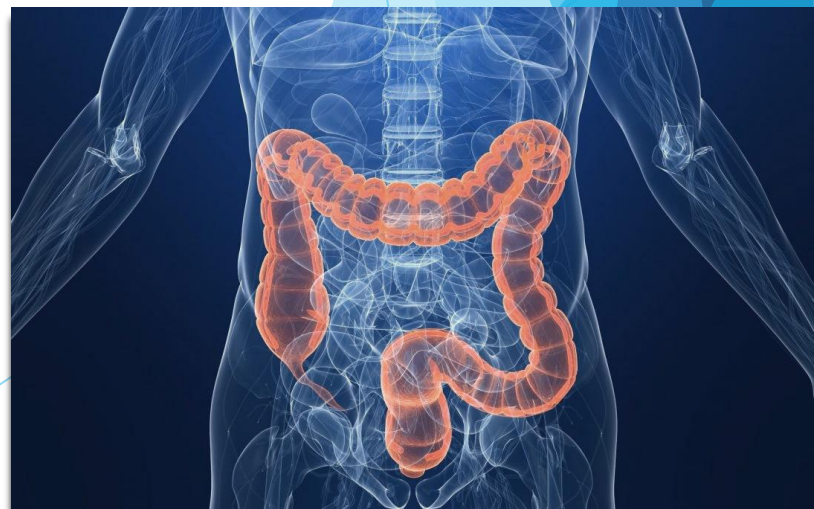
az sint-lucas
BRUGGE
Zorg is onze natuur

Behandeling van dikke darmkanker

Annelies Holvoet

Donderdag 24/05/2018



Dikke darmkanker

- Ontstaan
- Behandeling
- Preventie

Dikkedarmkanker in Vlaanderen

Jaarlijks wordt in Vlaanderen bij meer dan 5.000 mannen en vrouwen dikkedarmkanker ontdekt

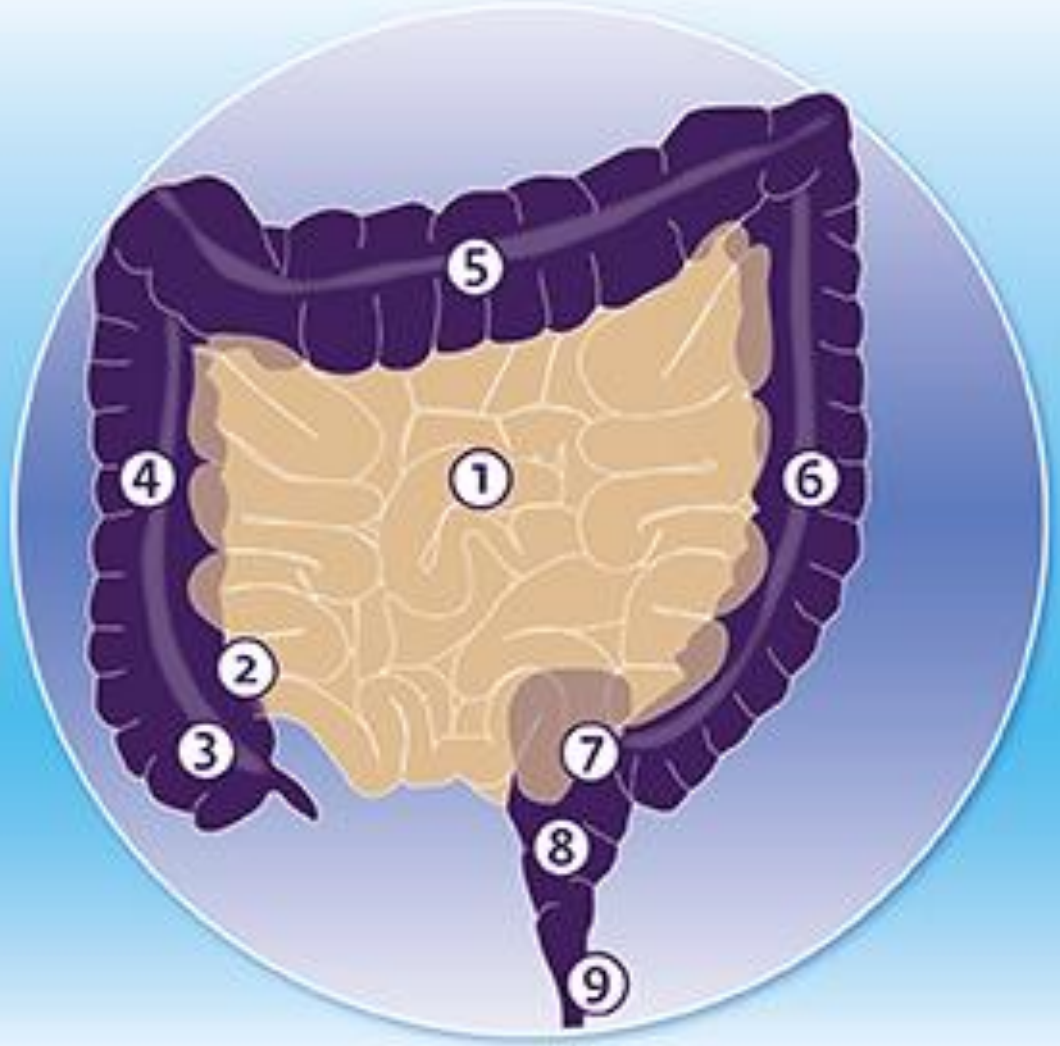
2012: 5438 **3048** **2390**

Jaarlijks sterven er in Vlaanderen ongeveer **1800** personen aan deze kanker

2012: 1806 **991** **815**

Sterfte 1/3 of bijna 5 per dag!

Stichting Kankerregister, 2014

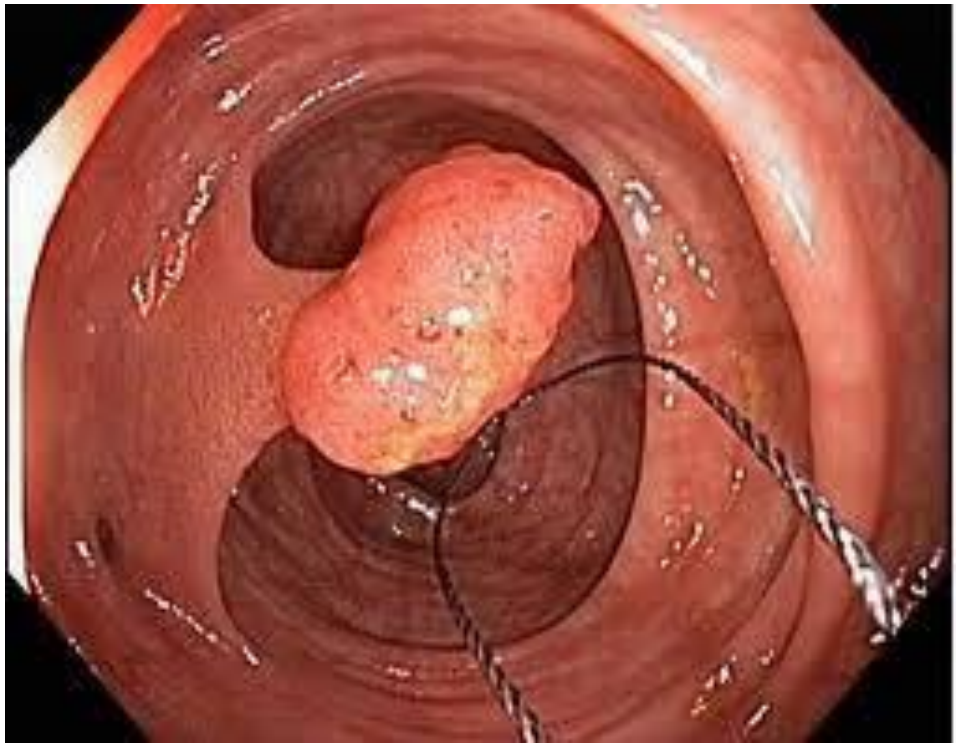


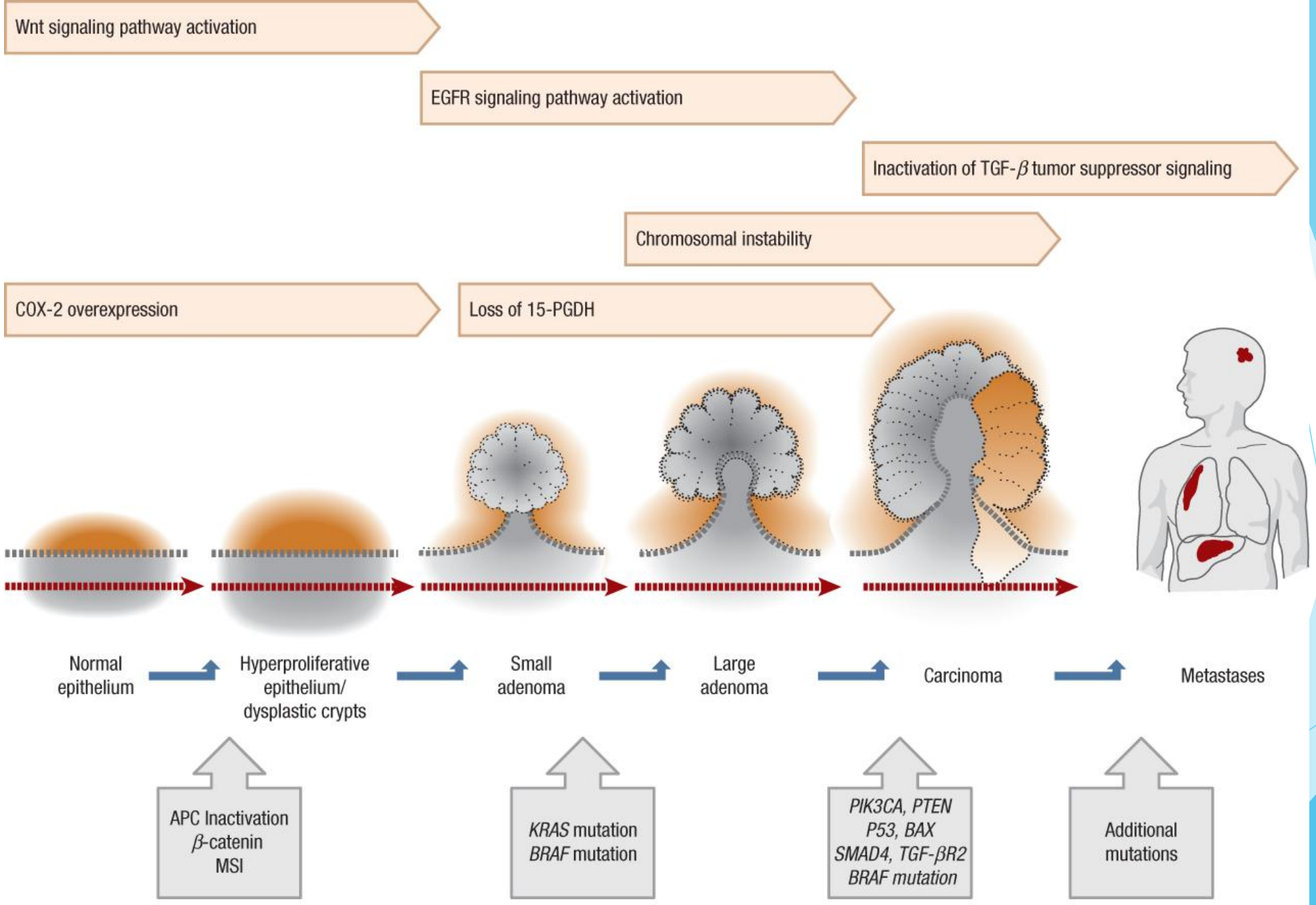
1. Dunne darm
2. Verbinding dunne darm - dikke darm
3. Blinde darm
4. Stijgende deel
5. Dwarslopende deel
6. Dalende deel
7. S-vormige deel
8. Endeldarm
9. Anus met sluitspier

kanker.nl

Ontstaan

- Voorloper van dikke darmkanker = poliep





Source: DiPiro JT, Talbert RL, Yee GC, Matzke GR, Wells BG, Posey LM: *Pharmacotherapy: A Pathophysiologic Approach, Ninth Edition:* www.accesspharmacy.com

Copyright © The McGraw-Hill Companies, Inc. All rights reserved.

Adenoma to Carcinoma Pathway

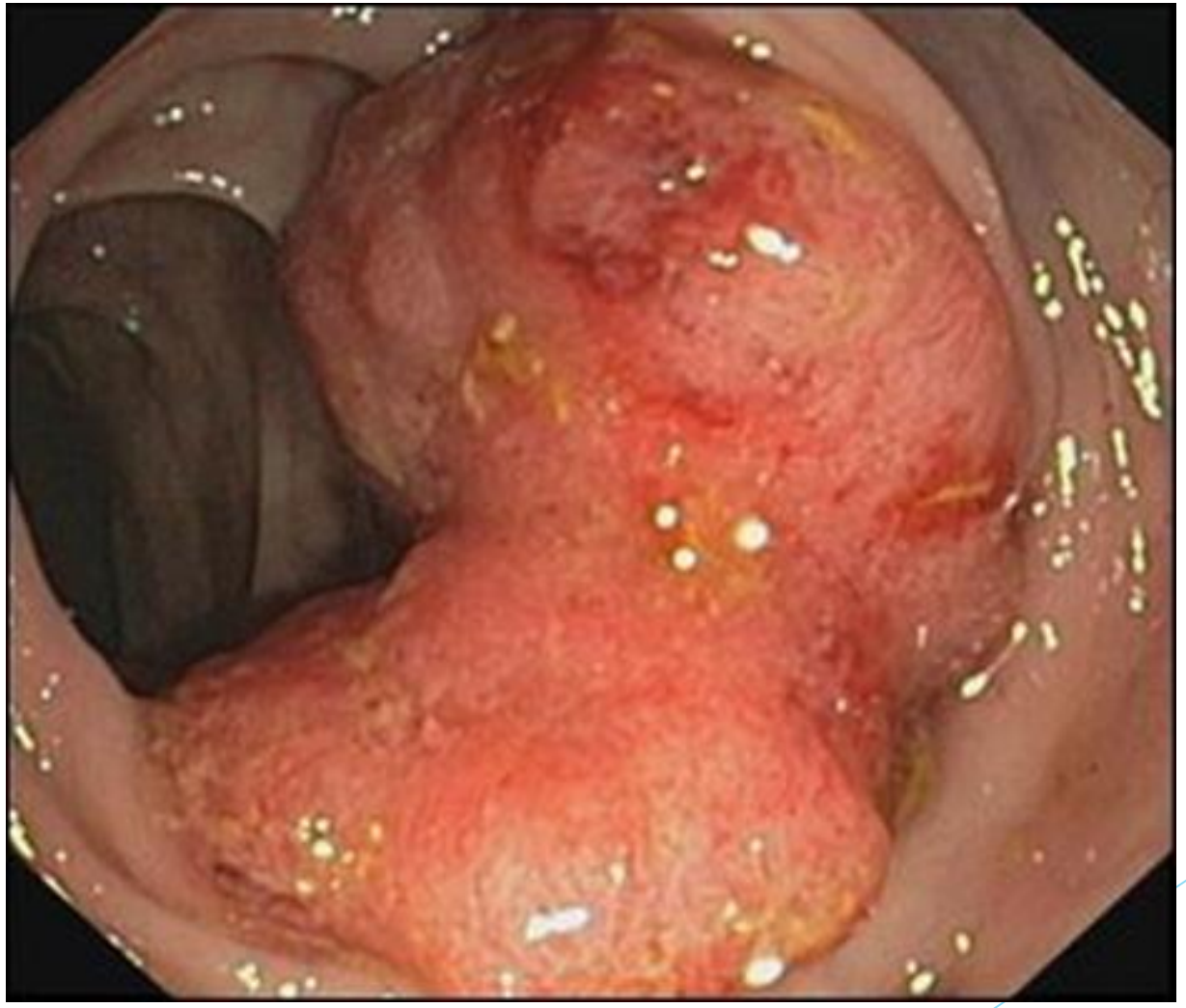
APC loss

K-ras mutation

Chrom 18 loss

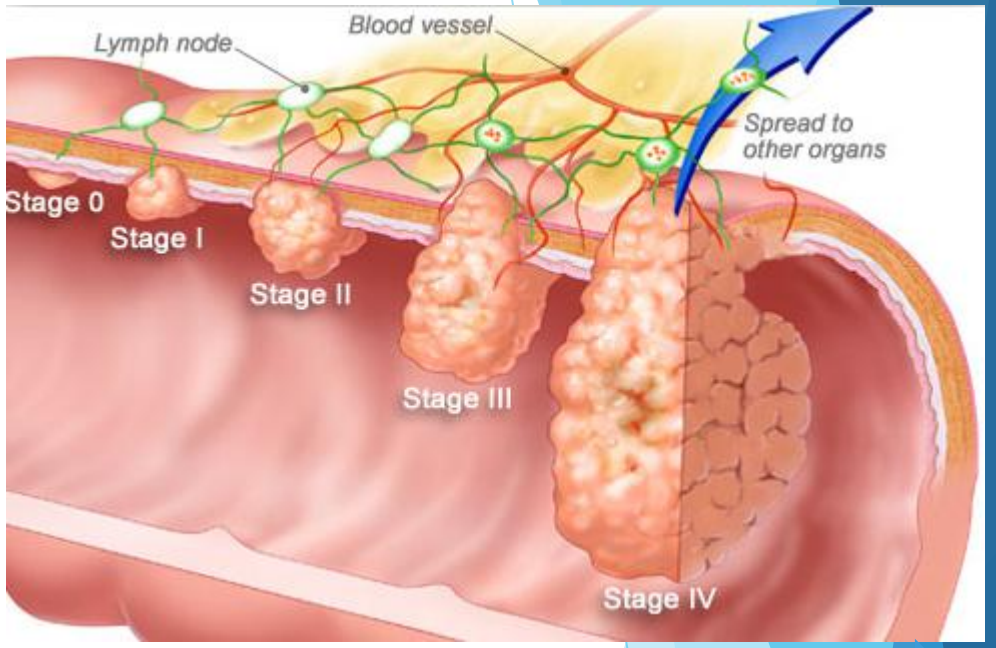
p53 loss

Normal Epithelium → Hyper-proliferation → Early Adenoma → Intermediate Adenoma → Late Adenoma → Cancer



