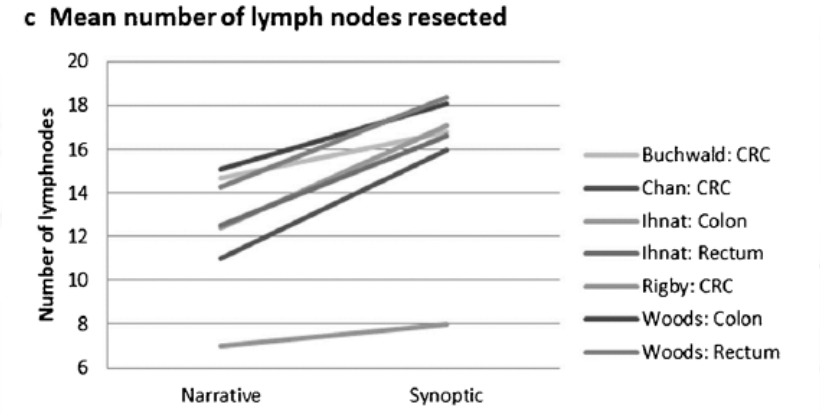
What is Synoptic Reporting and why is it important?

Important factors in colorectal cancer: increased reporting







Sluiter CE, Virchows Arch 2016

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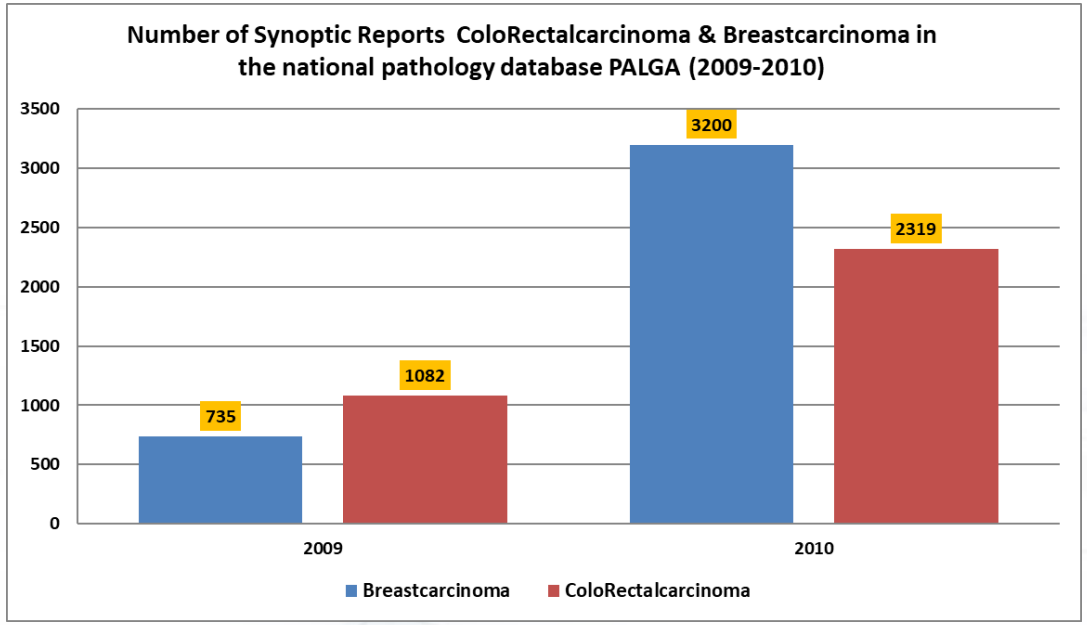
Implementation of Synoptic Reporting

- Development of de PALGA Protocol Module (PPM) from 2008
- First national availability at Q4 2009
- 2 national protocols, CRC & breast cancer
- 2010: in 59% of the labs both protocols were (not always) used



Q4 2012: only 4 nationals potocols where available !

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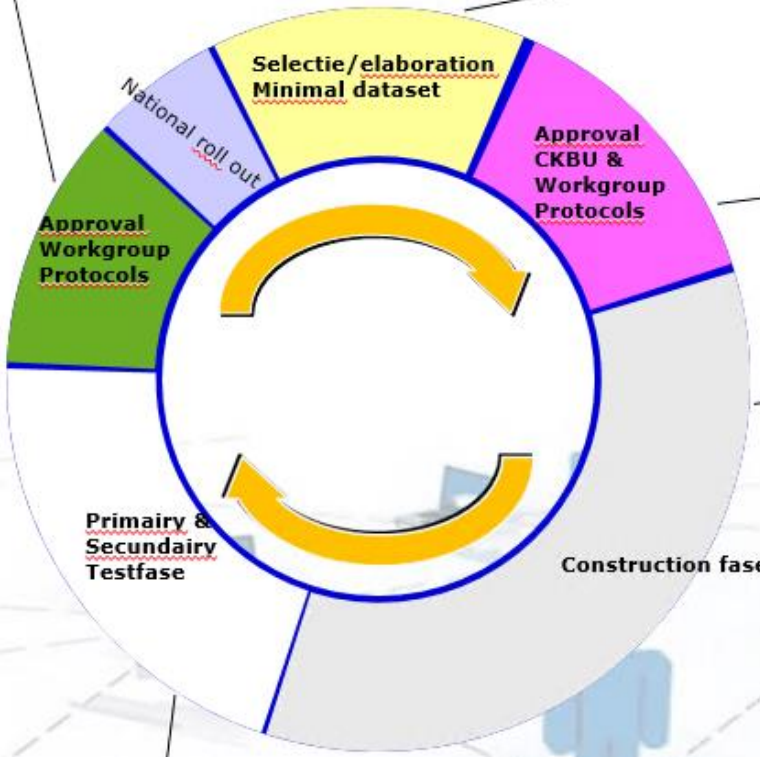
Implementation of Synoptic Reporting

