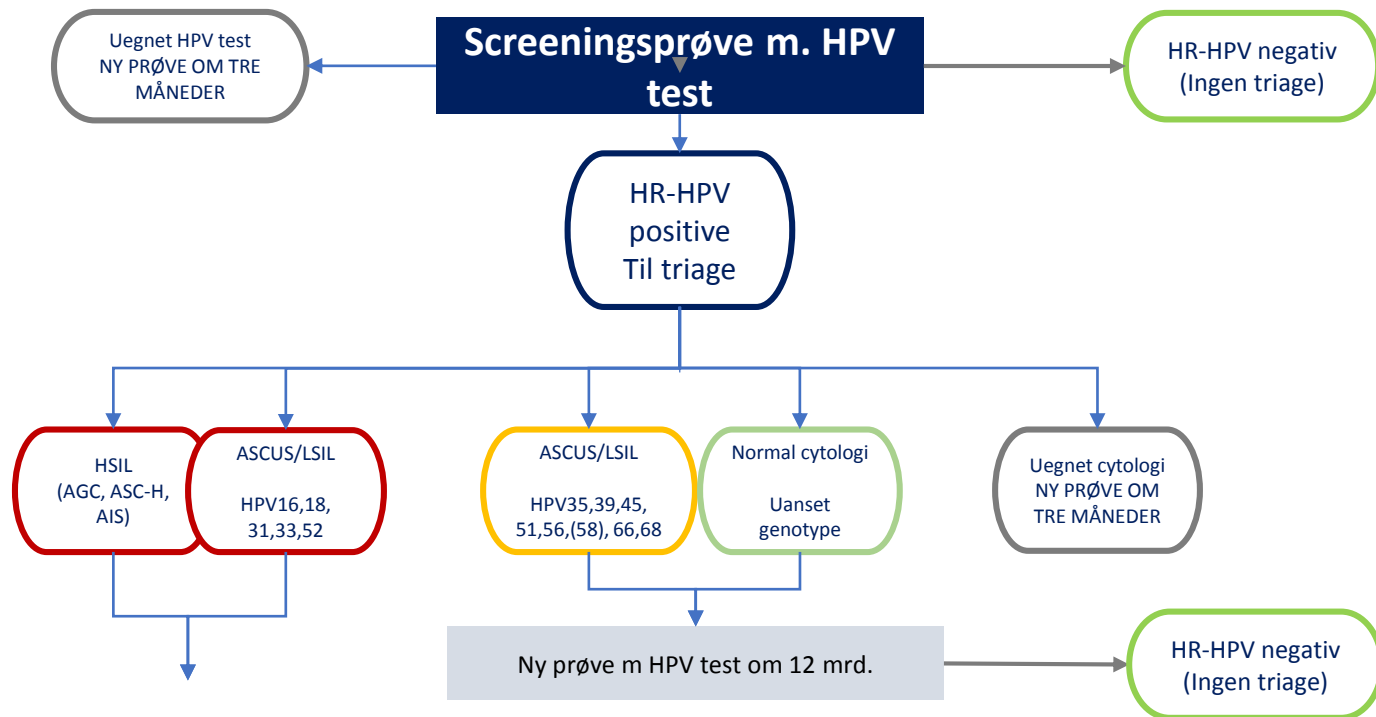


BRUG AF HPV GENOTYPE INFORMATION I SCREENINGSALGORITMER

-RISIKOSTRATIFICERING-



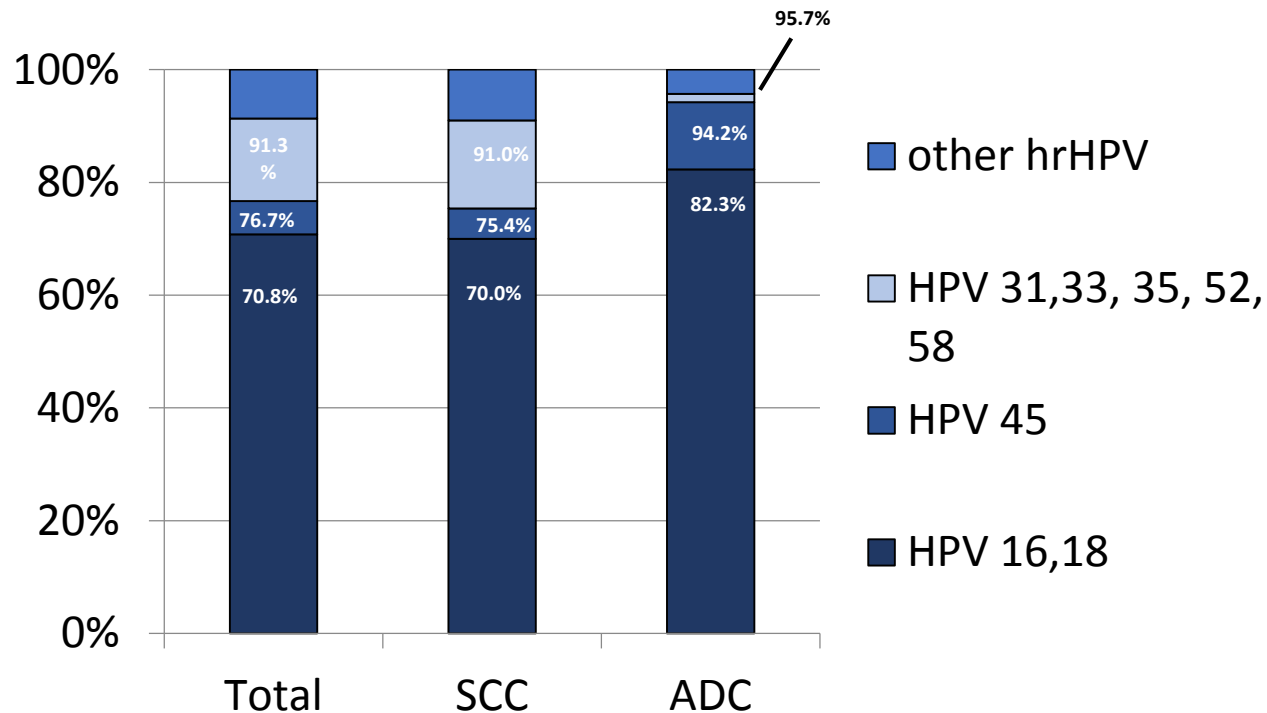
Classification of HPV types by alpha species and carcinogenicity according to IARC Monograph 100B (2012)

Alpha species	Carcinogenic to humans (Group 1)	Probably carcinogenic to humans (Group 2A)	Possibly carcinogenic to humans (Group 2B)		
9	16 31 33 58 52 35		67		
7	18 45 39 59	68	70	85*	97*
5	51		26	82	69*
6	56		53	66	30*
11			73	34*	
HPV genotypes = 12 13 14					
Included in EU/USA HPV IVD assays					

de Sanjose 2010, Smelov IJC 2014

*based on phylogenic analogy to known oncogenic HPV types, but with limited evidence in humans

Contribution of HPV Genotypes to Squamous Carcinoma (SCC) and Adenocarcinoma (ADC) of the Cervix