Dikkedarmkanker: stadia

Ontwikkeling van poliep naar dikkedarmkanker zeer traag proces



8-10 jaar

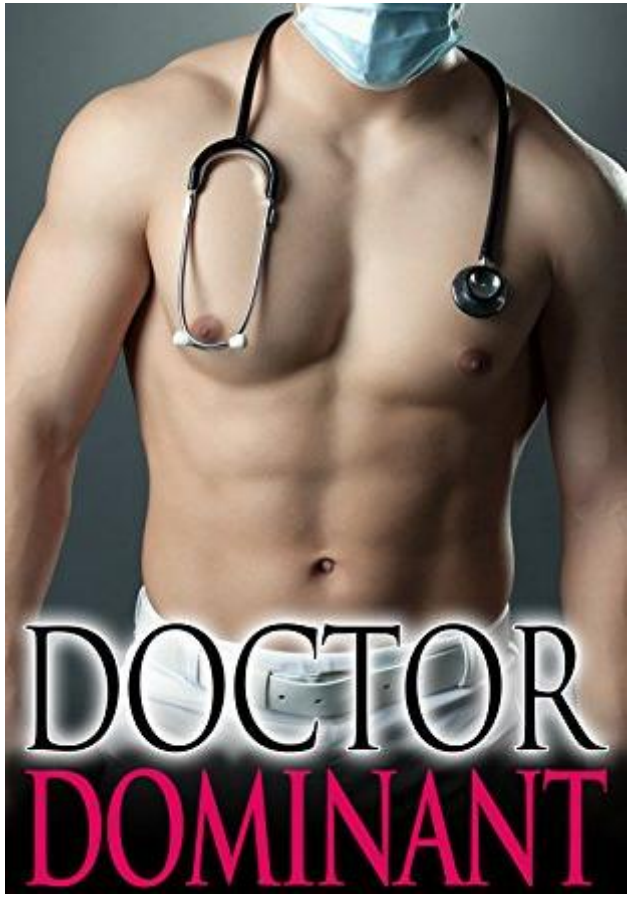
Verschillende stadia

Stadium 0: poliep, enkel in binnenste slijmvlies (nog geen DDK)
Stadium I: al in wand van dikkedarm
Stadium II: door darmwand heen gegroeid (in spierlaag)
Stadium III: in lymfeklieren in nabije gebied
Stadium IV: uitgezaaid naar andere lichaamsdelen (lever, longen, botten)

Referentie afbeelding www.helpbijkanker.nl

Behandeling

- Multidisciplinair
- Afhankelijk van
  - Stadium
  - Plaats (endeldarm of colon)
  - Andere factoren



Stadium: TNM

- Tumor: doorgroei door de wand
- Nodes: klieren
- Metastasen: uitzaaiingen

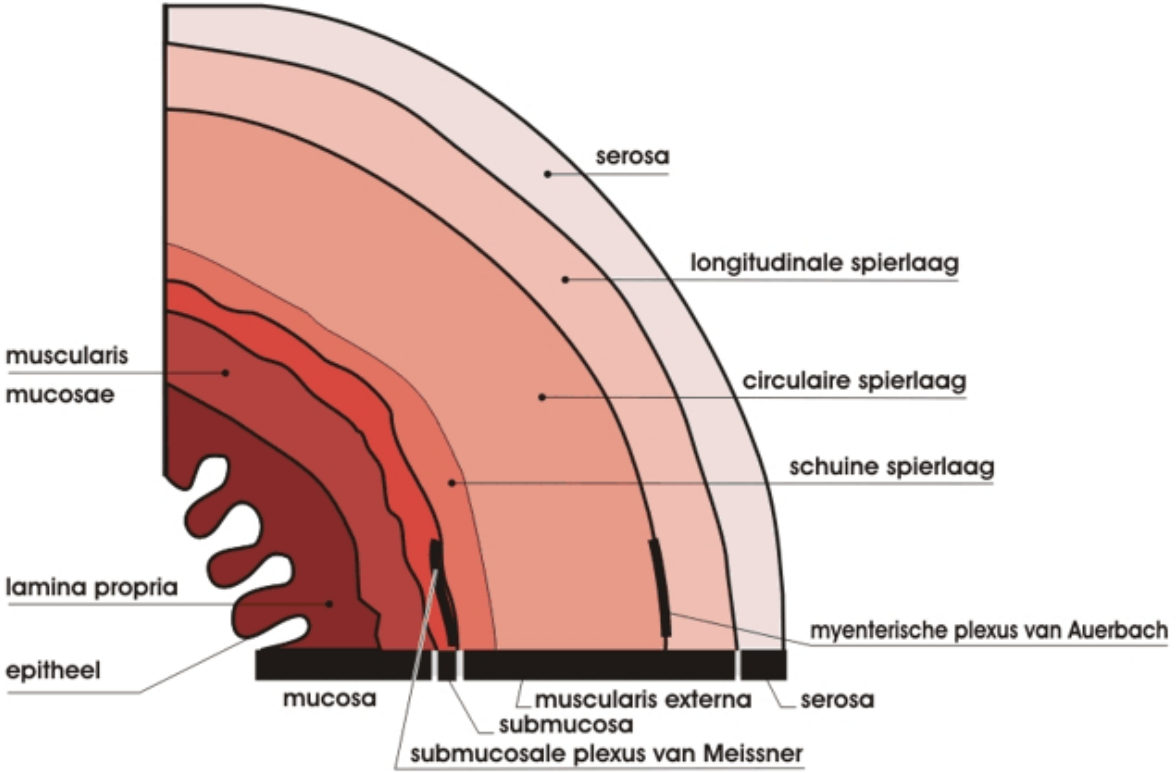
Table 4: TNM Staging System for Colorectal Cancer[43]

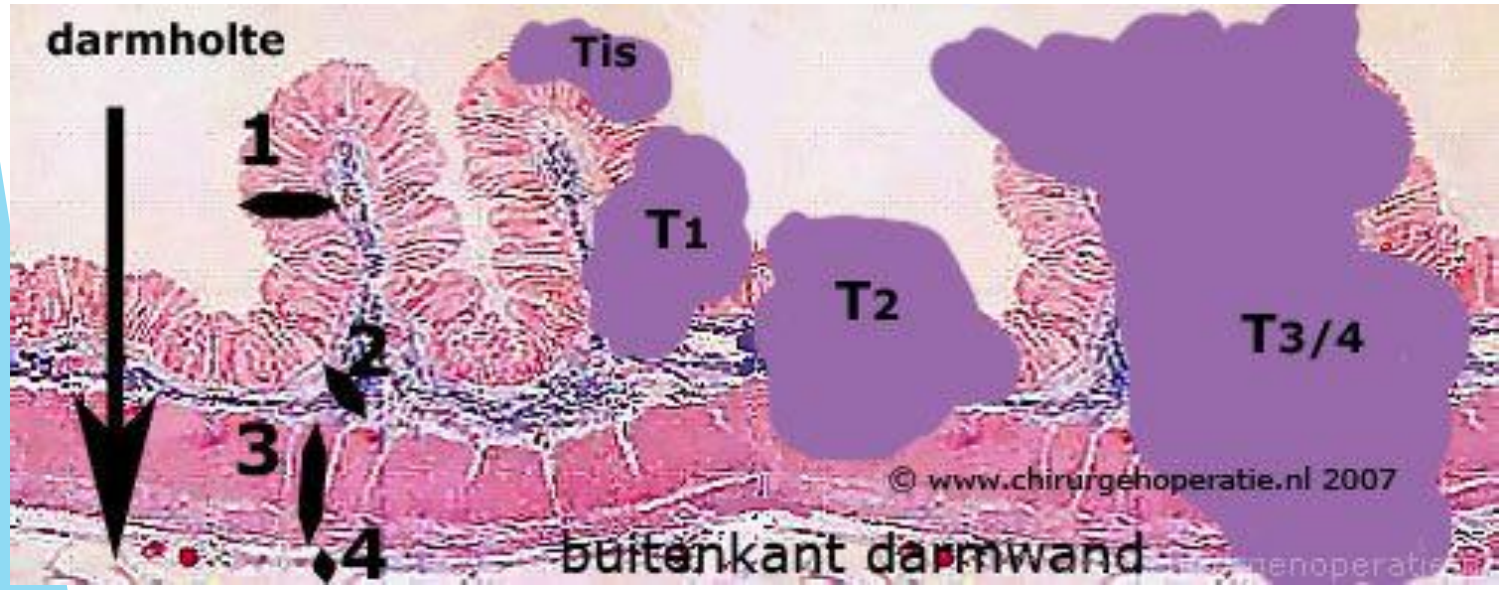
Primary tumor (T)	
T_x	Tumor cannot be assessed
T_{is}	Carcinoma in situ
T_1	Tumor invades submucosa
T_2	Tumor invades muscularis propria
T_3	Tumor invades subserosa
T_4	Tumor directly invades adjacent organs/structures or through the visceral peritoneum
Regional lymph nodes (N)	
N_x	Lymph nodes cannot be assessed
N_0	No lymph node metastases
N_1	Metastases in 1-3 lymph nodes
N_2	Metastases in ≥4 lymph nodes
Distant metastases (M)	
M_x	Metastases cannot be assessed
M_0	No distant metastases
M_1	Distant metastases present

Stage	TNM classification	5-year survival (%)
I	T_1, T_2	>90
IIA	T_3, N_0	87.5
IIB	T_4, N_0	71.5
IIIA	T_1, T_2, N_1	87
IIIB	T_3, N_1	68.7
IIIC	T_3, T_4, N_1, N_2	47-50
IV	Any T, M1	27

Stadia: T (tumor)

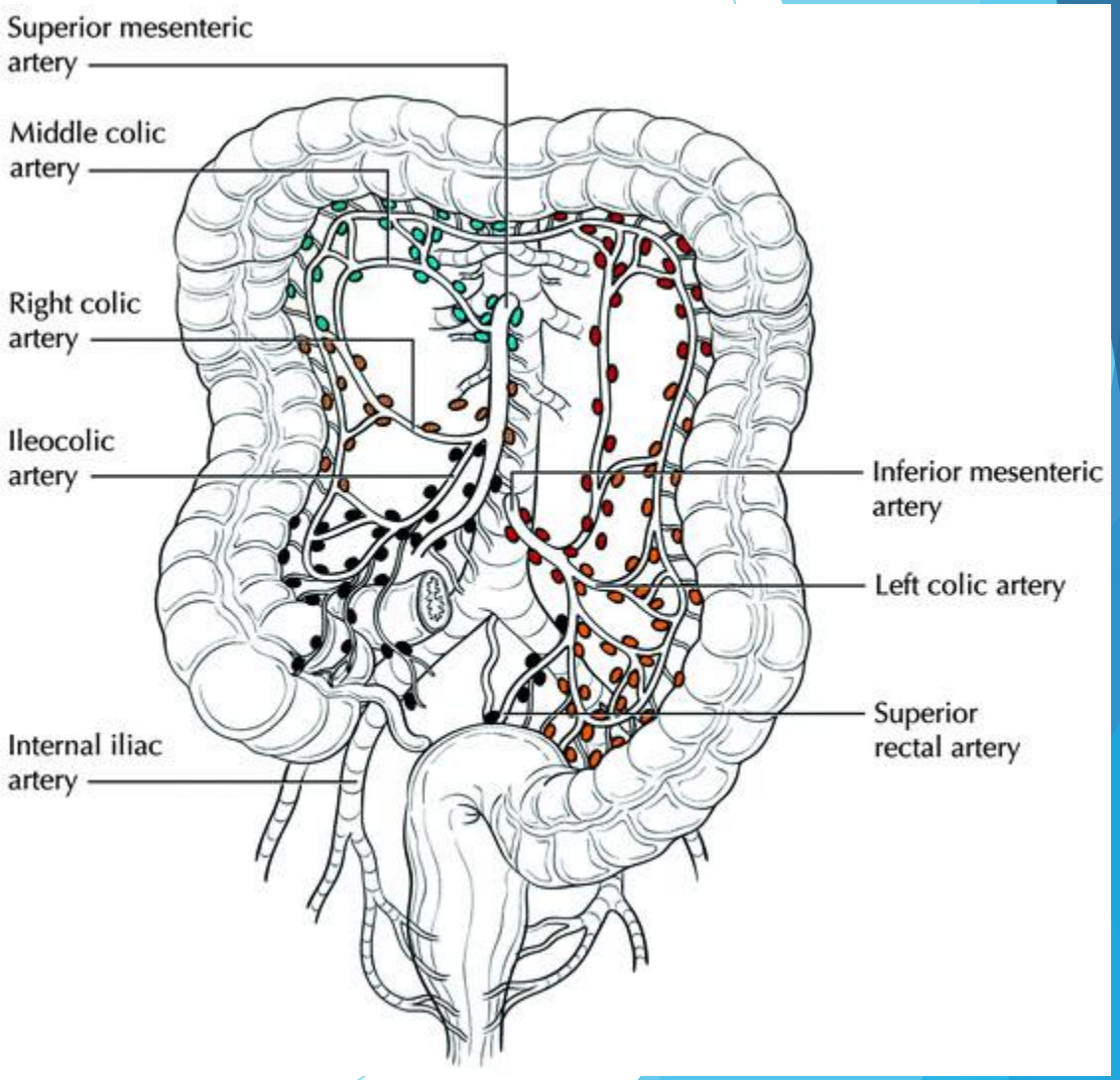
- Tis: in situ
- T1: tot in submucosa
- T2: tot in spierlaag
- T3: tot in serosa
- T4: ingroei in andere organen (vb prostaat, blaas)