- Present to NVVP



- IKNL guidelines
- Pathologist guidelinecommittee
- Thesauruscommittee
- CMDP / Wcyt (sub committiees)

- Minimal dataset for guidline
- Optional choices
- Complete functional design

- Modular building
- Headings uniform
- Uniform units (cm / mm)
- PV Structure and Conclusion
- TNM / FIGO (Other)
- Diagnosis Codes (SNOMED-2)

- Mutations and bugfixes
- Testlaboratories
- Documentation

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Implementation of Synoptic Reporting

Development of de PALGA Protocol Module (PPM), example CRC protocol

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Opslaan | Annuleren | Versturen
Feedback | Controle

Rapport Nummer: T99-TEST
Patient Naam: TestTestTest

Patient Nummer: 1234567890
Geslacht: O
Geboorte Datum: 24/07/1989

protocol versie 3.0.61
ColonRectumcarcinoom

- Macro
- Tumor1
- Lymf Overig
- Lynch
- Moleculair
- Immuno
- Aanvulling

Microscopie (1ste) tumor

Respons op eerdere (neo-adjuvante) therapie: (•) geen regressie ( ) partiele regressie

Type (1ste) tumor (WHO): (•) adenocarcinoom ( ) adenosquameus carcinoom ( ) NET/NEC ( ) mucineus carcinoom ( ) medullair carcinoom ( ) kleincellig carcinoom ( ) zegelringcelcarcinoom ( ) ongedifferentieerd carcinoom ( ) overige

Differentiatiegraad: ( ) goed / matig (•) weinig / niet ( ) niet te beoordelen

Diepste tumordoorgroei: ( ) intramucosaal / lamina propria (•) pericolisch (vet)weefsel ( ) submucosa ( ) peritoneum ( ) muscularis propria ( ) andere organen

Angio-invasie: [x] niet aangetroffen [ ] lymfvat invasie [ ] intramurale veneuze invasie [ ] extramurale veneuze invasie

Tumor budding: (•) laag (Bd1) (0-4) ( ) hoog (Bd3) (10 of >10) ( ) intermediair (Bd2) (5-9) ( ) niet beoordeelbaar

Lymfocytaire infiltratie: ( ) ja ( ) nee

Dichtstbijzijnde darmsnijvlak: (•) vrij ( ) niet vrij ( ) niet te beoordelen ( ) exact

PV | Conclusie | Informatie

TNM colorectaal carcinoom 5de editie
pTis: invasie beperkt tot lamina propria
pT1: invasie in de submucosa
pT2: invasie in de muscularis propria / lamina muscularis
pT3: invasie in de subserosa / pericolisch (vet)weefsel
pT4: doorbraak van de serosa en/of doorgroei in aangrenzende structuren
N0: geen lymfkliermetastasen
N1: 1 t/m 3 lymfkliermetastasen
N2: > 3 lymfkliermetastasen
M0: geen metastasen op afstand
M1: metastasen op afstand

Definitie van Tumordeposits (TNM 5, 1997):
Haardvormige tumorlokalisaties in het pericolische (vet-)weefsel zonder histologisch herkenbare (rest van een) lymfklier.
Een tumordeposit wordt als een positieve lymfklier geclassificeerd als deze haard 3 mm of groter is.
Een tumordeposit van < 3 mm wordt beschouwd als discontinue groei en dus als (onderdeel van) pT3.

Literatuur (advies CBU):
Assessment of Serosal Invasion and Criteria for the Classification of Pathological (p) T4 Staging in Colorectal Carcinoma: Confusions, Controversies and Criticisms; Cancer 2011

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Implementation of Synoptic Reporting

Development of de PALGA Protocol Module (PPM), example CRC protocol

(level 6+ protocol, generates conclusion, TNM/FIGO and SNOMED-2 codes)

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PV | Conclusie | Informatie

Conclusie
Hemicolectomie rechts: type tumor (WHO): adenocarcinoom; differentiatiegraad: weinig / niet; maximale diameter tumor 2,3 cm; diepste tumor doorgroei: pericolisch (vet)weefsel; eerdere neo-adjuvante therapie: chemotherapie, respons op eerdere neo-adjuvante therapie: geen regressie.
Dichtstbijzijnde darmsnijvlak vrij (afstand <= 0,1 cm); retroperitoneaal klievingsvlak vrij (afstand 0,2 cm).
Angio-invasie: geen lymfvat invasie of extramurale veneuze invasie aangetroffen.
Aantal lymfklieren: 10 waarvan met metastasen: 0.

TNM classificatie (5e editie): ypT3N0.

De afwezigheid van MLH1 en PMS2 in de tumorcelkernen maakt het ontstaan van de tumor als gevolg van een defect in de DNA mismatch repair waarschijnlijk en is reden om nader onderzoek naar aanleg voor erfelijke darmkanker en daarmee verwijzing naar een klinisch geneticus te overwegen.
NB Het betreft een hoog risico stadium II tumor.

Diagnoseregel(s)
colon*rechts*resectie*systeem*adenocarcinoom*therapie effect*snijvlak vrij lymfklier*mesocolon*excisie*systeem*geen maligniteit

Validated

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Implementation of Synoptic Reporting

Biopsy:
Colon biopsy (2 protocols) (population screening for bowel cancer)
Endometrial biopsy
Breast biopsy
Lung biopsy
Urinary bladder biopsy
Cervical biopsy
Pancreas biopsy
Prostate biopsy

Molecular testing

DDF: > 10,900 !