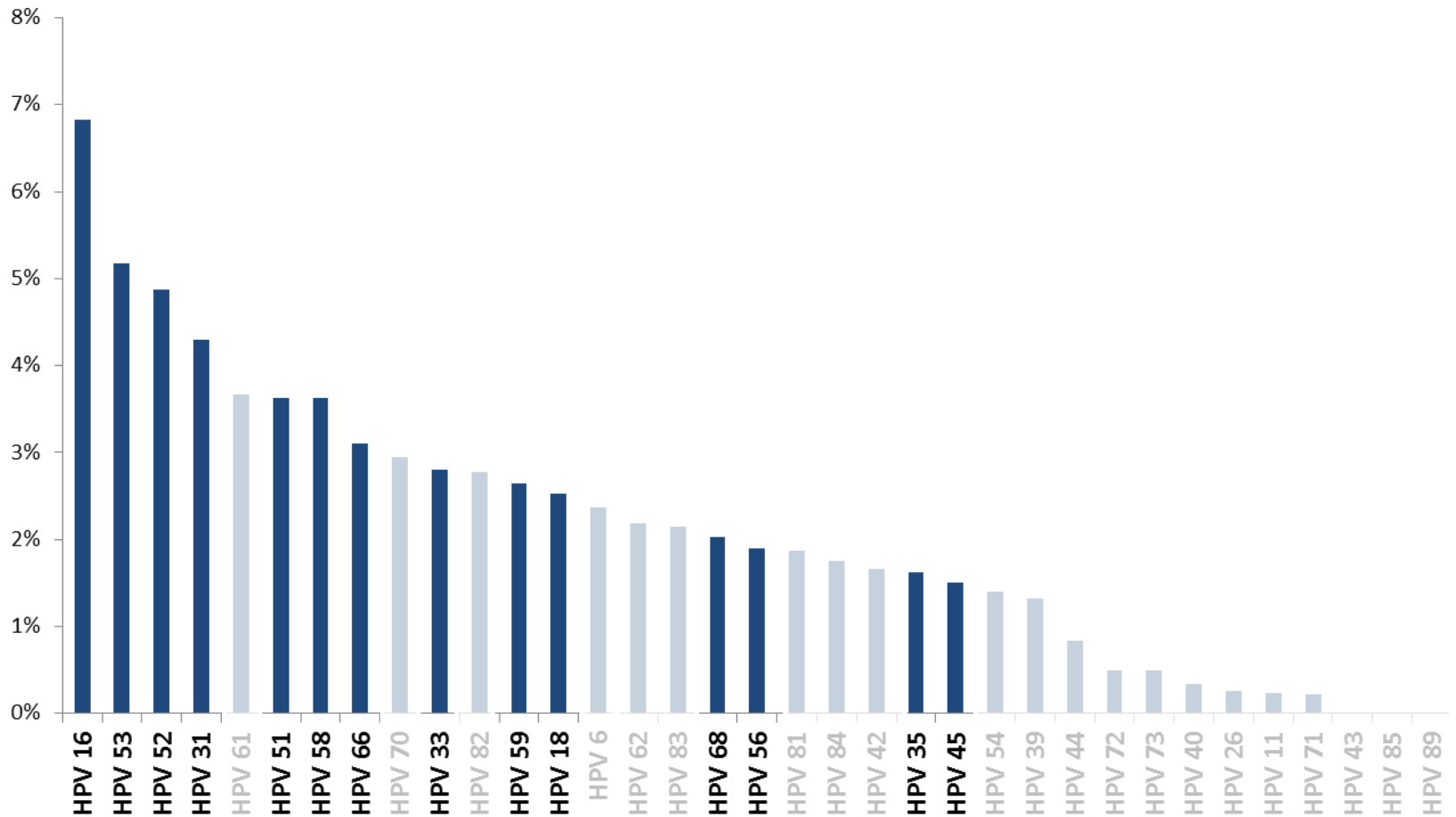


de Sanjose et al. Lancet Oncology (2010)

HPV 45 contributes to:

- 5.9% of total cervical cancer
- 5.4% of squamous cell carcinoma
- 11.9% of adenocarcinoma