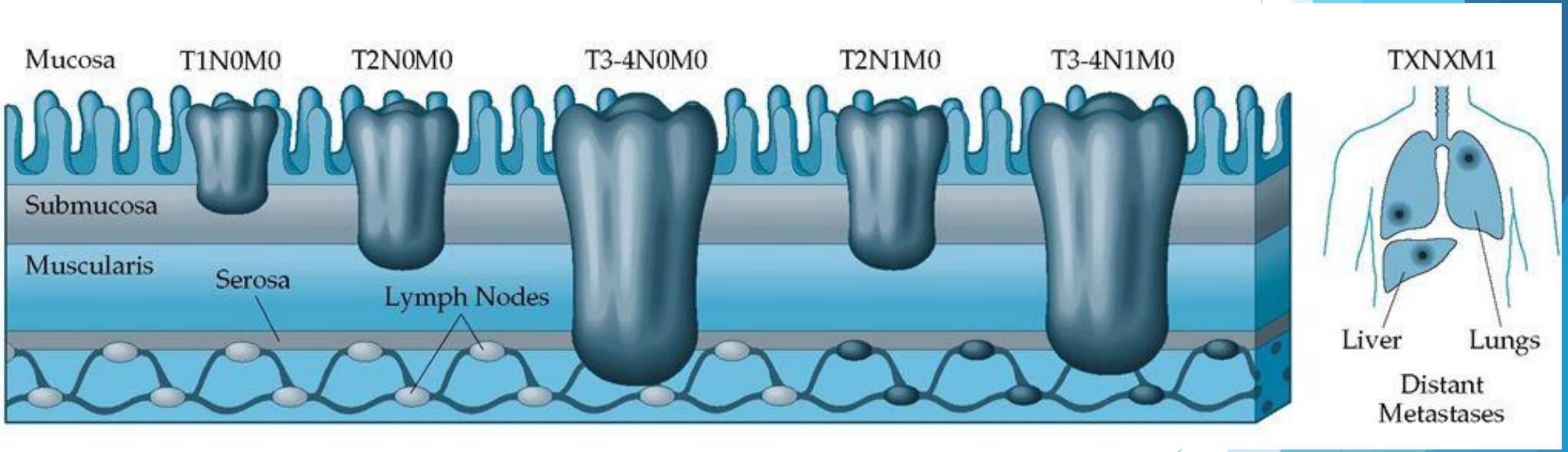




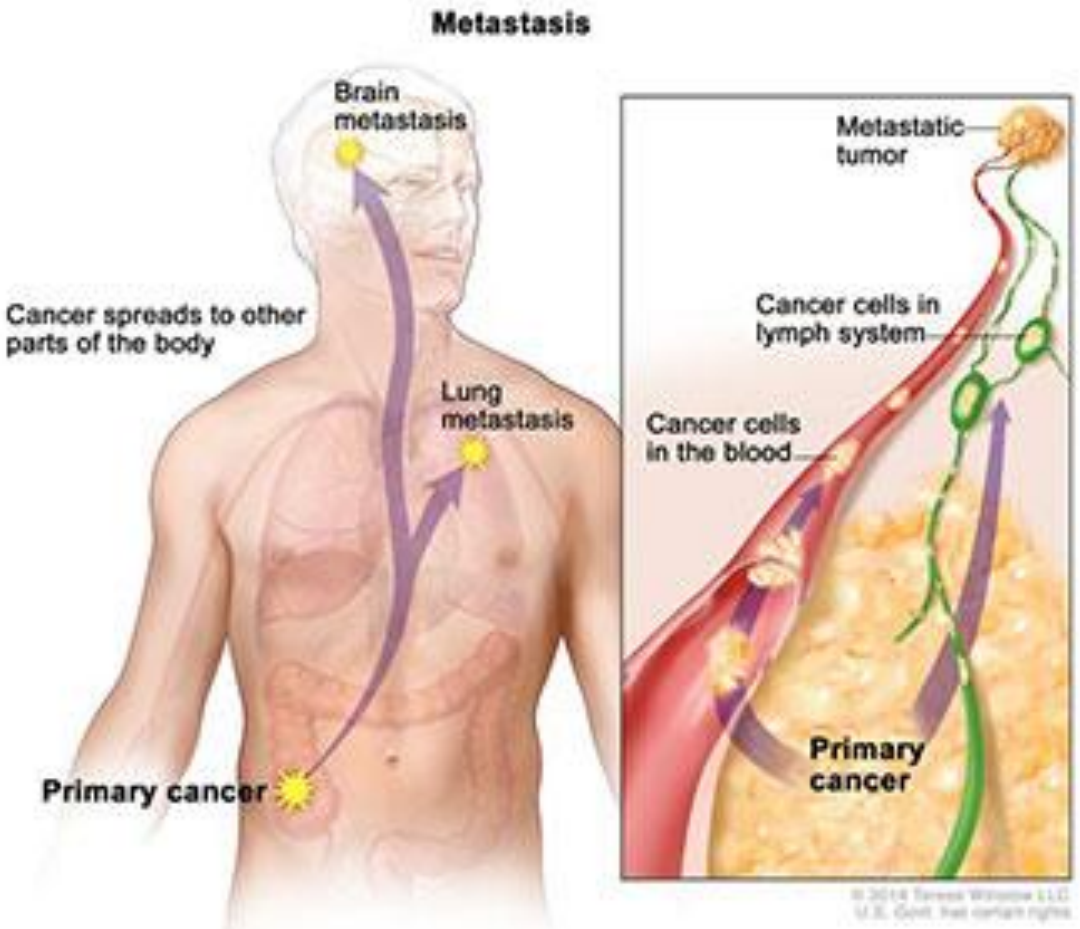
Stadia: N (klieren lokaal)

- N0: geen klieren
- N1: 1-3 klieren
- N3: meer dan 3 klieren




Mucosa
T1N0M0
T2N0M0
T3-4N0M0
T2N1M0
T3-4N1M0
TXNXM1
Submucosa
Muscularis
Serosa
Lymph Nodes
Liver
Lungs
Distant
Metastases

Stadia: M (uitzaaiingen)

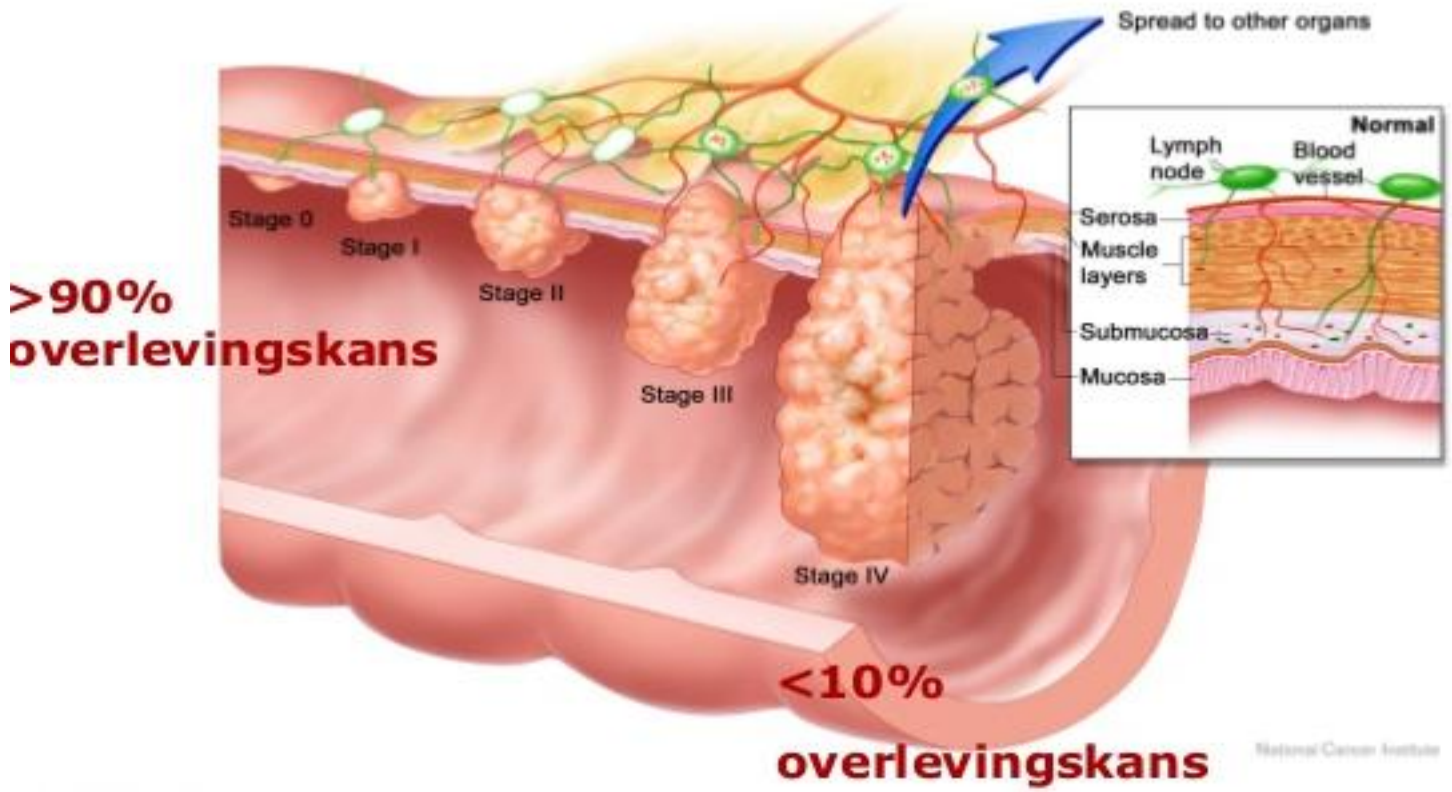


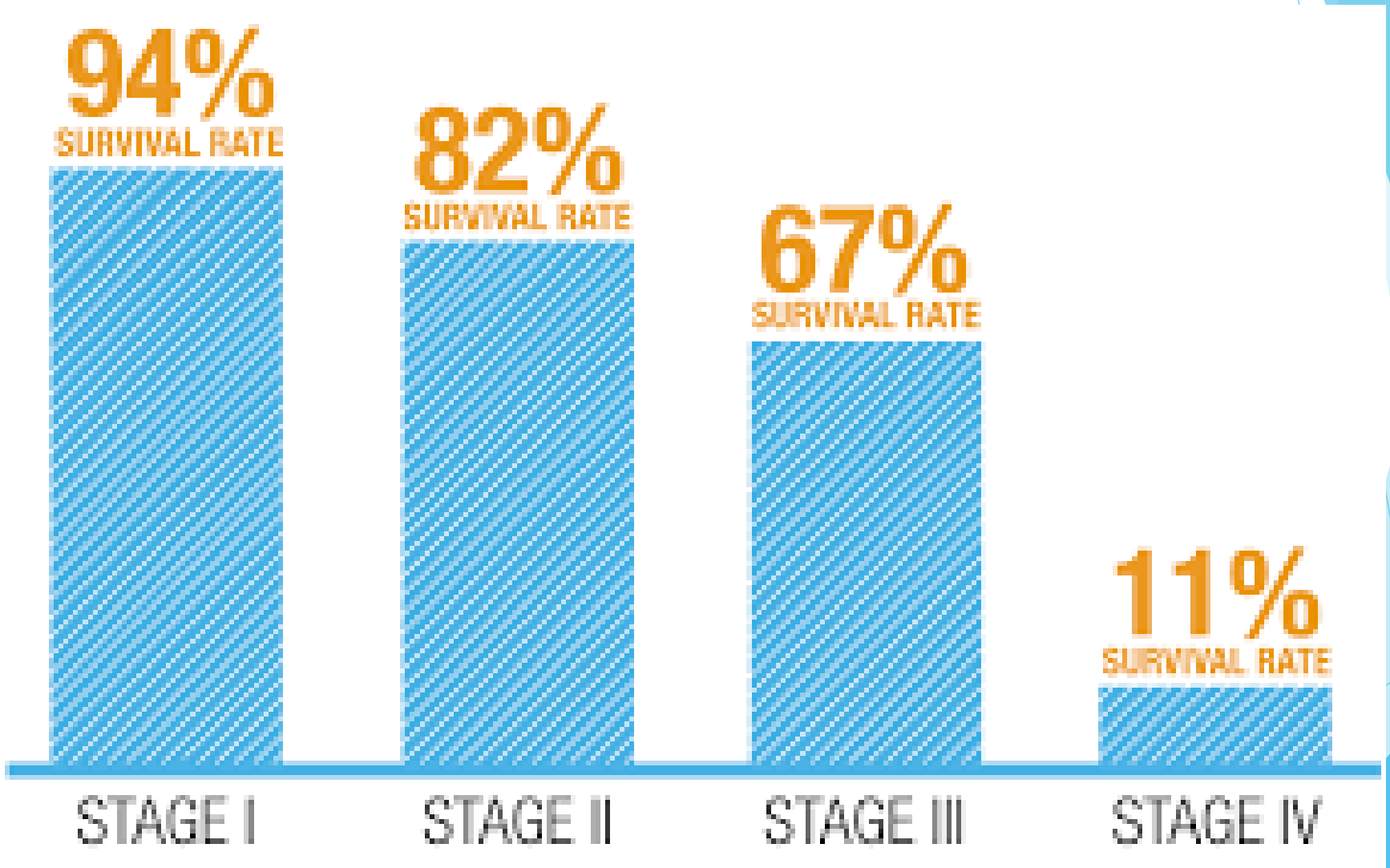
- Colon (dikke darm)
  - Lever (70%)
  - Long (32%)
  - Buikvlies (21%)
- Rectum (endeldarm)
  - Lever (70%)
  - Long (47%)
  - Bot (12%)

Stadia

- TNM

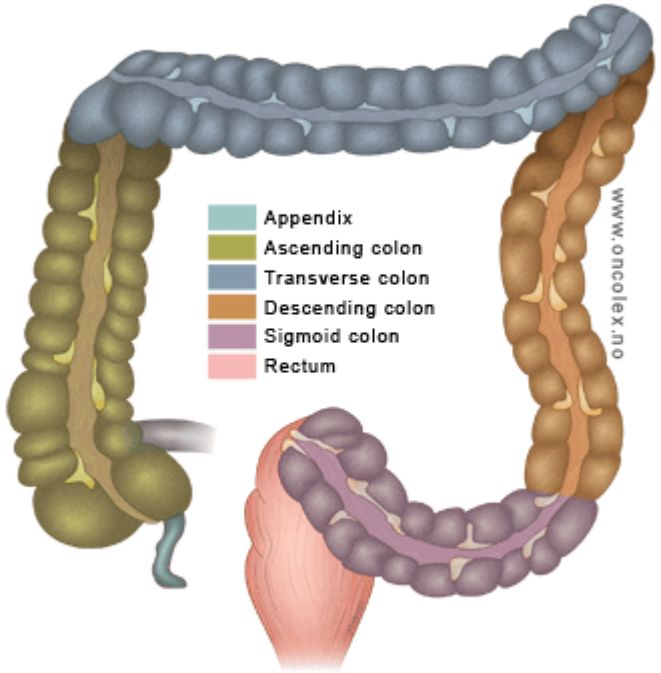
- 0: Tis
- I: T1-T2 N0
- II: T3-T4N0
- III: N+: klieren lokaal
- IV: M+: uitzaaiingen