Cytology:
CRIS4 (population screening for cervical cancer)
Urine cytology (Paris System)
Thyroid FNA

Resections:
Colon-Rectal
Breast resection
Placenta
Endometrial resection
Bladder resection, TUR
Ovaries
Cervix Uteri resection
Lung resection
Oesophagus-gastric resection
Kidney resection
Pancreas resection
Prostate resection
Melanoma (skin)
Melanoma (eye)
Squameus cell carcinoma (skin)
Testis

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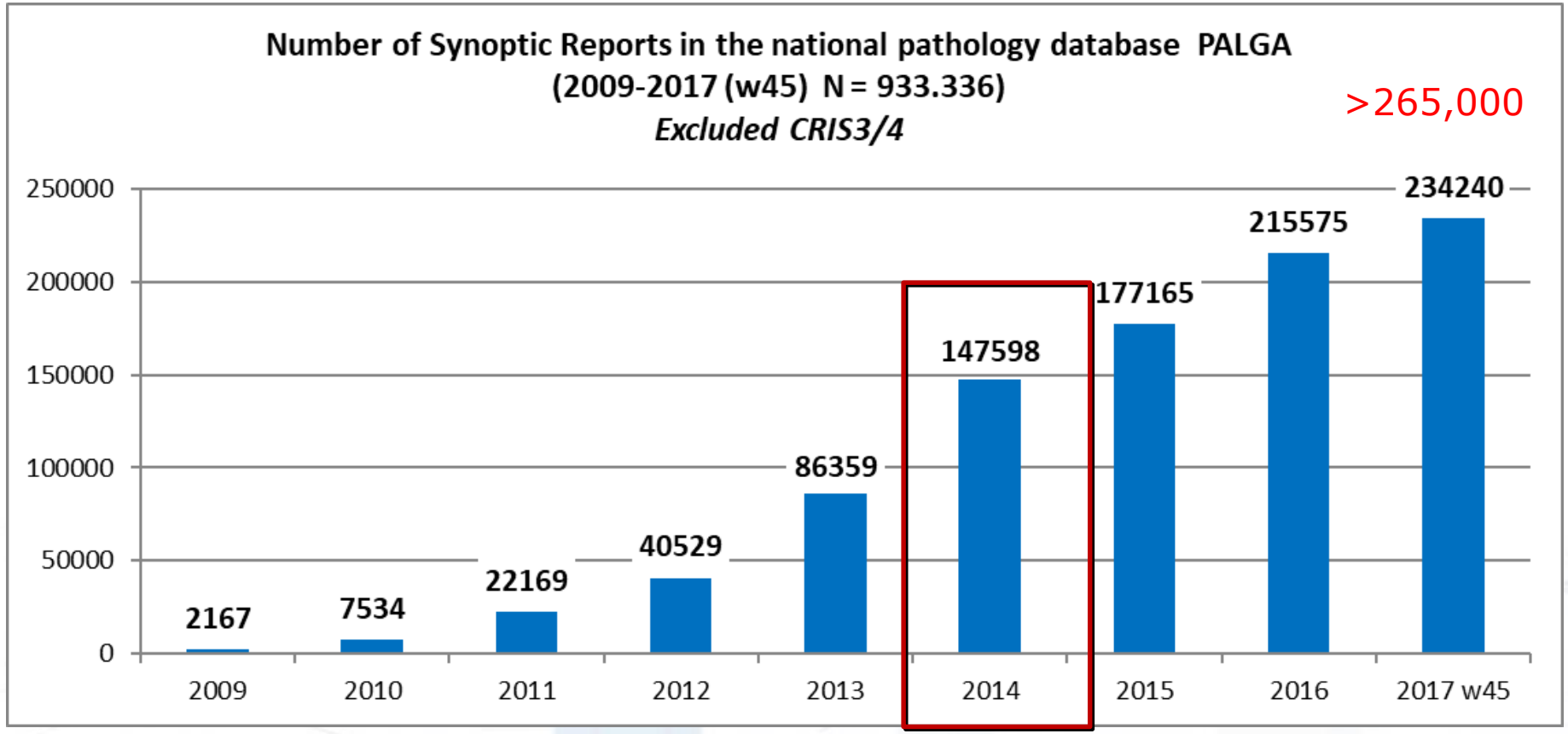
Implementation of Synoptic Reporting



20-25% daily workload of a pathologist is done with Synoptic Reporting

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  Highlights from studies:

  - Comparing study NR en SR for colon and breast
  - Standardisation HGD adenomas in population screening bowel cancer with E-learning
- Where are we today ?

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Insights using Synoptic Reporting

Study design – colorectal cancer study

Submitted for publication

- Narrative Report (NR) (N= 32,079) versus Synoptic Report (SR) (N= 24,237) 2009-2014
- To detect ongoing trends: Reference group (N = 17,489) 2007-2008
- Completeness (parameter/total), according to guidelines
- Quality of pathology: indicators (Lymph node count, CRM EMVI)
- Stage II colon cancer: selection and treatment
- Overall survival NR versus SR

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Insights using Synoptic Reporting

Completeness (parameter/total), according to guidelines

	Reference	NR	SSR	Crude OR (95%CI)	Adjusted OR (95%CI)	p-value Reference vs NR	p-value NR vs SSR
Overall completeness	90.6%	89.8%	95.8%	2.58 (2.40-2.78)	2.33 (2.15-2.52)	0.006	< 0.0001
Parameter specific completeness							
Histological type	100%	100%	100%	NA	NA	NA	NA
Histological grade	96.9%	92.1%	95.8%	1.96 (1.80-2.14)	1.97 (1.79-2.18)	< 0.0001	< 0.0001
Invasion depth	100%	99.9%	100%	NA	NA	0.20	0.07
Nodal status	98.4%	99.0%	99.7%	3.38 (2.61-4.39)	2.98 (2.24-3.96)	< 0.0001	< 0.0001
Lymph node count	98.8%	99.5%	99.9%	6.24 (3.83-10.2)	4.56 (2.69-7.73)	< 0.0001	< 0.0001
EMVI	-	88.9%	96.9%	3.86 (3.55-2.41)	2.17 (1.98-2.38)	NA	< 0.0001
CRM	75.5%	84.9%	96.1%	4.34 (3.73-5.06)	3.63 (3.06-4.30)	< 0.0001	< 0.0001
Quality indicators							
At least 10 lymph nodes investigated	63.3%	77.3%	89.3%	2.46 (2.34-2.58)	1.77 (1.68-1.87)	< 0.0001	< 0.0001
Presence of EMVI	-	16.1%	17.1%	1.08 (1.03-1.13)	1.08 (1.02-1.14)	NA	0.003
Negative CRM	88.5%	94.3%	95.5%	1.27 (1.08-1.50)	1.13 (0.94-1.37)	< 0.0001	0.004