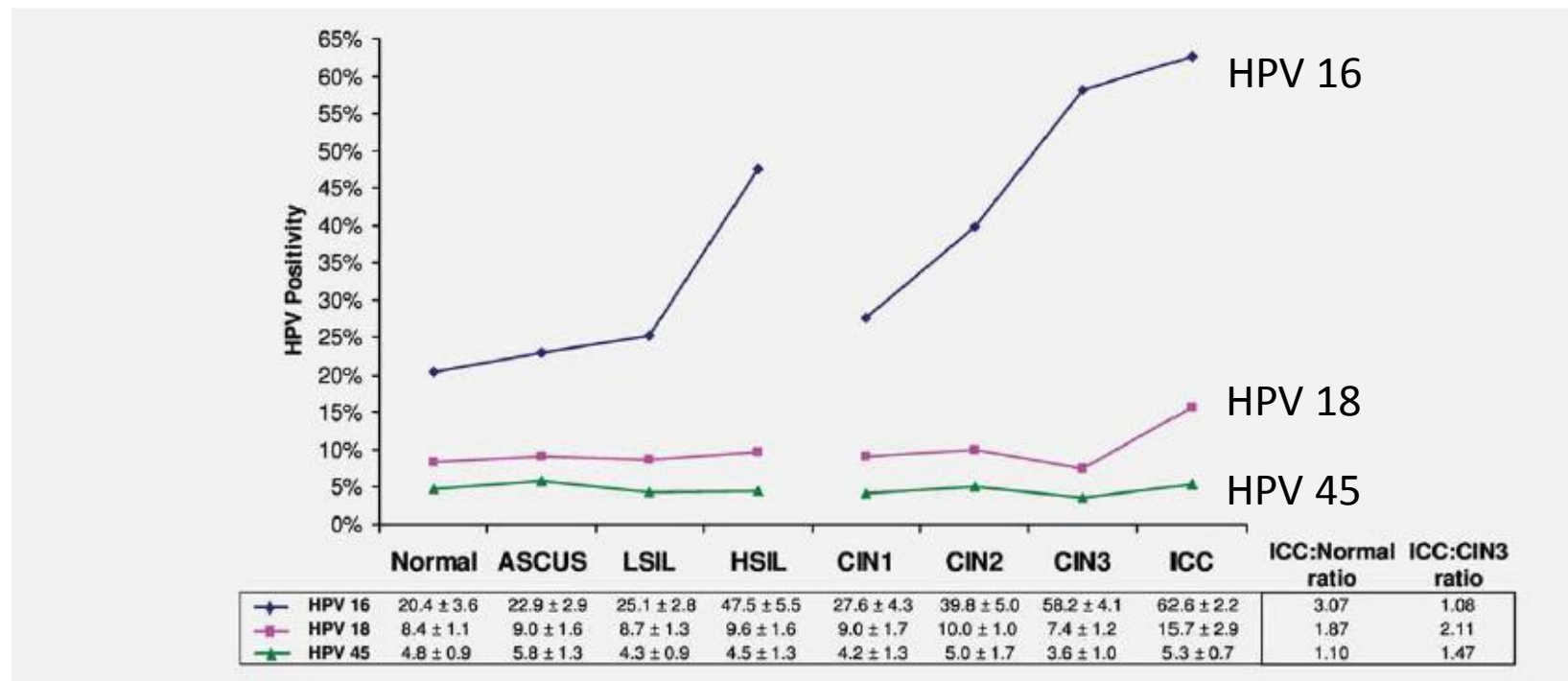
Genotype distribution on 5,064 Danish women