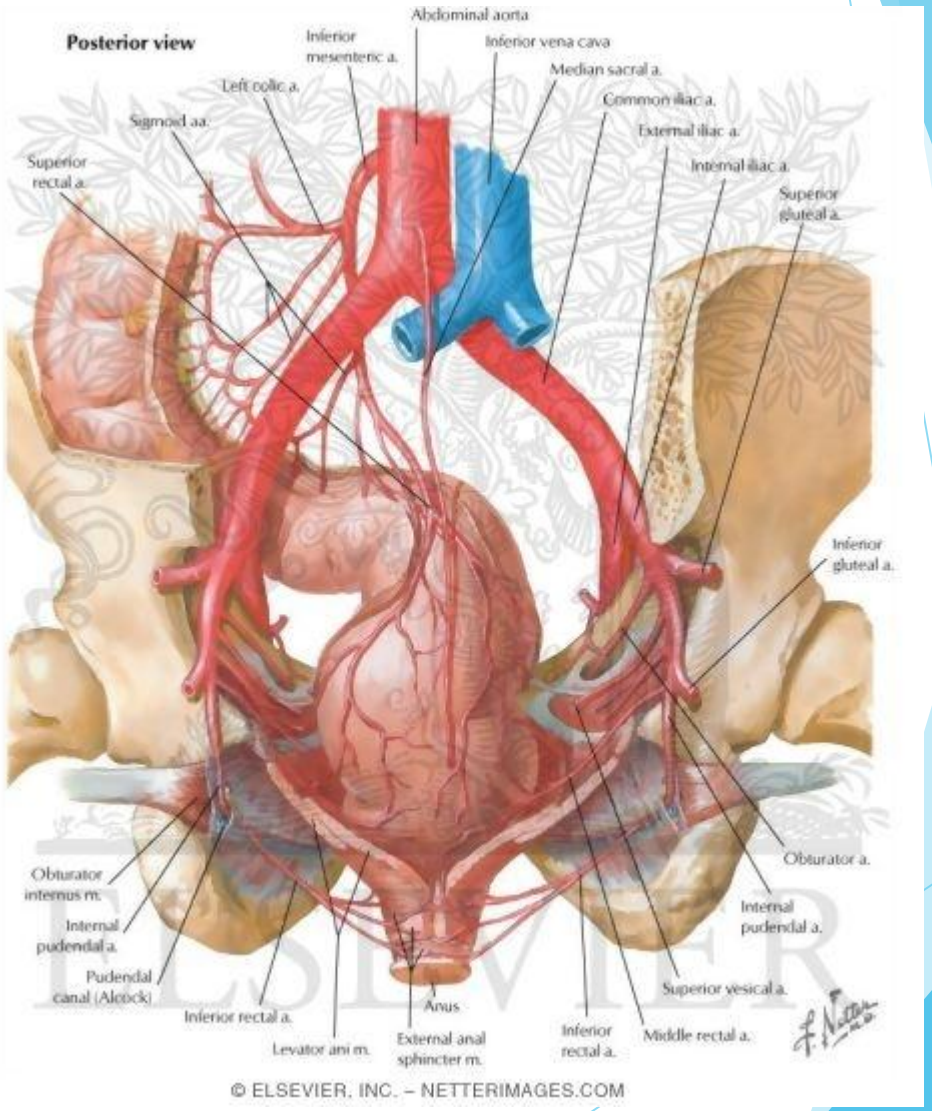



94%
SURVIVAL RATE
82%
SURVIVAL RATE
67%
SURVIVAL RATE
11%
SURVIVAL RATE
STAGE I
STAGE II
STAGE III
STAGE IV

Behandeling

- Locatie





Behandeling

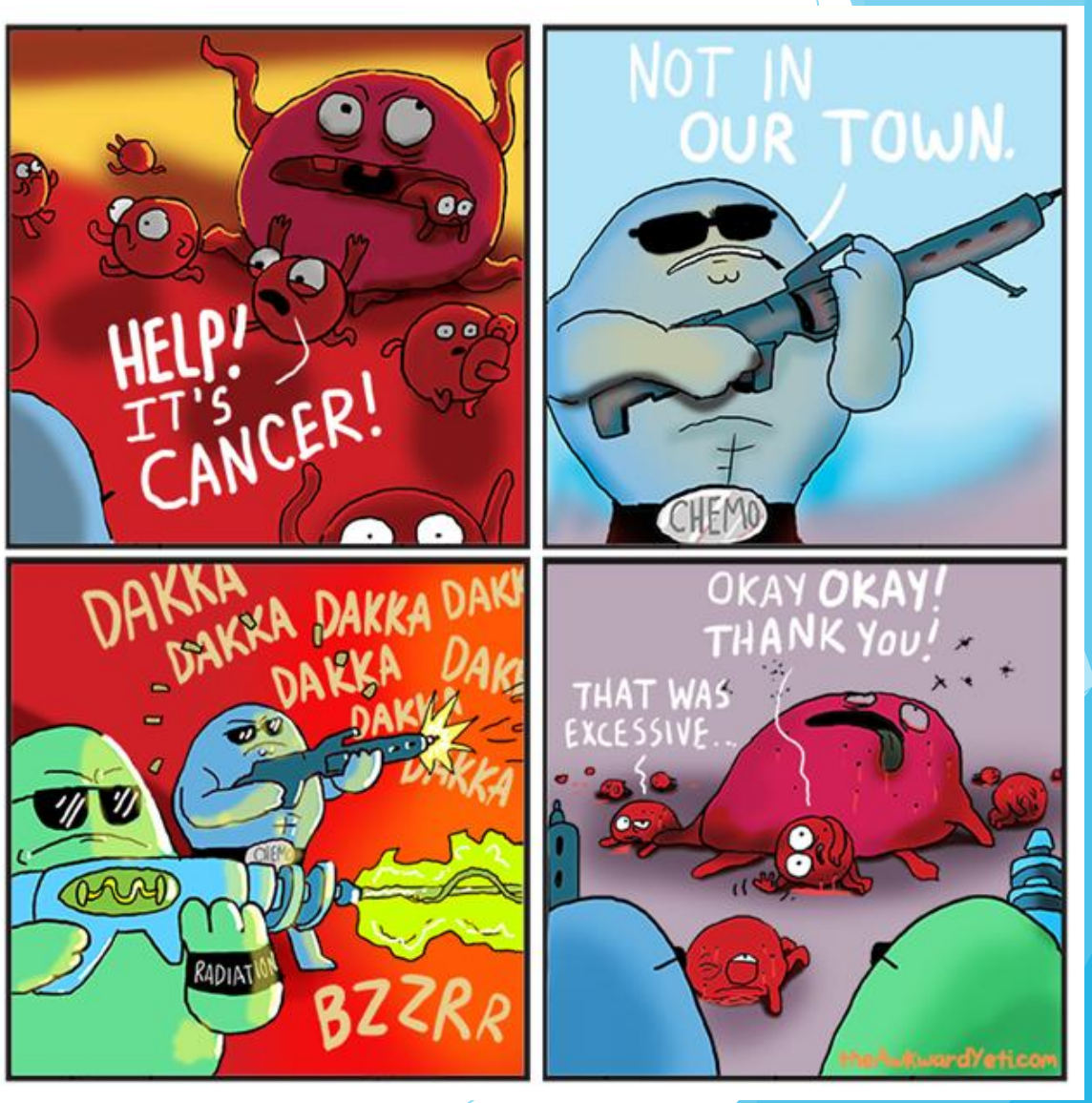
- Afhankelijk van
  - TNM
  - Locatie
  - Individueel !!

Behandeling

Behandeling

- Lokale therapie
  - Heelkunde of chirurgie
  - Radiotherapie of bestraling

- Systemische therapie
  - chemotherapie
  - (immunotherapie)



Behandeling: heelkunde

1, niet gemetastaseerd (I-III)

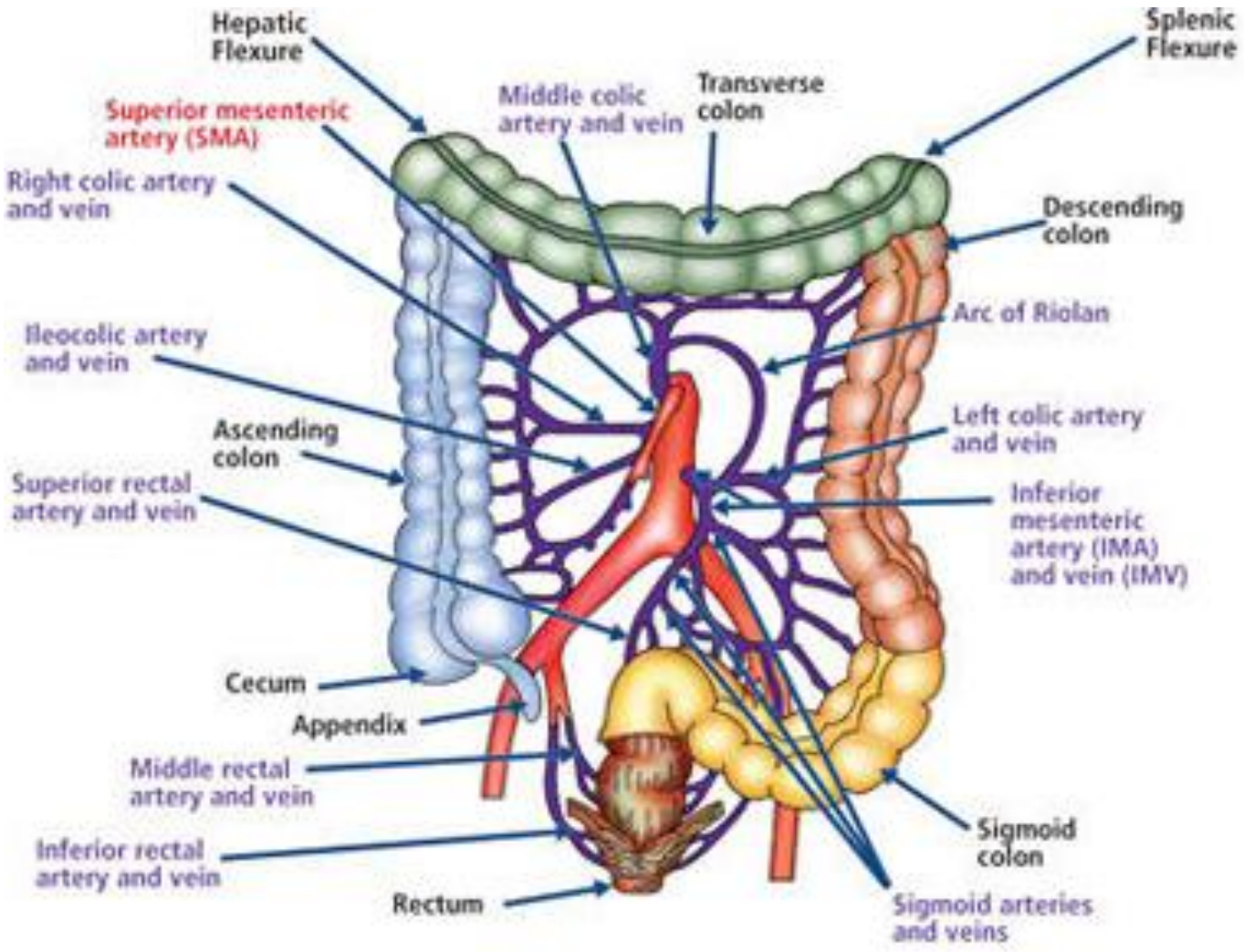
dikke darm: altijd heelkunde

endeldarm: stadium II en III: eerst bestraling

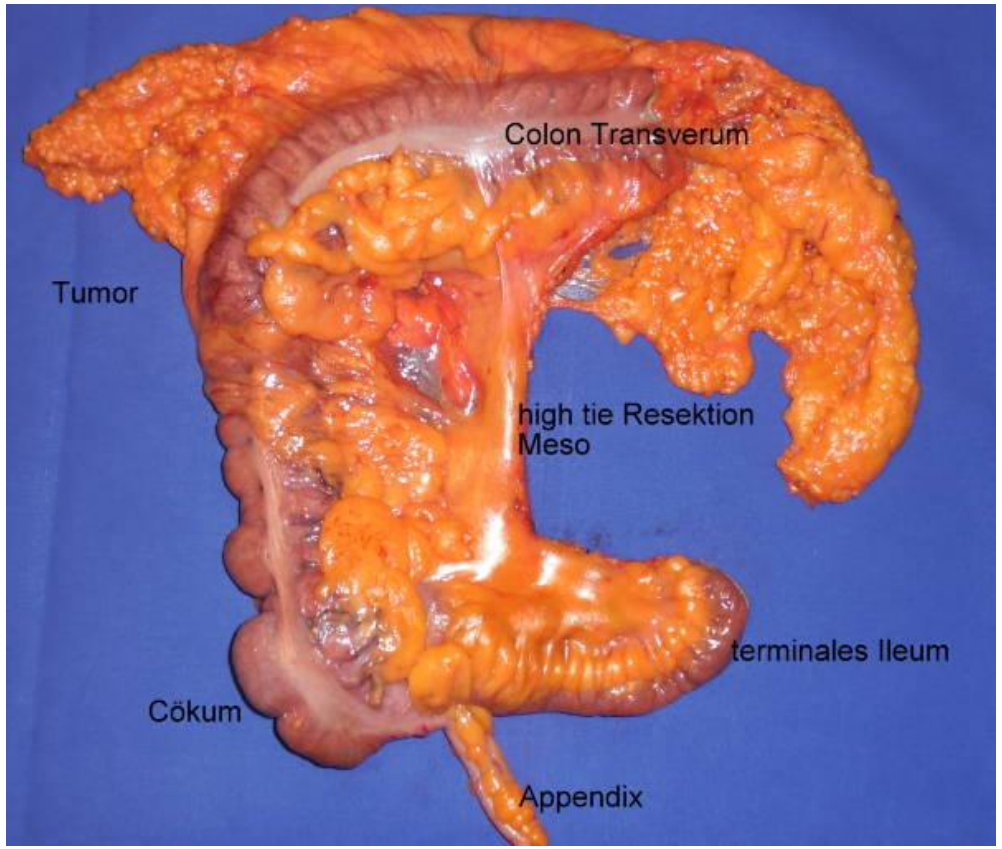
2, gemetastaseerd (IV)

soms heelkunde zo operabel, zo goed als altijd eerst chemotherapie

Behandeling: heelkunde



Behandeling: rechtszijdig: rechter hemicolectomie



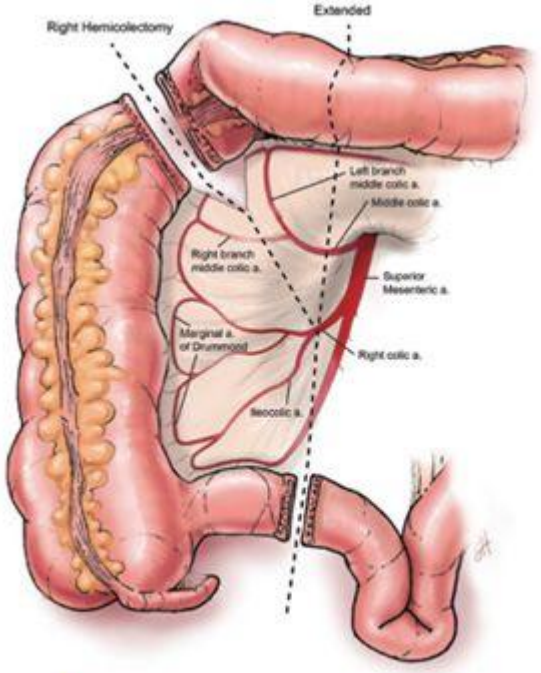
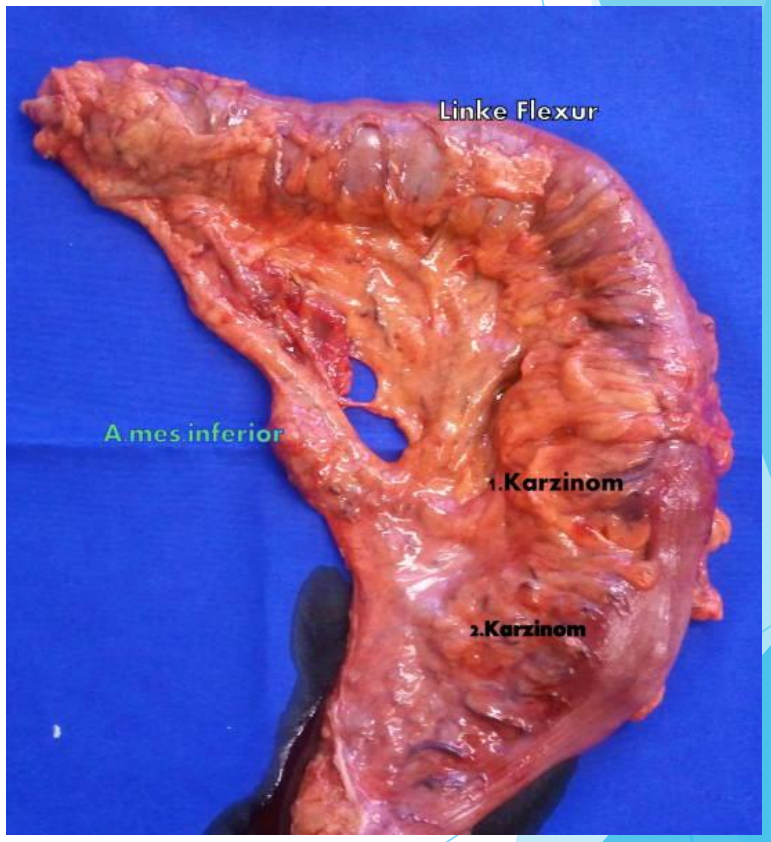


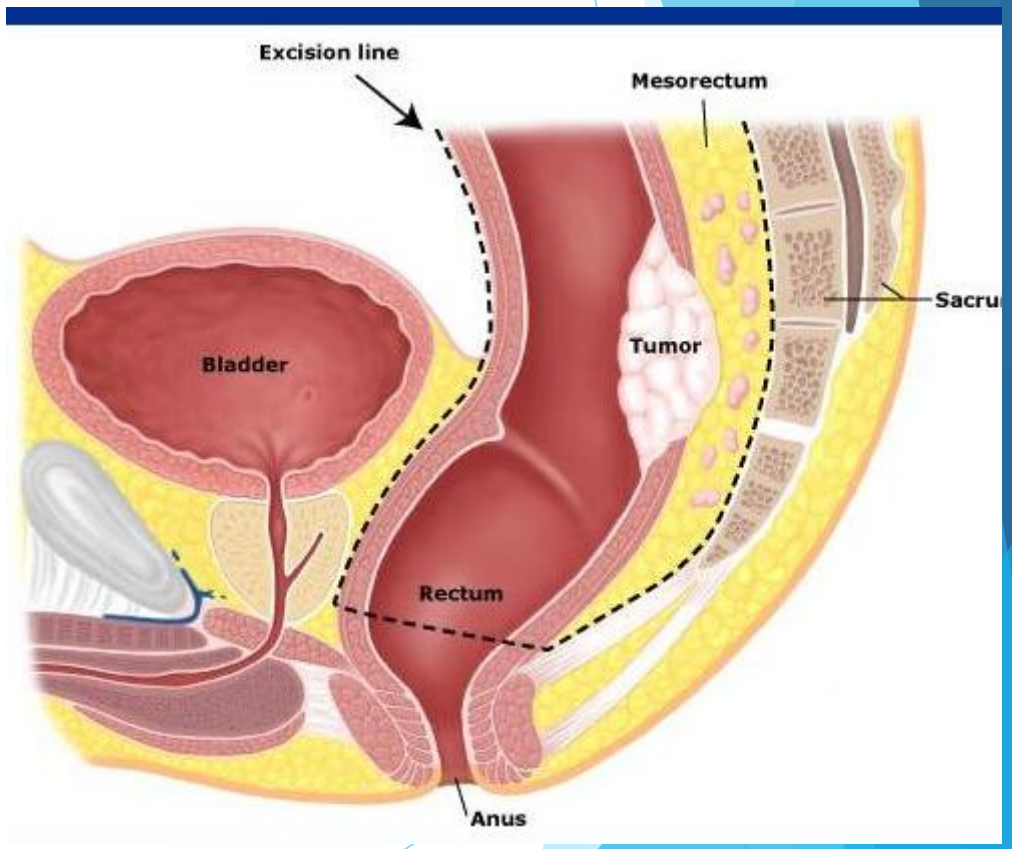
FIG 1 • Vascular anatomy of a right hemicolectomy. (Printed with permission from Baylor College of Medicine.)