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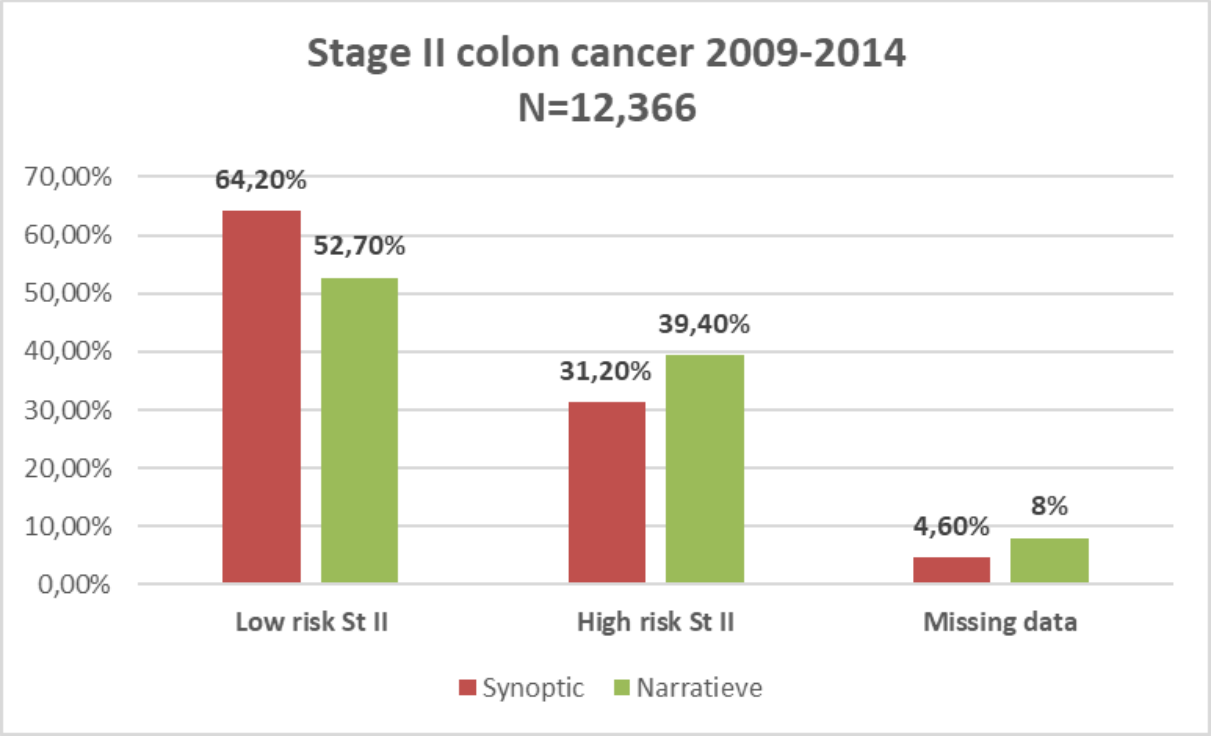
Insights using Synoptic Reporting

Stage II colon cancer



- Adjuvant chemotherapy for high risk:
  - More in SR group: 19,6% versus 15,1% in NR group
  - Overall survival in this group: 65,0 % versus 62,1% (NR), p=0,026

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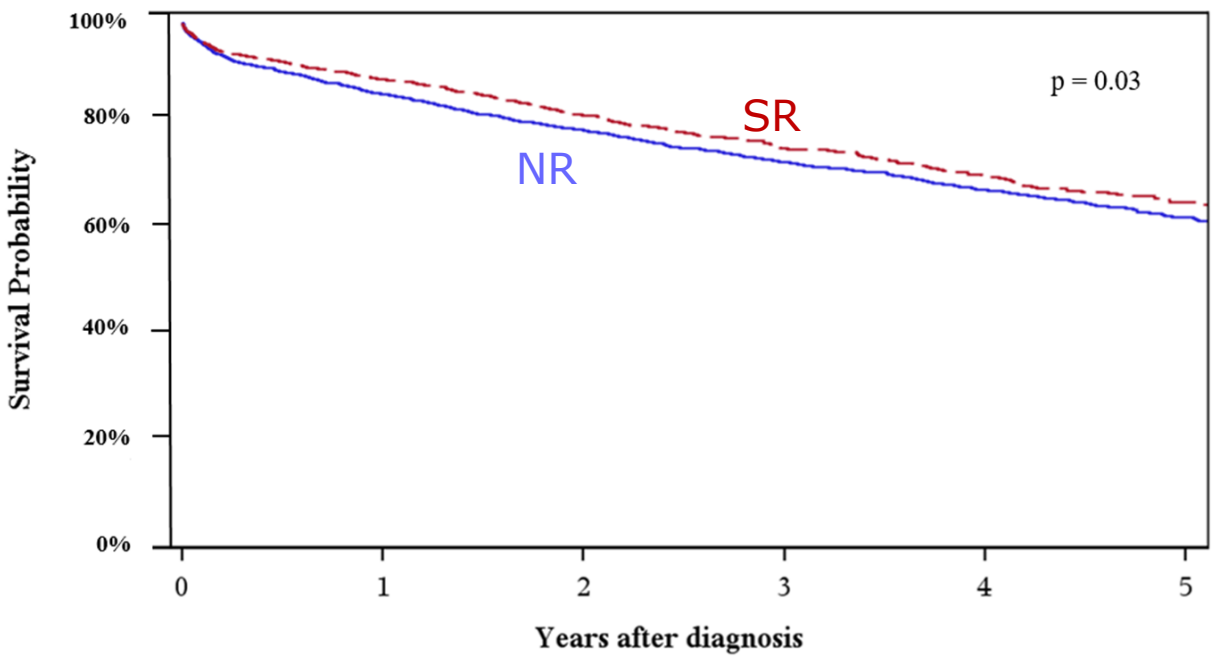
Insights using Synoptic Reporting