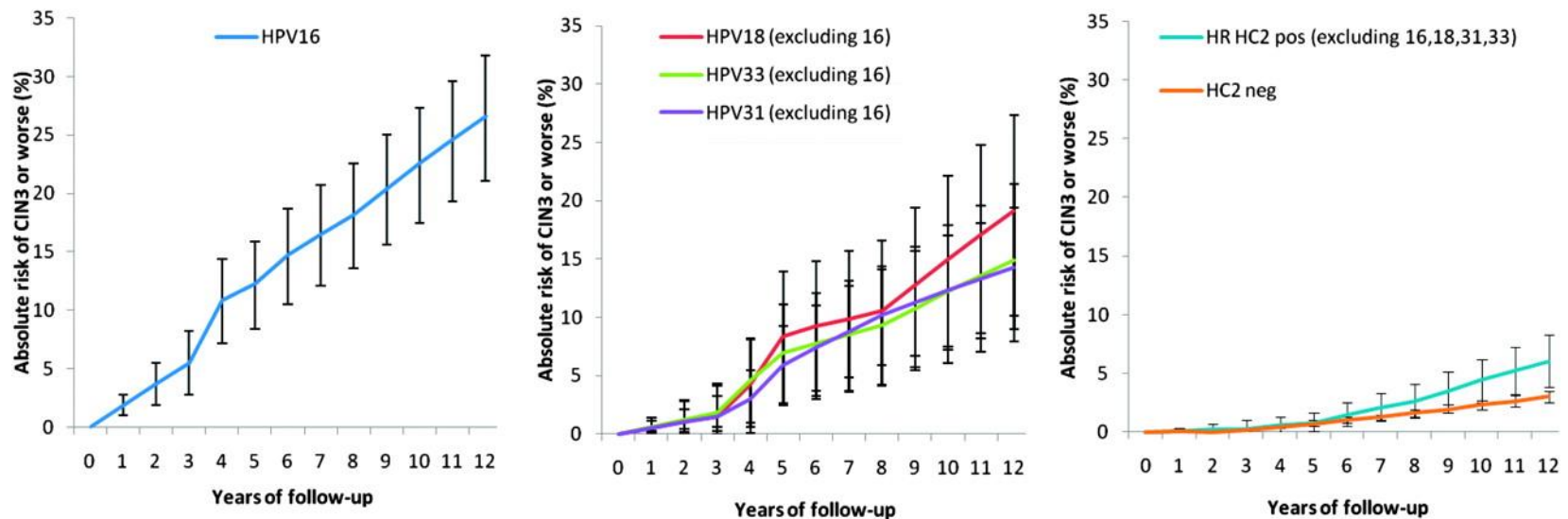
Bonde et al., BMC Inf. Dis. 2014



HPV Genotype Prevalence and Severity of Cervical Dysplasia and Invasive Cervical Carcinoma



Absolute risks of cervical intraepithelial neoplasia grade 3 (CIN3) or worse after infection with different high-risk human papillomavirus (HPV) types in women with normal cytological findings at baseline.