Behandeling: linkszijdig: linker hemicolectomie



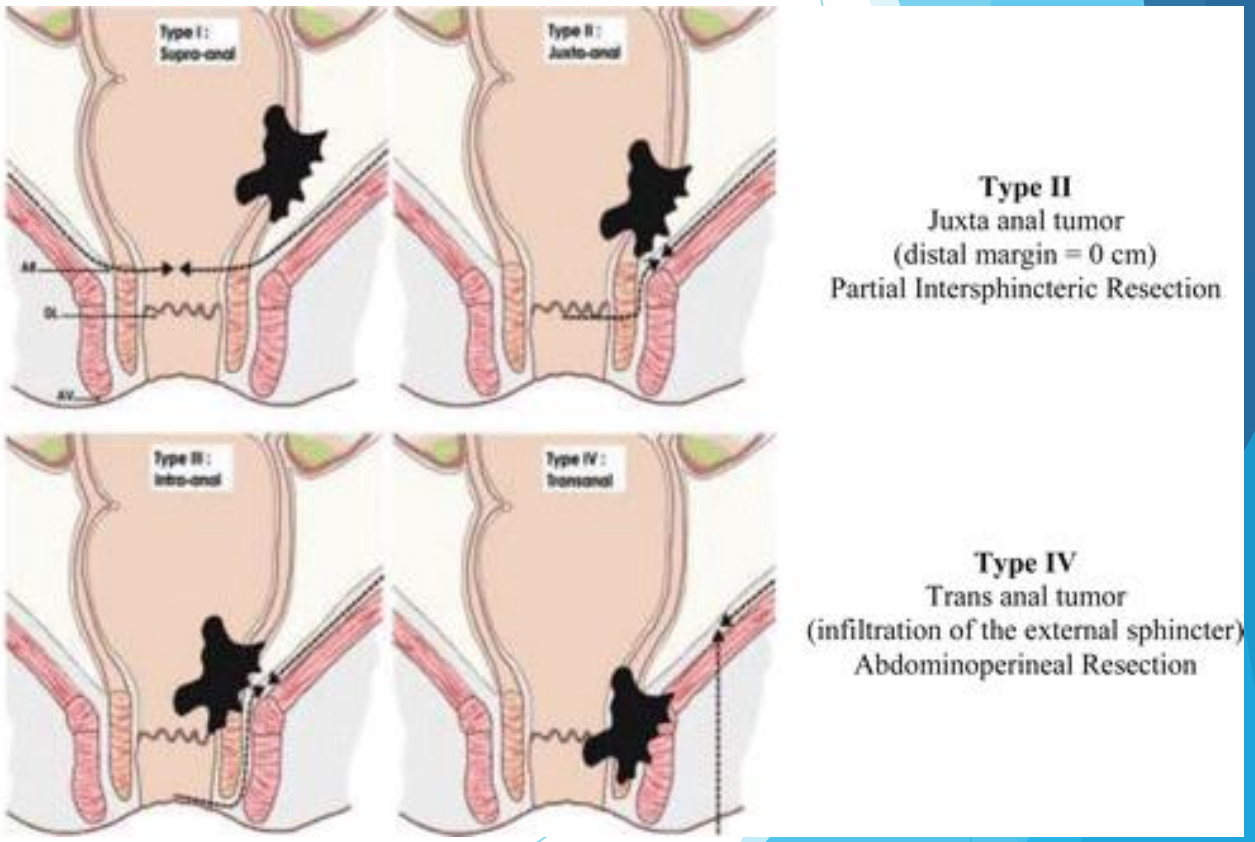
Behandeling: heelkunde: rectum

- Endeldarm:
  - Rectumresectie met of zonder tijdelijk (ileo)stoma
  - APRA: sluitspier wordt mee weg-genomen, definitief colostoma



Behandeling: heelkunde: rectum

Type I
Supra anal tumor
(distal margin < 1-2 cm)
Colo-Anal Anastomosis

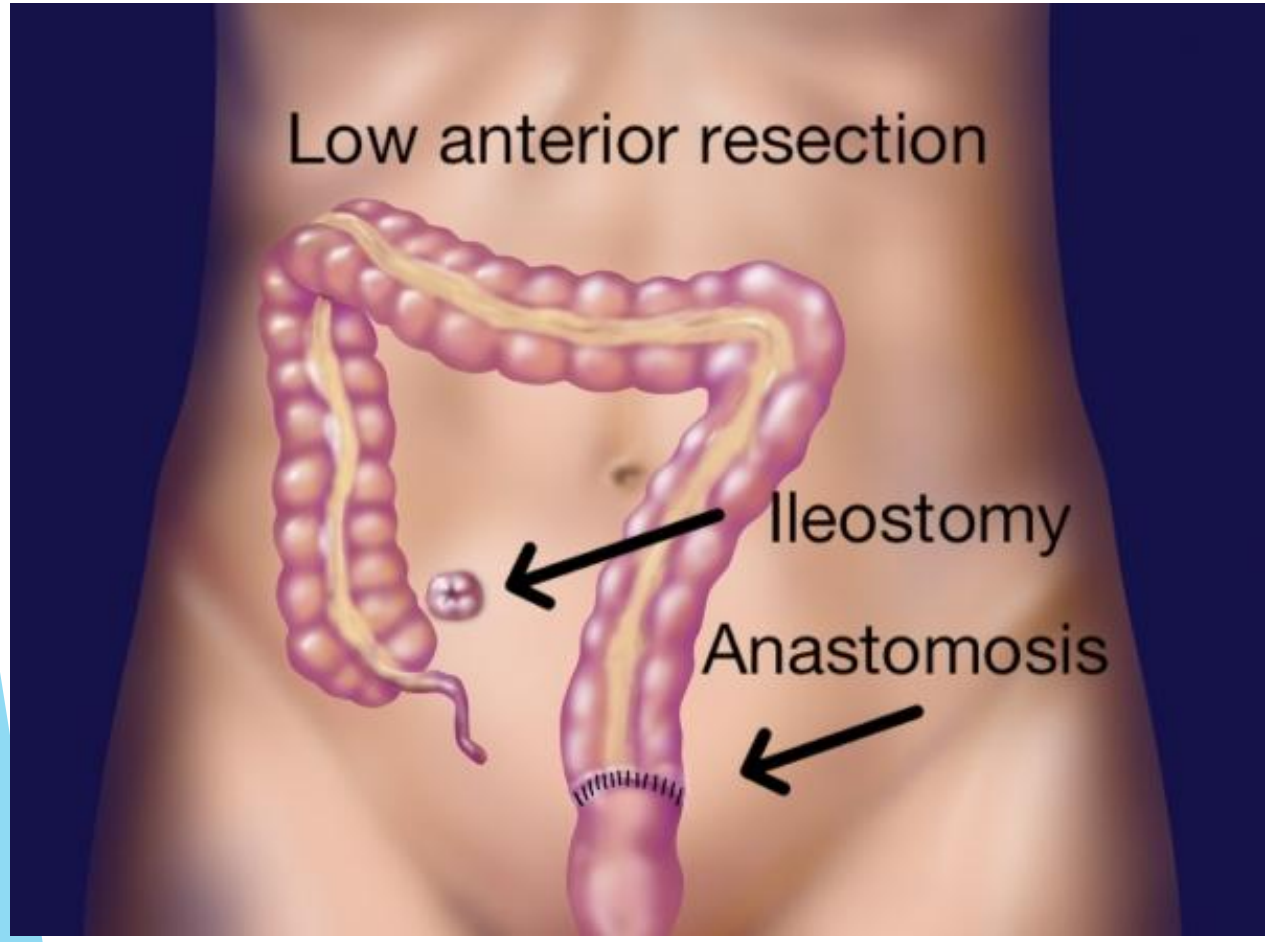


Type II
Juxta anal tumor
(distal margin = 0 cm)
Partial Intersphincteric Resection

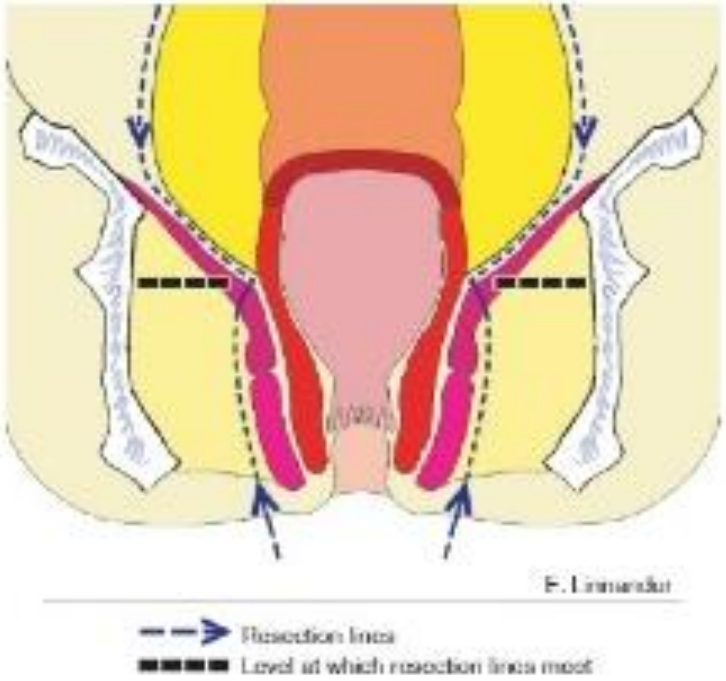
Type III
Intra anal tumor
(infiltration of the internal sphincter)
Total Intersphincteric Resection

Type IV
Trans anal tumor
(infiltration of the external sphincter)
Abdominoperineal Resection

TME (totale mesorectale excisie)

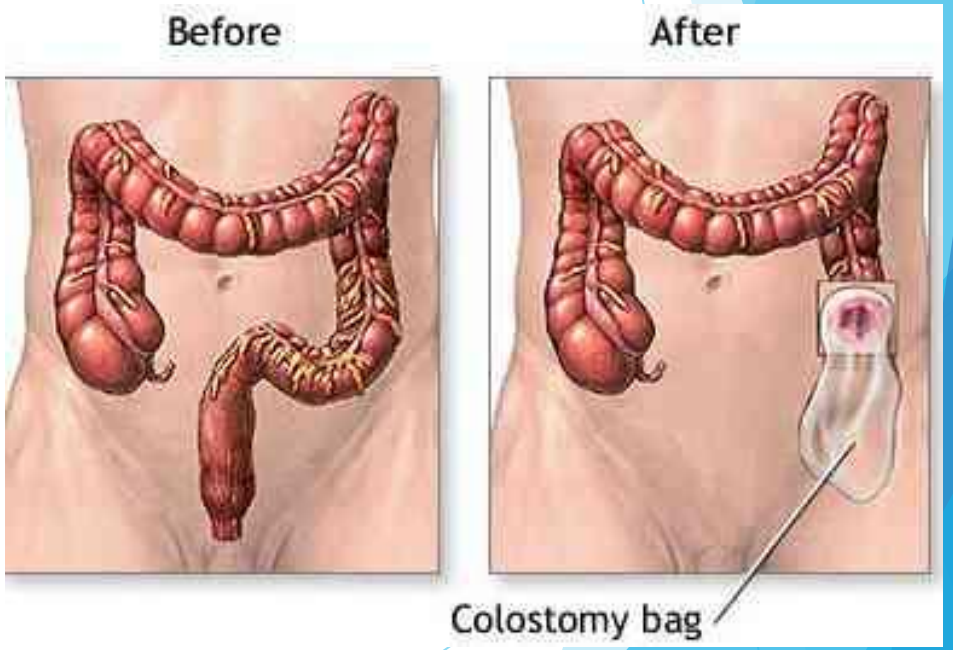


APRA: abdominoperineale rectumresectie



a Resection lines

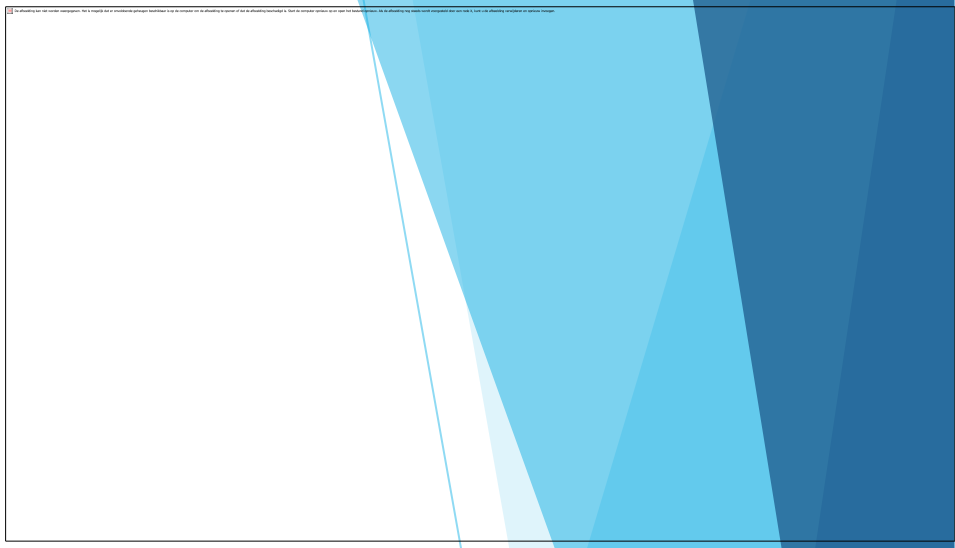
b Specimen

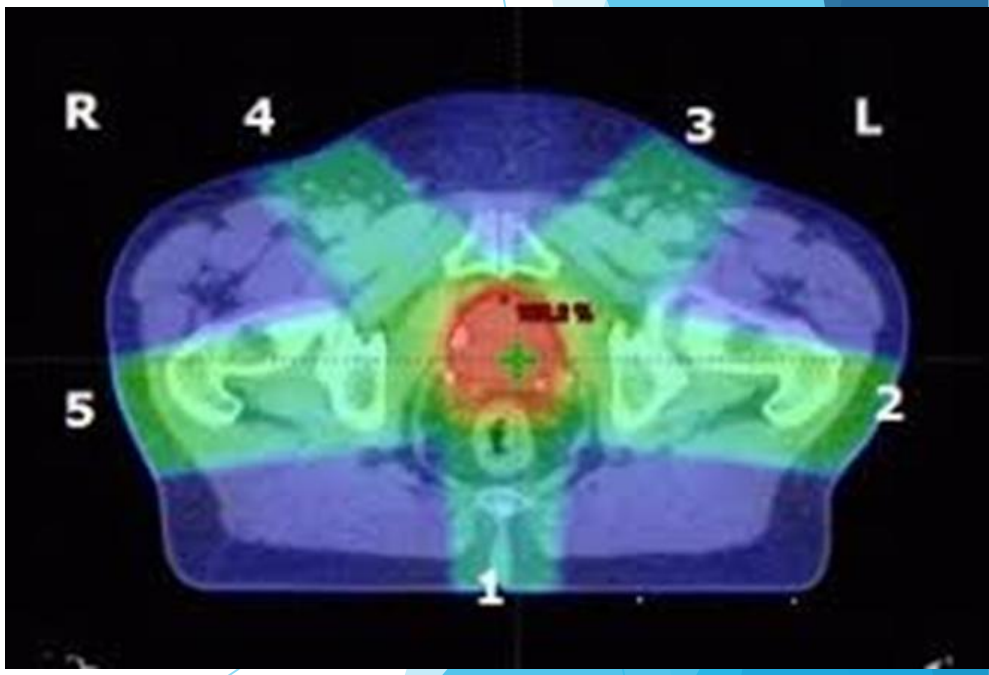


LARS

Behandeling: bestraling

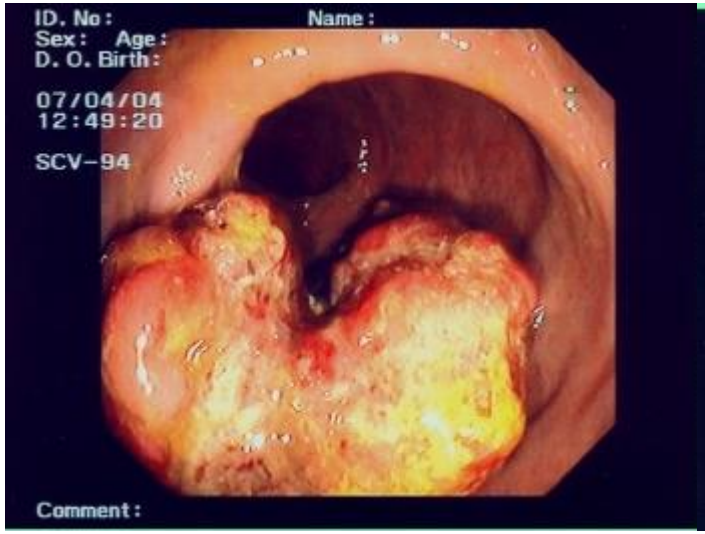
- Tumor krijgt max dosis
- Omgevend weefsel dosis binnen aanvaard-bare limieten
- Kankercellen (snel delende cellen) zijn gevoeliger voor RT
- Gezonde cellen kunnen beter herstellen (sublethal dose)