Overall survival difference



64.9% versus 62.2%, $p < 0.0001$

Adjustment for stage, grade, neoadjuvant therapy, age, gender, year of diagnosis, location of the tumor, histological type and type of pathology lab
HR = 0.94, 95% CI 0.90-0.97

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Insights using Synoptic Reporting

Same study design – breast cancer study

Submitted for publication

- Narrative Report (NR) (N= 42,682)versus Synoptic Report (SR) (N= 31,284) 2009-2014
- To detect ongoing trends: before (N=21,741) 2007-2008
- Completeness (parameter/total), according to guidelines
  - Increase in completeness overall (9 parameters) from 91.5% to 94.4%
- Quality of pathology: indicators
- HER2: Changes in treatment ; HER2 and treatment
- Overall survival

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Insights using Synoptic Reporting

Changes in treatment

	No	Yes	X2-value (NR vs SR)	p-value NR vs SR	OR NR vs SR adj voor incjr
Chemotherapy			**38.2**	**<0.0001**	**1.40 (1.32-1.50)**
BEFORE	4660 (67.7%)	2223 (32.3%)			
NR	8531 (65.0%)	4599 (35.0%)			
SR	5263 (60.9%)	3386 (39.1%)			
Hormonal therapy			**0.08**	**0.76**	**1.00 (0.94-1.07)**
BEFORE	3209 (46.6%)	3674 (53.4%)			
NR	5139 (39.1%)	7991 (60.9%)			
SR	3368 (38.9%)	5281 (61.1%)			
Radiotherapy			**103.43**	**<0.0001**	**0.62 (0.58-0.66)**
BEFORE	5209 (75.7%)	1674 (24.3%)			
NR	9359 (71.3%)	3771 (28.7%)			
SR	6701 (77.5%)	1948 (22.5%)			
Targeted therapy			**5.80**	**0.016**	**1.20 (1.07-1.33)**
BEFORE	6382 (92.7%)	501 (7.3%)			
NR	12049 (91.8%)	1081 (8.2%)			
SR	7856 (90.8%)	793 (9.2%)			

HER2 and treatment

In case of a HER2 negative tumor

- NR: 0,25 % are still treated
- SR: 0,16% are still treated

In case of a HER2 positive tumor

- NR: 58,7% are treated
- SR: 69,2% are treated

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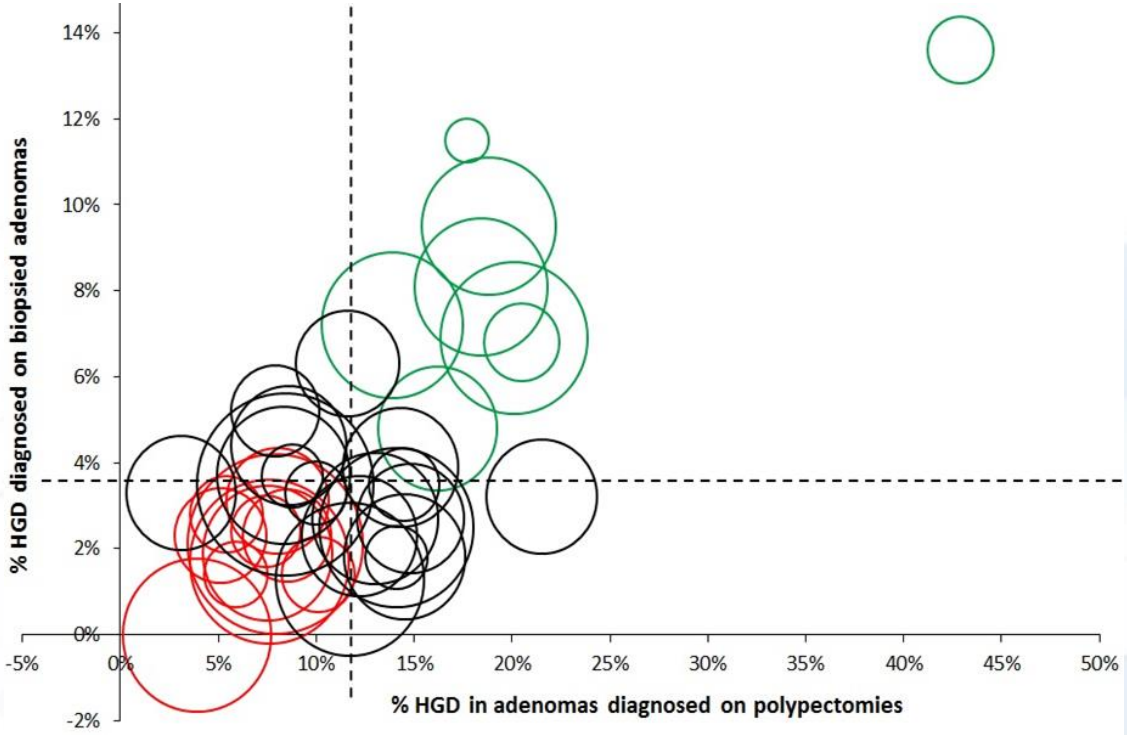
Insights using Synoptic Reporting