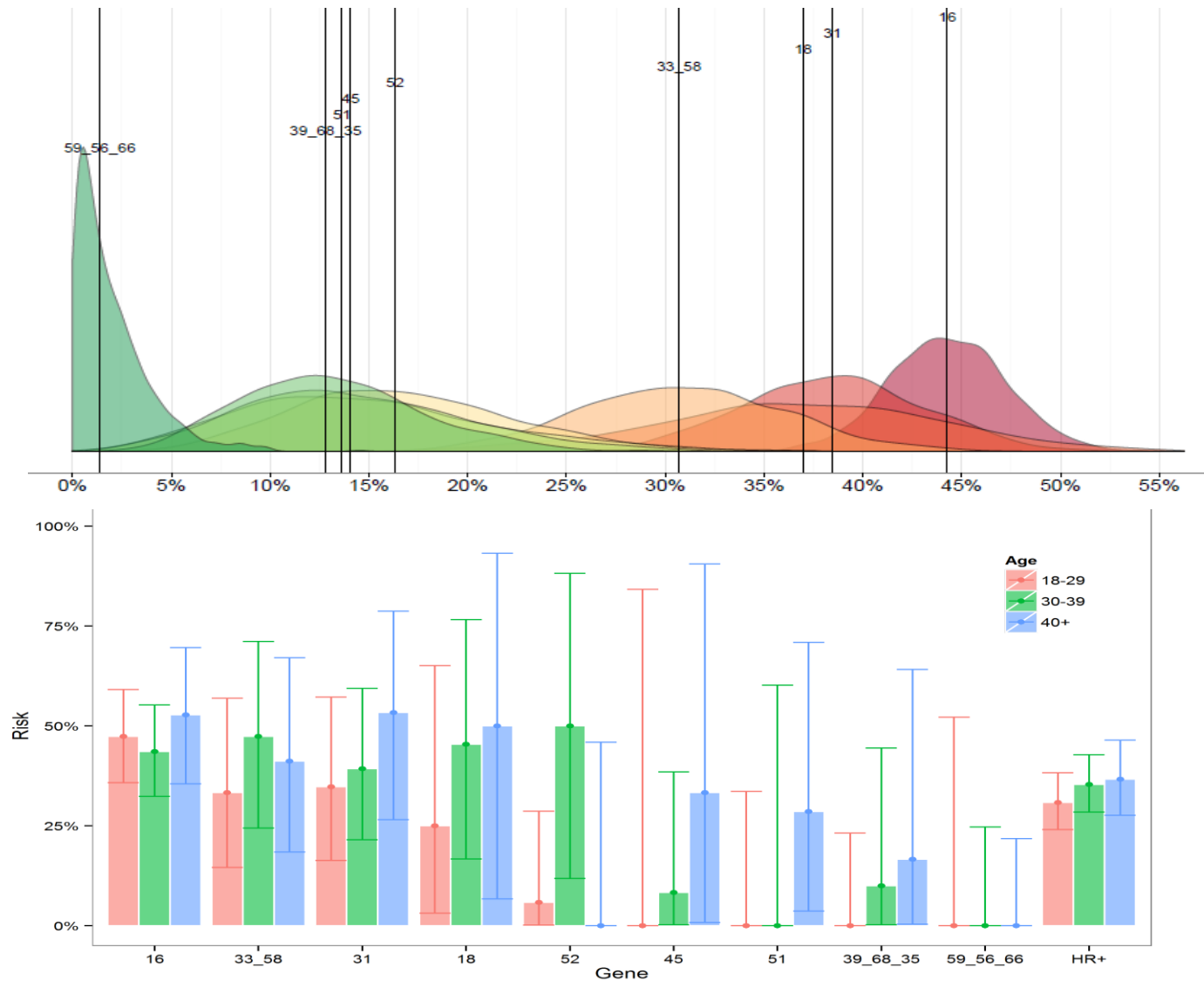
HPV Genotyping and Clinical Actions

HPV Genotype	Cytology Result	Clinical Action
HPV 16	HSIL	LEEP
	All other	Colposcopy
HPV 18, 45	All	Colposcopy
HPV 31,33/58,52	$\geq$ LSIL	Colposcopy
	$\leq$ ASCUS	1 yr re-screen
"Lower 7"	HSIL	Colposcopy
	All other	1 yr re-screen

Schiffman et al. Intl J Cancer (2016)

Predictive Value of HPV Genotype in women with positive screening findings

RISK of $\geq$ CIN3



Systematic review on risk stratification by HPV genotype

Studies of women receiving cervical cancer screening, with extended genotyping test and a clinical endpoint of $\geq$ CIN2/CIN3											
Article	Study type	N	HPV genotype assay	NILM	ASC-US	LSIL	ASC-US /LSIL	all	Study Years	Follow-up duration (years)	Country
Monsonogo 2015 GO	Post-hoc ATHENA clinical trial	40901	Linear Array	√				√	2008-2009	baseline	USA
unpublished raw data	clinical trial	33858	Onclarity	√	√	√		√	2014-2018	baseline	USA
Schiffman 2015 JCM	KPNC screening Retrospective	4602	Linear Array	√					2007-2011	1.3	USA
Berkhof 2006 CEBP	Prospective RCT	21996	GP5+/6+ PCR	√			√		1999-2002	1.5	Netherlands
Wheeler 2006 JID	Post-hoc ALTS clinical trial	5060	L1 PCR				√		1996-2000	2	USA
Wheeler 2014 IJC	Screening Registry Retrospective	47541	Linear Array	√	√	√		√	2007-2009	3	USA
Schiffman 2016 IJC	KPNC screening Retrospective	8664	Onclarity	√			√	√	2003-2014	3.5	USA
Schiffman 2015 GO	KPNC screening Retrospective	1903	Onclarity		√				2003-2014	3.6	USA
Naucler 2007 BrJC	Prospective SWEDESCREEN	5696	GP5+/6+ PCR	√					1997-2002	4.1	Sweden
Kitchener 2014 NHR	Prospective cohort screening	8873	Roche LBA & LA					√	2007-2013	6	England
Thomsen 2015 IJC	Prospective cohort	33288	INNO-LiPA	√					2002-2014	8	Denmark
Kjaer 2010 JNCI	Prospective cohort	7482	line probe	√					1991-1993	13.4	Denmark
Smelov 2015 IJC	Prospective SWEDESCREEN	11683	GP5+/6+ PCR					√	1997-2014	14	Sweden
		231547									