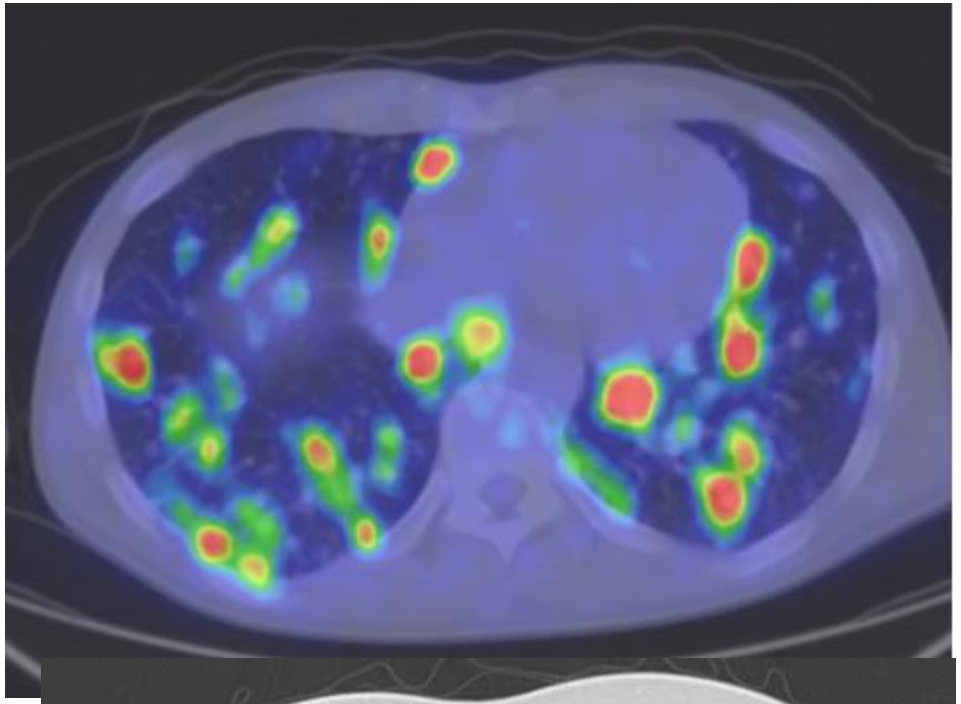


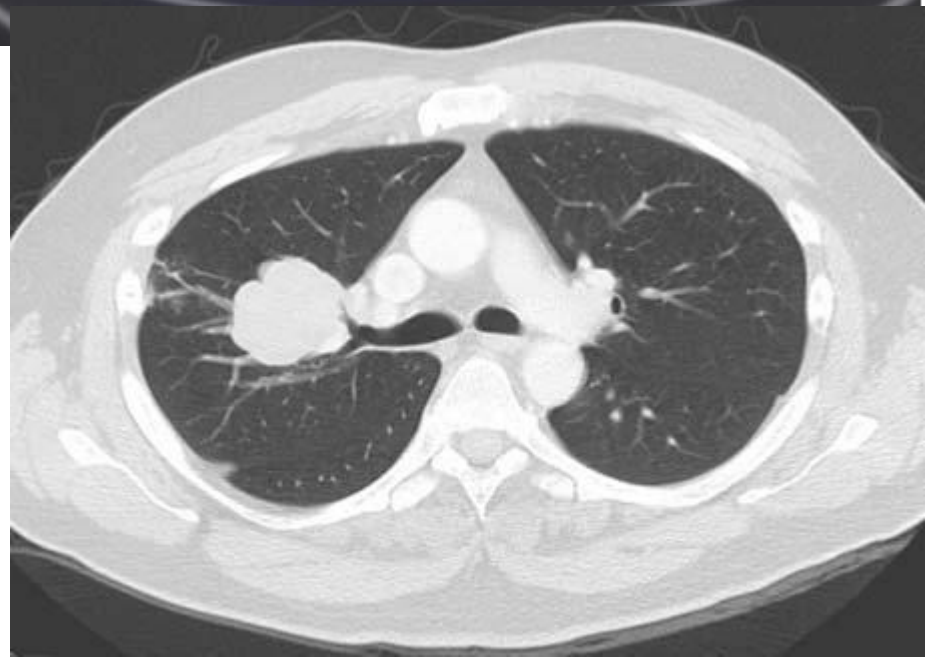
Behandeling: bestraling: indicaties

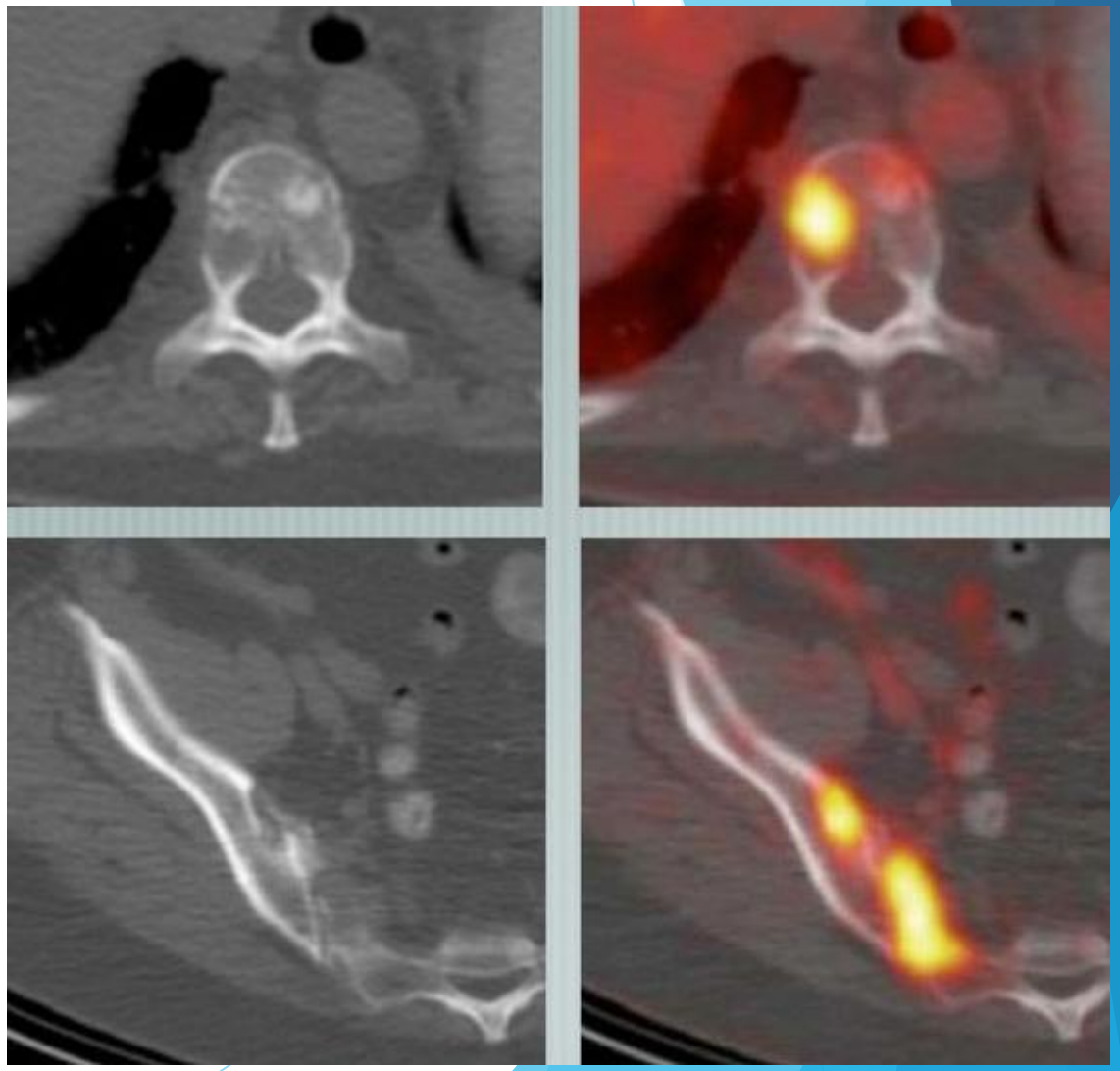
- Rectumtumoren (endeldarm)
  - Stadium II en III (dus T3 en/of N+)
    - Minder plaats in klein bekken
    - Sparen sluitspier
    - Minder kans op lokaal recidief



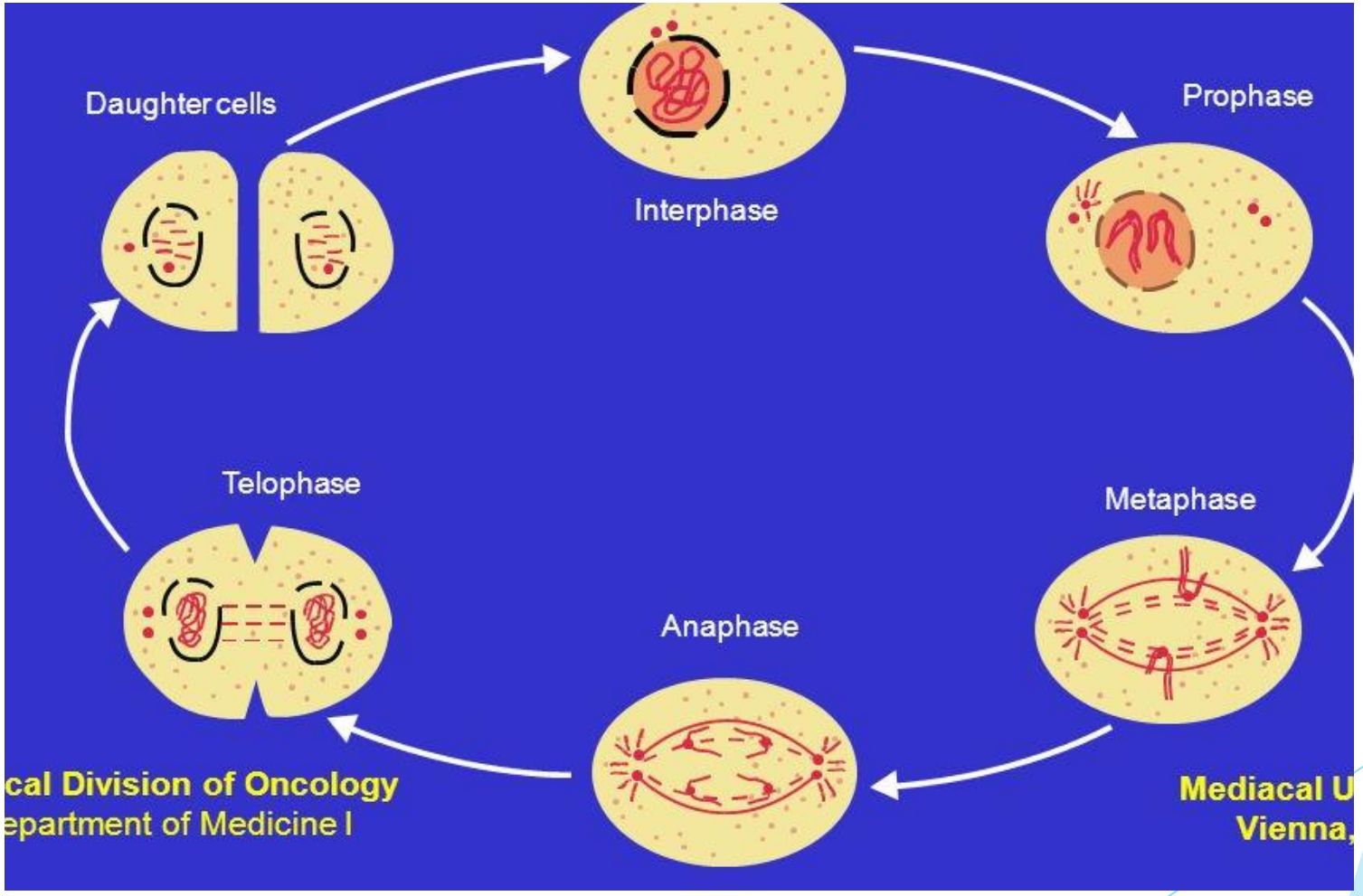
- Uitzaaiingen:
  - Als lokale therapie: enkel zo beperkt tot 1-2 plaatsen
  - Symptoomcontrole of preventief: vb bot, hersen en longmetastasen







Behandeling: chemotherapie



Chemotherapie: doel

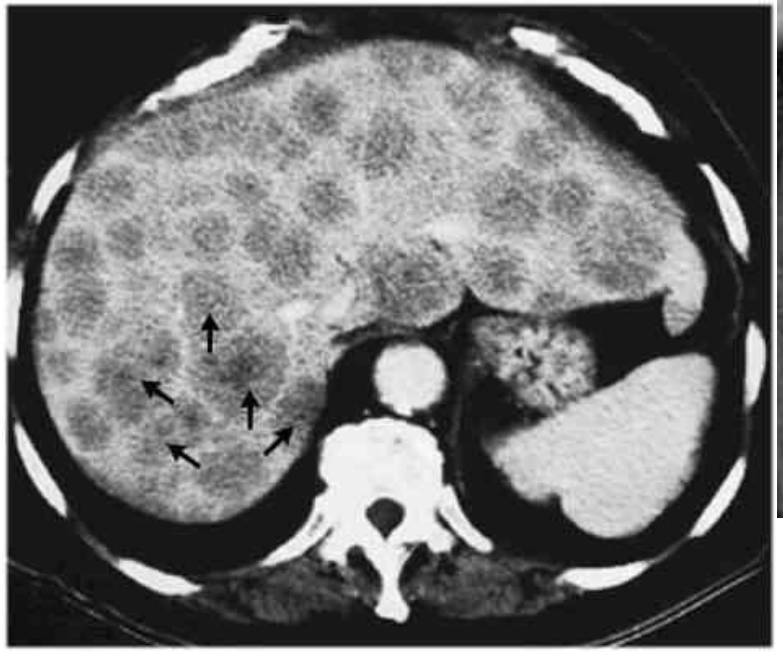
- Genezen
  - Lymfoom, lymfeklierkanker, leukemie
- Controleren
  - Remissie verlengen
  - Kans op herval verminderen
- Palliatie
  - Symptomen verminderen
  - Levenskwaliteit verbeteren

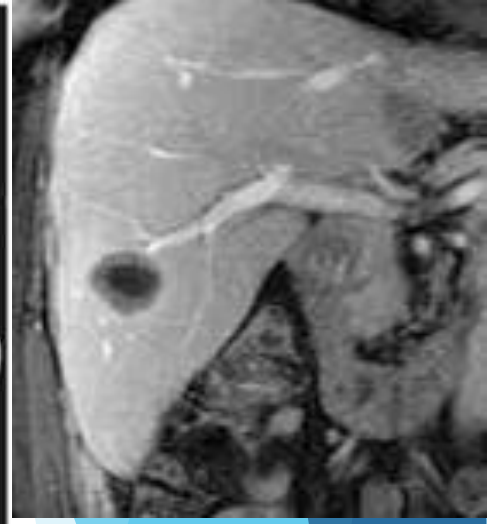
Gevoeligheid van weefsel voor chemotherapie

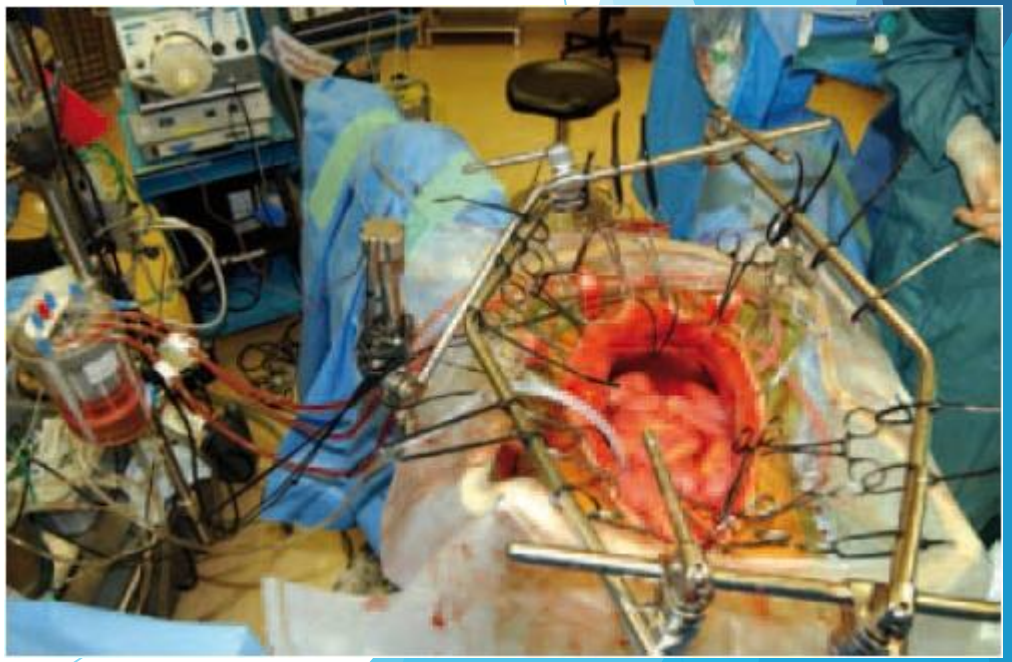
Hoog	Gemiddeld	laag
Lymfoom (lymfeklierkanker)	Borst	Hoofd en hals
Leukemie	Colon	Prostaat
Testis (teelbal)	Long	Maag
		Pancreas (alvleesklier)

Chemotherapie

- Primaire chemotherapie: alleen
  - Stadium IV (niet operabel)
- Adjuvant: na heelkunde
  - Stadium III (N+ of aangetaste klieren)
- Neo-adjuvant: voor heelkunde
  - Rectum of endeldarm: samen met radiotherapie
  - Stadium IV (operabel)
- Concomittant: samen met andere therapie
  - Samen met radiotherapie (endeldarm)
  - Samen met heelkunde (buikvliesuitzaaiingen)