Histopathology 2016 DOI: 10.1111/his.12923

Interlaboratory variability in the grading of dysplasia in a nationwide cohort of colorectal adenomas

Chantal C H J Kuijpers,[1,2,3] Caro E Sluijter,[2,4] Jan H von der Thüsen,[5,6] Katrien Grünberg,[6,7] Martijn G H van Oijen,[2,8] Paul J van Diest,[1] Mehdi Jiwa,[1,3] Iris D Nagtegaal,[2,4] Lucy I H Overbeek[2] & Stefan M Willems[1,2]



Before population screening

32,291 adenomas in 2013

37 laboratories

Standardisation is necessary !

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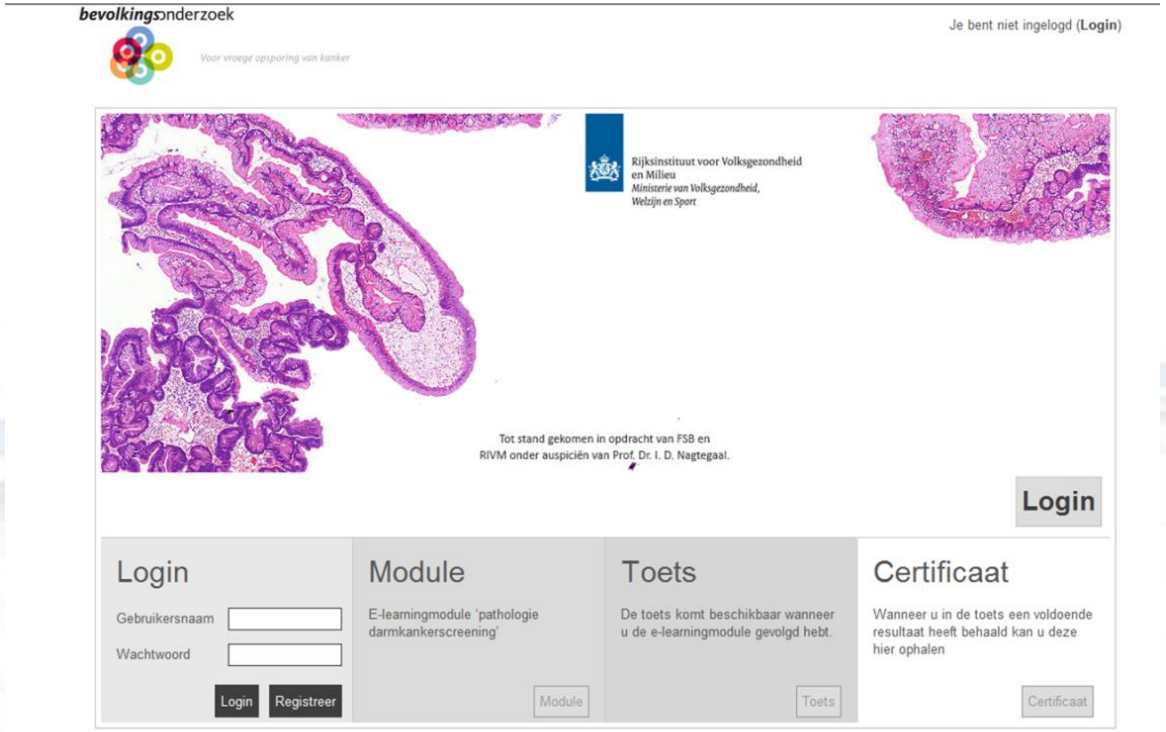
Insights using Synoptic Reporting

Population screening for bowel cancer started in 2014

E-learning was introduced



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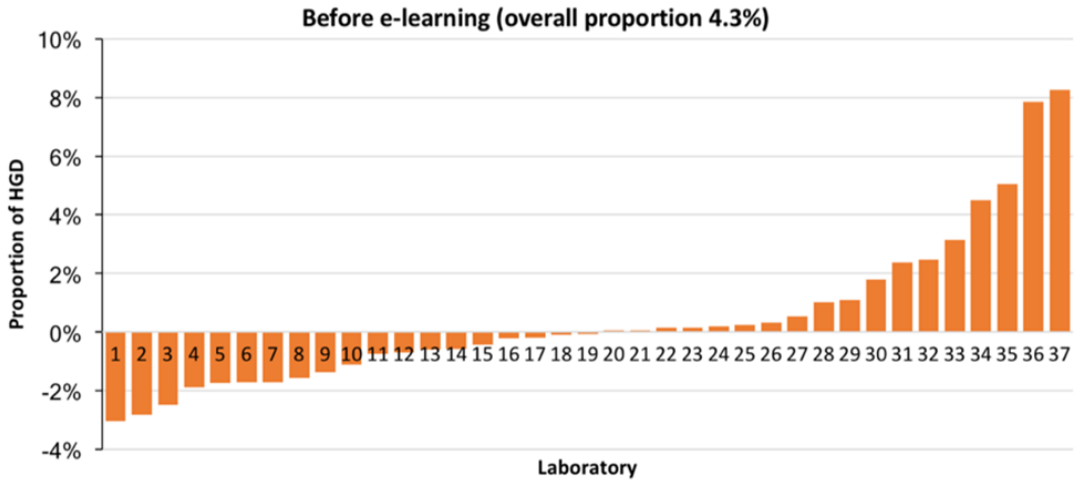
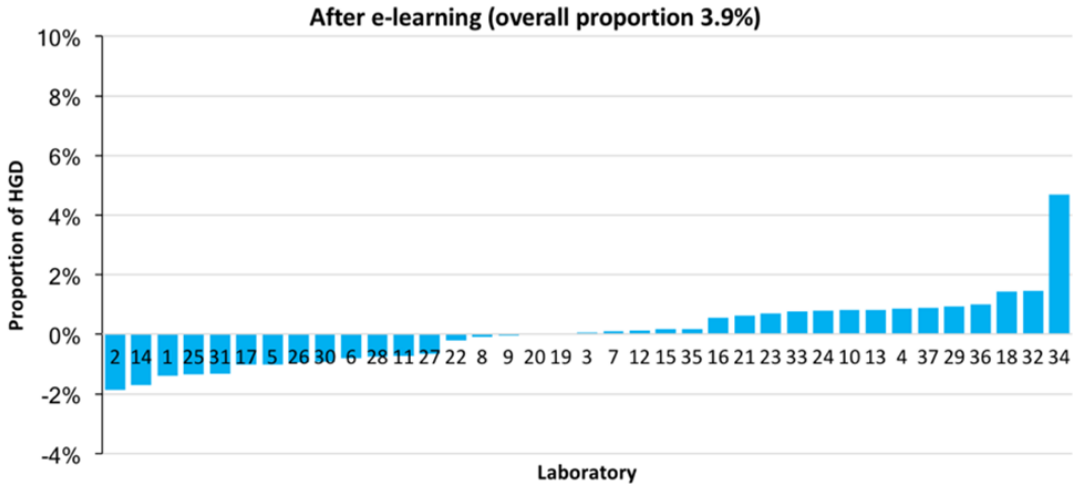
Insights using Synoptic Reporting