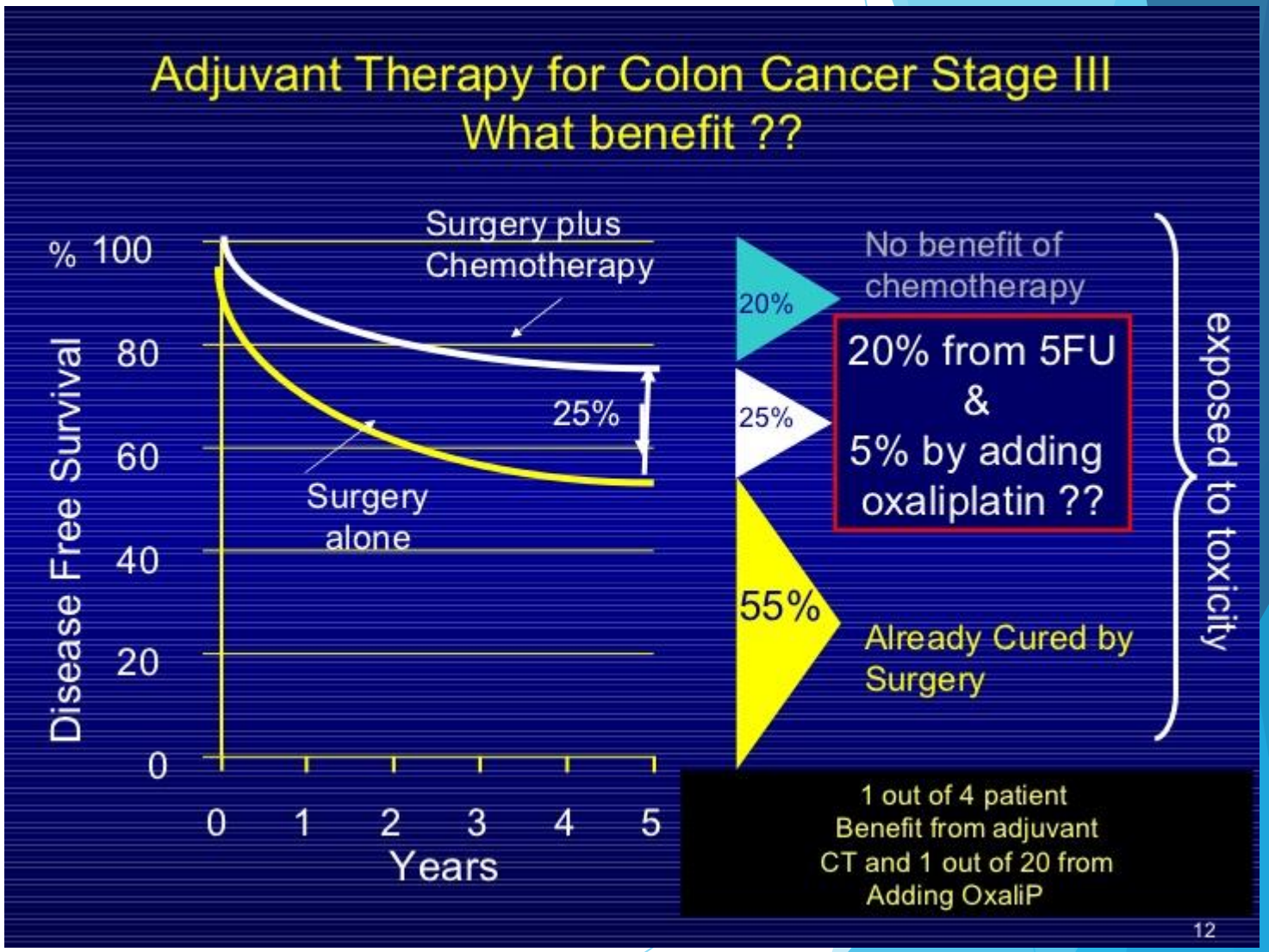
Chemotherapie: dikke darmkanker

- Chemotherapie:
  - Basis: 5 FU
  - Evt samen met
    - Oxaliplatin: FOLFOX
    - Irinotecan: FOLFIRI
    - Oxaliplatin en irinotecan: FOLFIRINOX

- Biological:
  - Avastin
  - Egfr inhibitor (ras status)

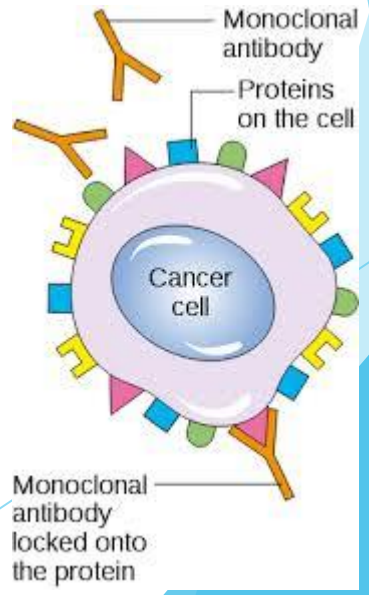
Chemotherapie

- Adjuvant (na chirurgie)
  - Wanneer ?
    - Stadium I: nooit
    - Stadium II: soms
    - Stadium III: altijd
  - Wat?
    - 5FU+oxaliplatin: folfox

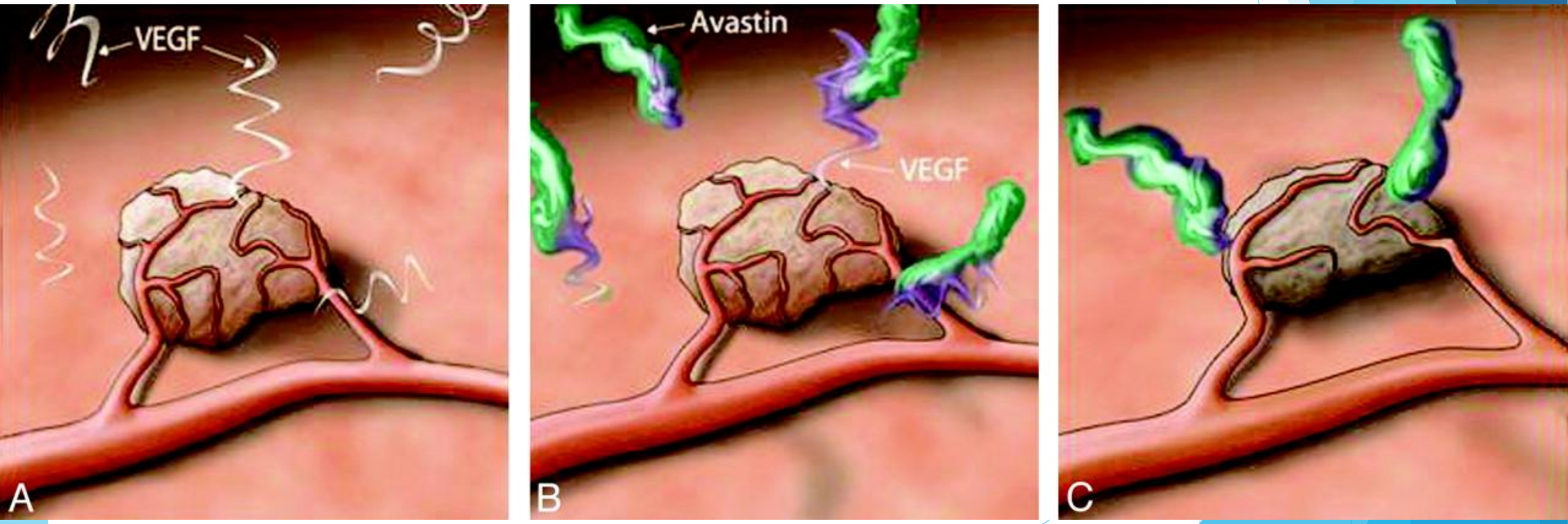


Chemotherapie

- Gemetastaseerd:
  - Chemotherapie:
    - 5FU met oxaliplatin (FOLFOX)
    - 5FU met irinotecan (FOLFIRI)
    - 5FU met oxaliplatin en irinotecan: FOLFIRINOX
  - Gecombineerd met biological
    - Avastin
    - EGFR inhibitor

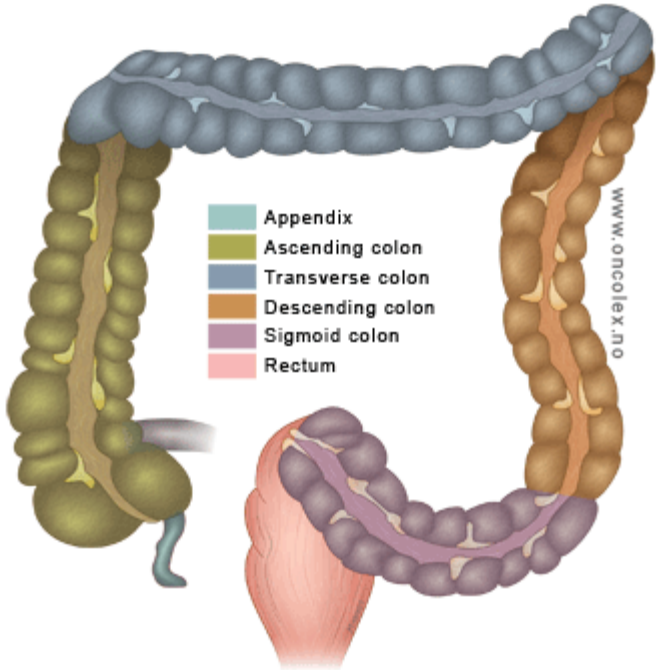


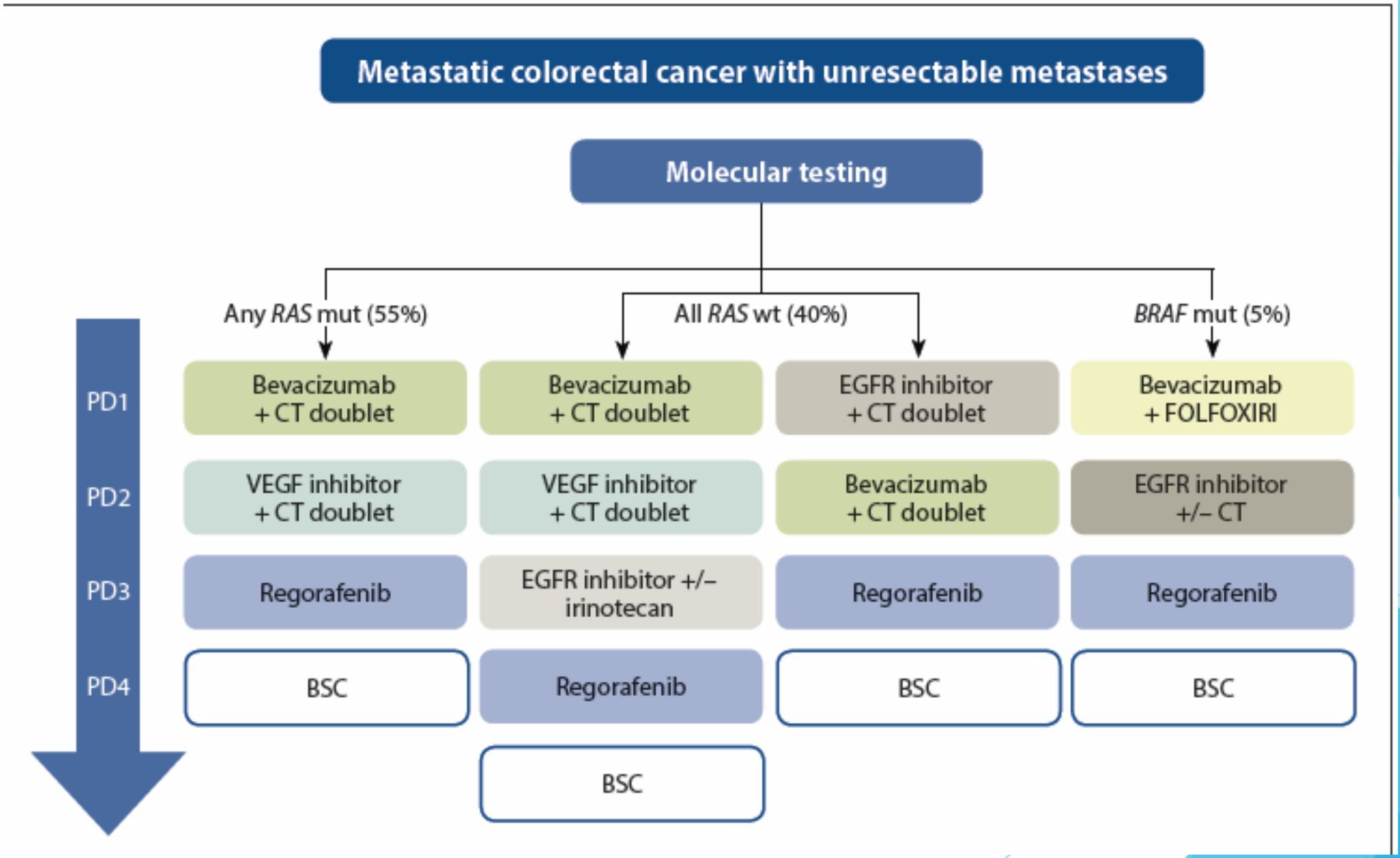
Avastin



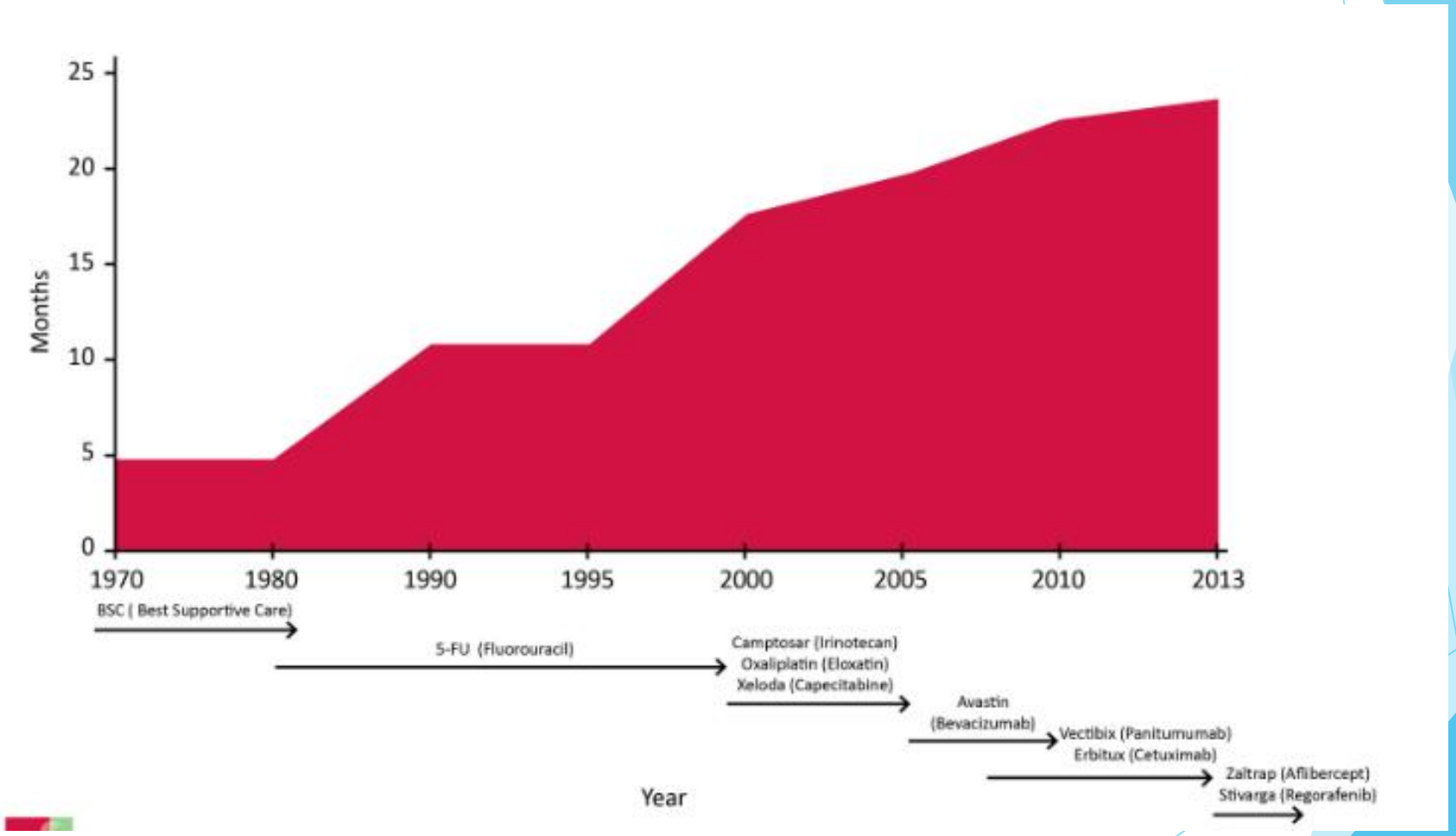
EGFR inhibitor

- Ifv ras status (nras - kras): 40%
- Huidtoxiciteit !!!!
- Linkszijdige tumoren



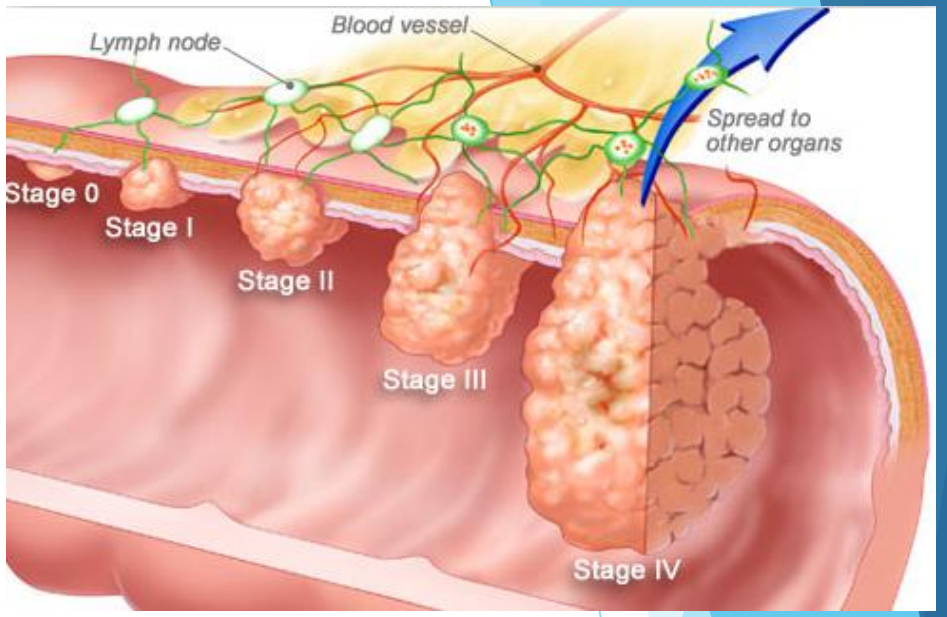

Metastatic colorectal cancer with unresectable metastases
Molecular testing
Any RAS mut (55%)
All RAS wt (40%)
BRAF mut (5%)
PD1
PD2
PD3
PD4
Bevacizumab + CT doublet
Bevacizumab + CT doublet
EGFR inhibitor + CT doublet
Bevacizumab + FOLFOXIRI
VEGF inhibitor + CT doublet
VEGF inhibitor + CT doublet
Bevacizumab + CT doublet
EGFR inhibitor +/– CT
Regorafenib
EGFR inhibitor +/– irinotecan
Regorafenib
Regorafenib
BSC
Regorafenib
BSC
BSC
BSC

chemotherapie



Nevenwerkingen !!

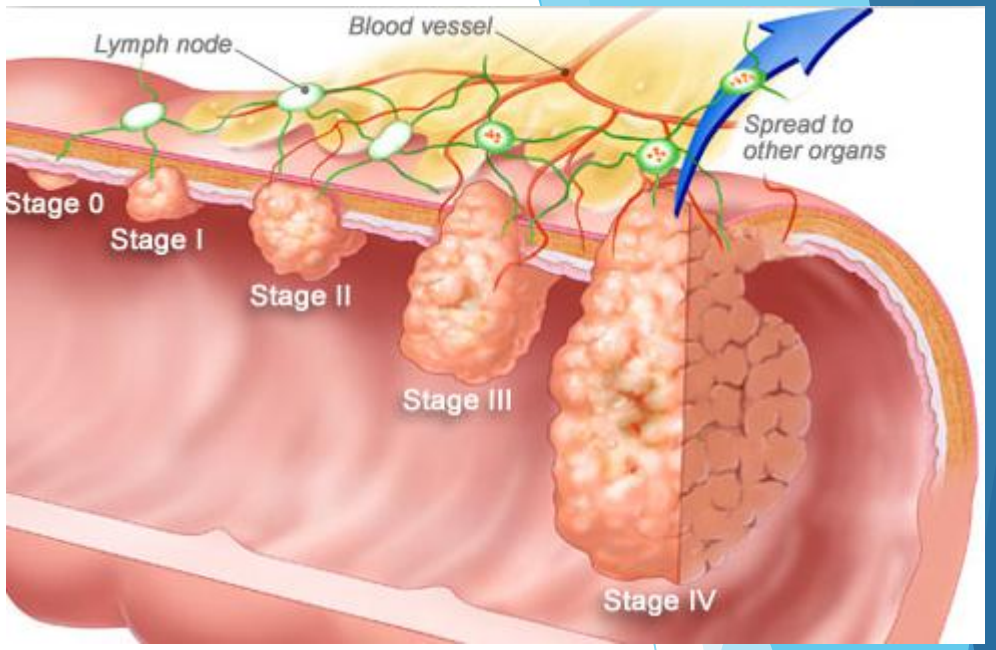
Behandeling



1, colon

- stadium I:
  - heelkunde
- stadium II:
  - heelkunde (evt + chemotherapie zo prognostisch ongunstige kenmerken)
- Stadium III: (pos klieren)
  - 1 heelkunde gevolgd door
  - 2 chemotherapie (FOLFOX)
- Stadium IV: (uitzaaiingen)
  - Chemotherapie (FOLFOX of FOLFIRI) met avastin / egfr inhibitor
  - evt gevolgd door lokale behandeling (radiotherapie of heelkunde zo beperkte ziekte)

Behandeling

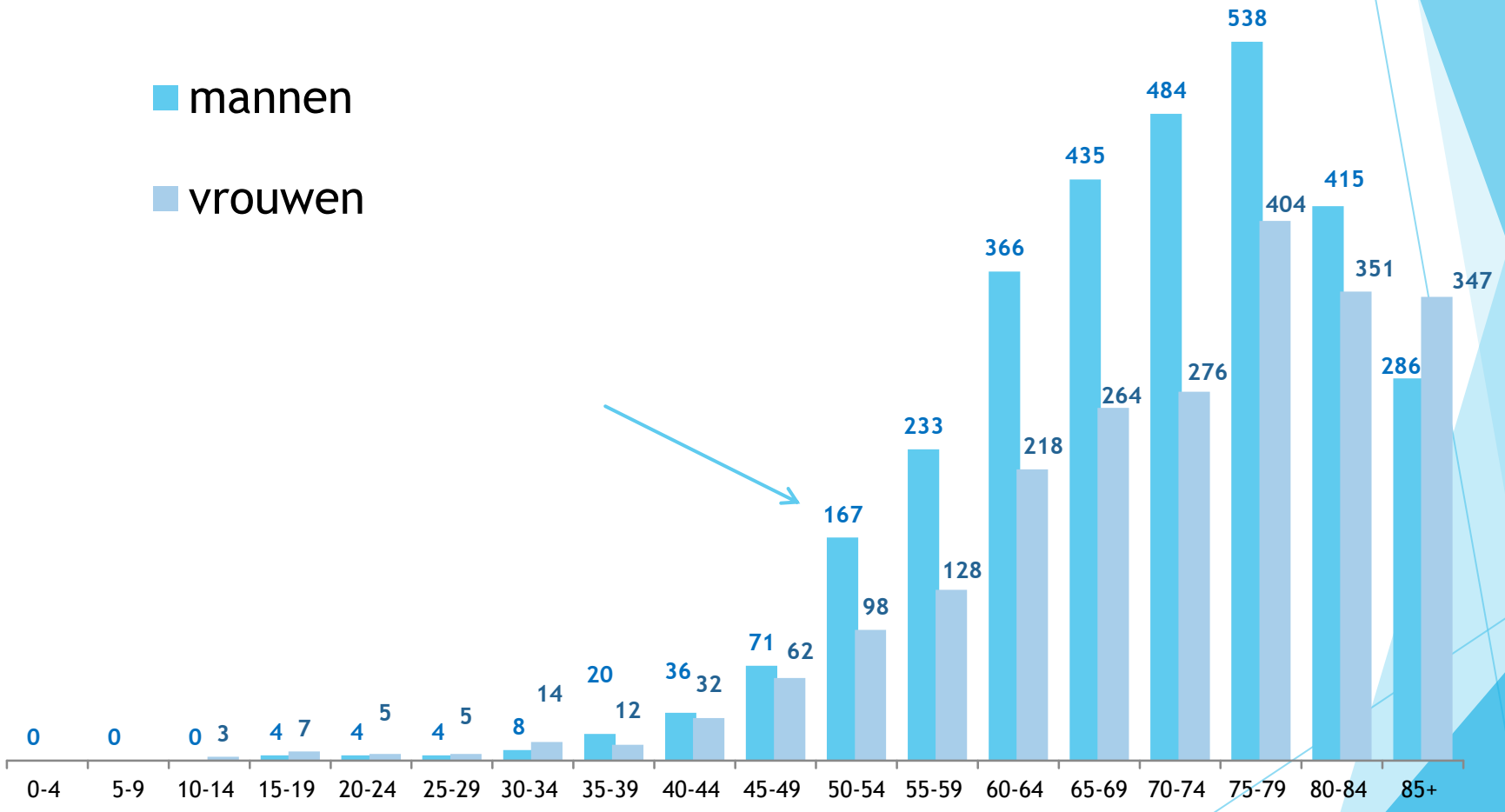


2, rectum (endeldarm)

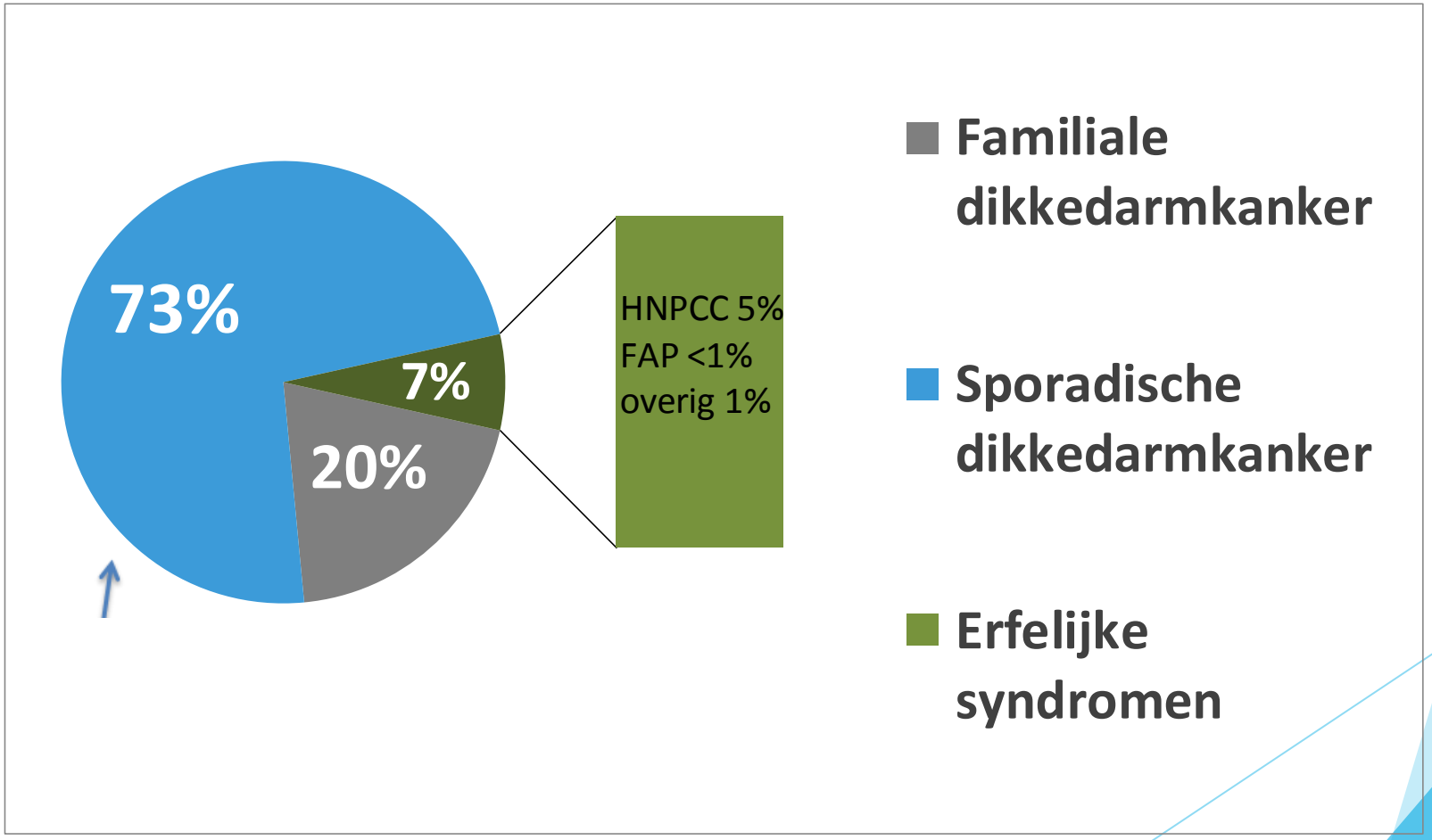
- Stadium I:
  - heelkunde
- Stadium II:
  - heelkunde
  - zo T3 en laag gelegen (dicht bij sfincter): chemoradiotherapie gevolgd door heelkunde
- Stadium III:
  - 1 chemoradiotherapie
  - 2 heelkunde
  - 3 chemotherapie (uitz T0N0)
- Stadium IV:
  - Idem als colon: chemotherapie, evt gevolgd door lokale behandeling
  - Evt radiotherapie zo laag gelegen en klachten (palliatief)

Preventie !!!!!

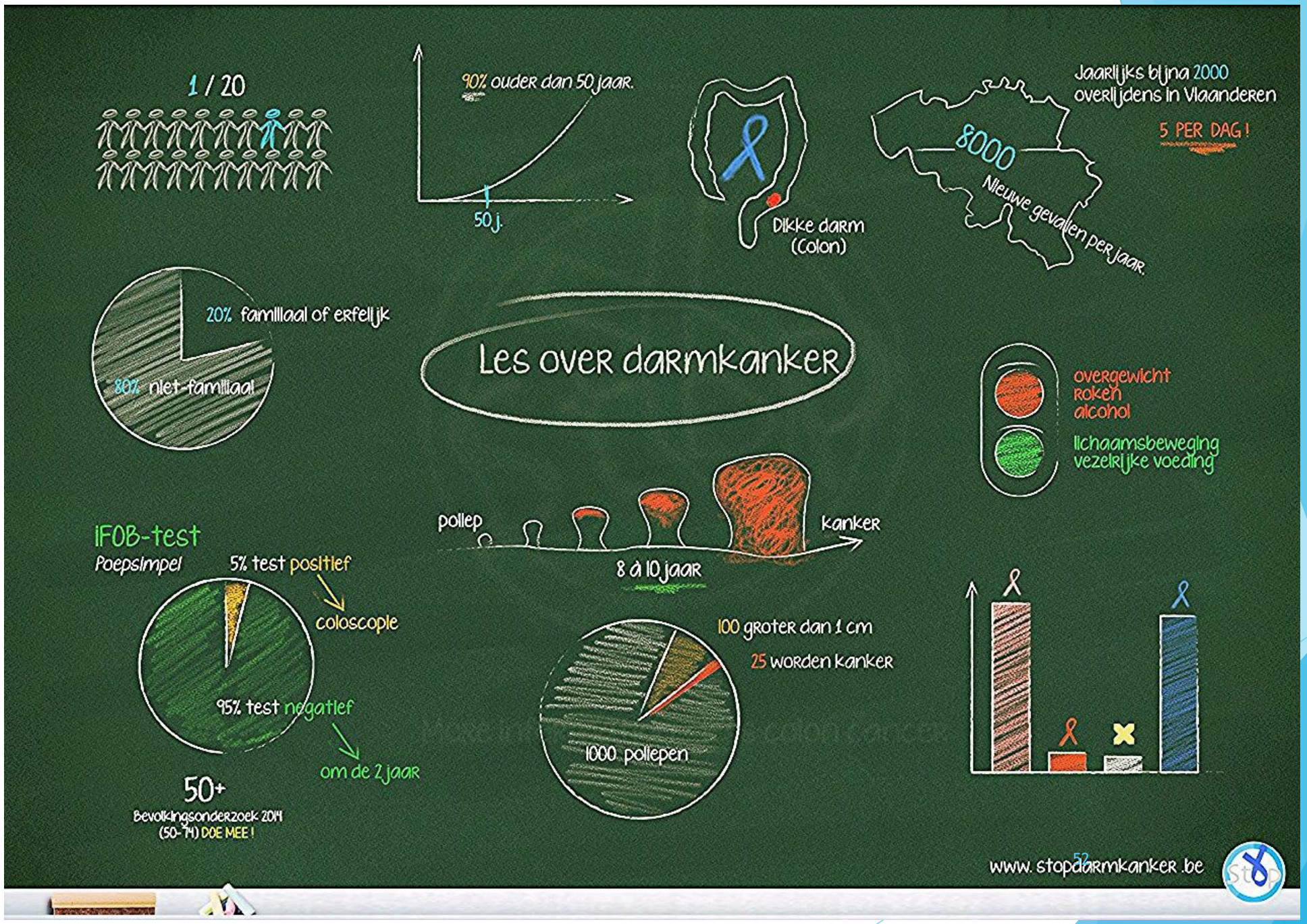
Dikkedarmkanker naargelang leeftijd – Vlaanderen 2011



Preventie - screening



Preventie


1 / 20
90% ouder dan 50 jaar.
50 j.
Dikke darm
(Colon)
Jaarlijks bijna 2000
overlijdens in Vlaanderen
5 PER DAG !
8000
Nieuwe gevallen per jaar.
20% familiaal of erfelijk
80% niet-familiaal
Les over darmkanker
overgewicht
roken
alcohol
lichaamsbeweging
vezelrijke voeding
pollep
kanker
8 à 10 jaar
iFOB-test
Poepsimpel
5% test positief
coloscopie
95% test negatief
om de 2 jaar
50+
Bevolkingsonderzoek 2014
(50-74) DOE MEE !
100 groter dan 1 cm
25 worden kanker
1000 pollepen
www. stopdarmkanker .be

Bedankt voor uw aandacht !!!