Interlaboratory variation of High Grade Dysplasia in adenomas diagnosed before implementation of the E-Learning(N=12,614) compared to adenomas diagnosed after implementation of the E-learning (N=43,741)





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Where are we today

Trial-alert SUBITO - trial

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Opslaan | Annuleren | Versturen | Feedback | Controle

Rapport Nummer: T17-12345 | Patient Naam: Rick

Patient Nummer: Patient Demo
Geslacht: M
Geboorte Datum: 12/10/1982
protocol versie 2.0.44
Mammacarcinoom

Macro | Tumor 1 | Receptor 1 | OKD | Overige | Aanvulling

Zijdigheid: links / rechts / niet vermeld
MARI-klier procedure (MKP): ja / nee

OKD

Partiele okselklierdissectie: ja / nee
Gewicht okselklierdissectie (gr):
SWK verricht: nee / ja, negatief / ja, metastasen aangetroffen / ja, geen lymfklieren aangetroffen / ja, geisoleerde tumorcellen aangetroffen / ja, voorafgaande aan de neo-adjuvantie therapie

Lymfklieren OKD

Aantal lymfklieren OKD: 5
Eerdere therapie: ☑ geen ☐ radiotherapie ☐ thermoablatie ☐ chemotherapie ☐ hormonale therapie ☐ onbekend
Aantal lymfklieren OKD met macrometastase > 2,0 mm: 4
Diameter grootste macrometastase OKD (mm):
Extranodale groei OKD: niet aangetroffen / ja, gering / matig en geen bedreiging van het snijvlak / ja, matig / massaal met mogelijk bedreiging van het snijvlak
Aantal lymfklieren OKD met micrometastase > 0,2 mm en <= 2,0 mm: 1
Aantal lymfklieren niet-OKD:
Detectie methode OKD: cytokeratine IHC / PCR
Topklier: negatief / positief / niet gemarkeerd
Lokalisatie topklier: mediaal / lateraal / Rotter
Clustervorming lymfklieren: aanwezig / niet aanwezig

Indien patiënt stadium III mamacarcinoom heeft (T0-2N2M0, T3N1-2M0, T4N0-2M0, TxN3M0), komt hij waarschijnlijk in aanmerking voor een BRCA1-like test. Bij een positieve test of BRCAg mutatie drager kan hij in mogelijk behandeld worden met hoge dosis chemotherapie gevolgd door stamceltransplantatie of chemotherapie gevolgd door een PARP-remmer. Voor informatie, neem zo spoedig mogelijk contact op met subito@nki.nl (zie ook clinicaltrials.gov NCT02810743).

PV | Conclusie | Informatie

Gebaseerd op de richtlijn Mammacarcinoom Versie 2.0 (2012)

Klinische gegevens en macroscopie
Preparaat: lumpectomie
Zijdigheid: links
Eerdere niet complete excisie: nee
Lokalisatie tumor: mediale bovenkwadrant
Eerdere therapie: geen

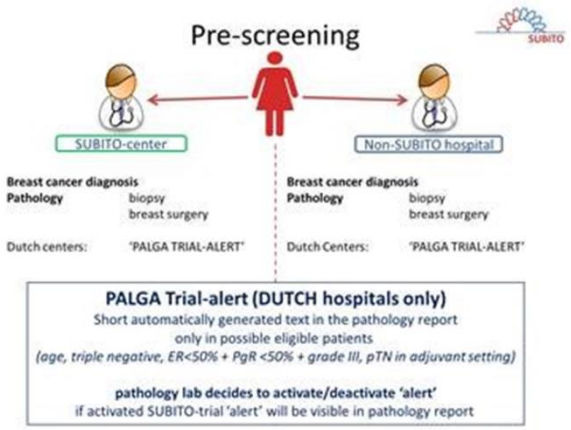
Tumor aanwezig
Dominante tumor: invasief carcinoom zonder CIS
Type invasieve tumor (WHO): Invasief carcinoom NST (voorheen infiltrerend ductaal carcinoom nos)
Afmeting dominante tumor: 5,3 cm
Tubulaire differentiatie: >75 %
Mitosen per 2mm2: 2
Kernpolymorfie: 1
Graad volgens Bloom Richardson: I
Kenmerken van T4 mammacarcinoom: geen

Snijvlakken 1e invasieve tumor
Snijvlak: meer dan focaal niet vrij

Receptoren 1e invasieve tumor
Oestrogeen receptor: negatief
Percentage Oestrogeen receptor positieve tumorcellen: 2%
Progesteron receptor: negatief
Percentage Progesteron receptor positieve tumorcellen: 5%
HER2 Immunohistochemie: negatief (score 0)
HER2 FISH: niet verricht
HER2 CISH / SISH: niet verricht
HER2 PCR: niet verricht
Status HER2: negatief

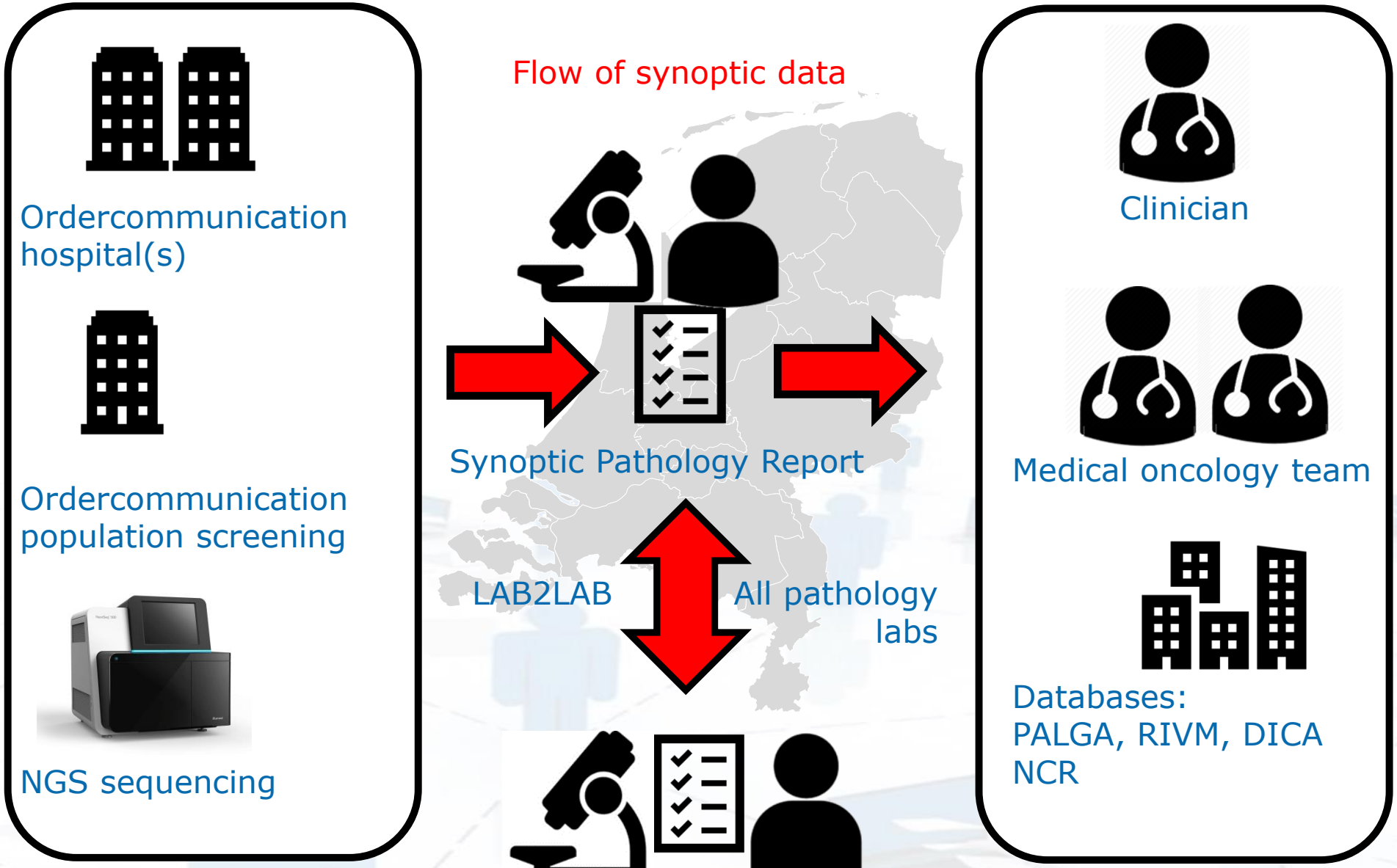
Okselklierdissectie
Zijdigheid: links
MARI-Klier Procedure (MKP): nee
SWK verricht: nee
Eerdere therapie: geen
Aantal lymfklieren OKD: 5
Aantal lymfklieren OKD met macrometastase (> 2,0 mm): 4
Aantal lymfklieren OKD met micrometastase (> 0,2 mm en <= 2,0 mm): 1
Detectie methode OKD: cytokeratine IHC

Trial-alert
Indien patiënt stadium III mamacarcinoom heeft (T0-2N2M0; T3N1-2M0; T4N0-2M0; TxN3M0), komt hij waarschijnlijk in aanmerking voor een BRCA1-like test. Bij een positieve test of BRCAg mutatie drager kan hij in mogelijk behandeld worden met hoge dosis chemotherapie gevolgd door stamceltransplantatie of chemotherapie gevolgd door een PARP-remmer. Voor informatie, neem zo spoedig mogelijk contact op met subito@nki.nl (zie ook clinicaltrials.gov NCT02810743).



palga
The best treatment begins with the best diagnosis

Where are we today



Acknowledgements

Iris Nagtegaal
Lucy Overbeek
Caro Sluijter
Rosella Hermens
Ariana Madani
Joep IJspeert
Chantal Kuijpers

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