Bonde, Sandri, Schiffman, Andrews, J Low Gen Trac Dis, 2019

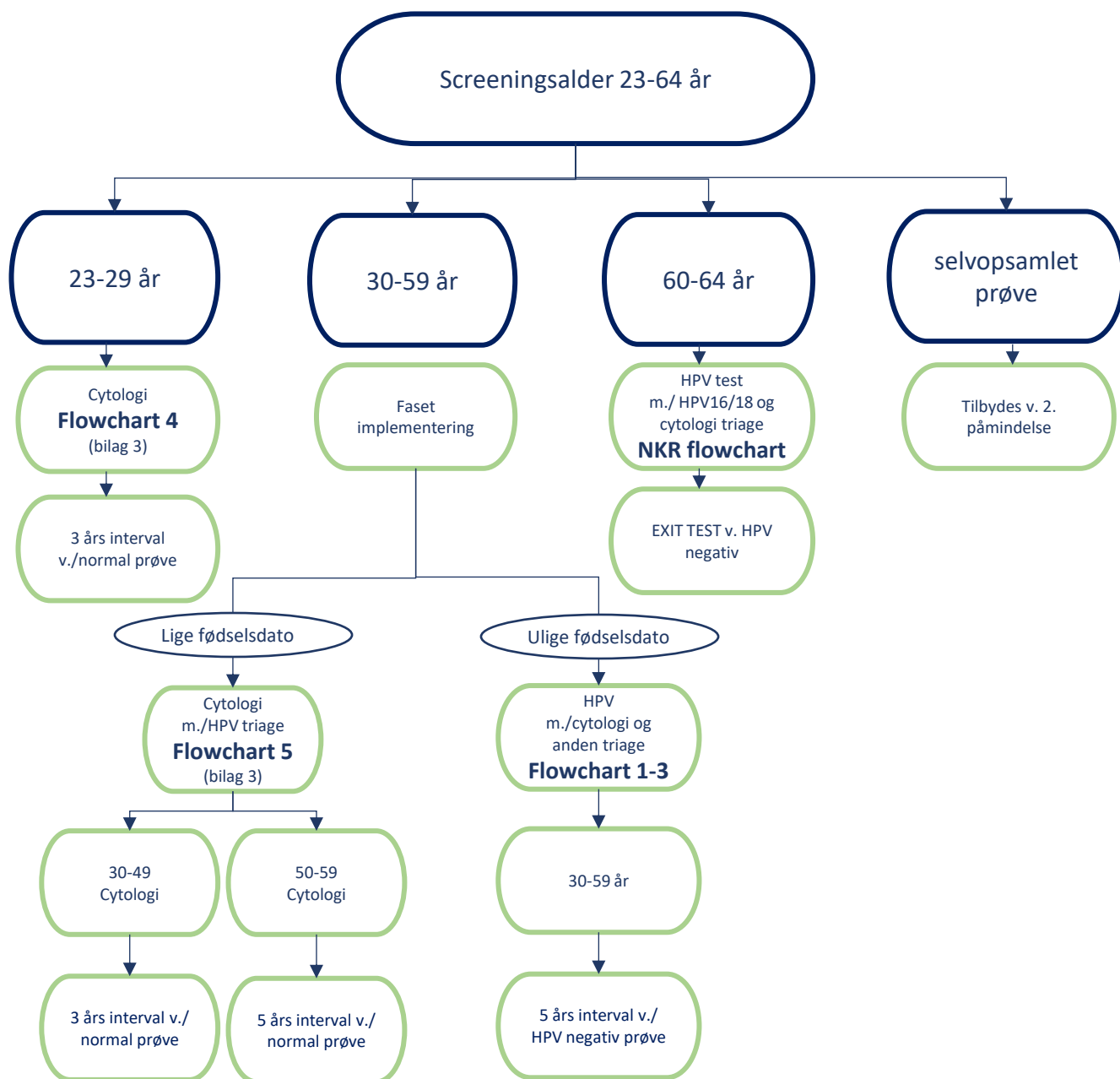
NSLS

NSLS

Bilag 2

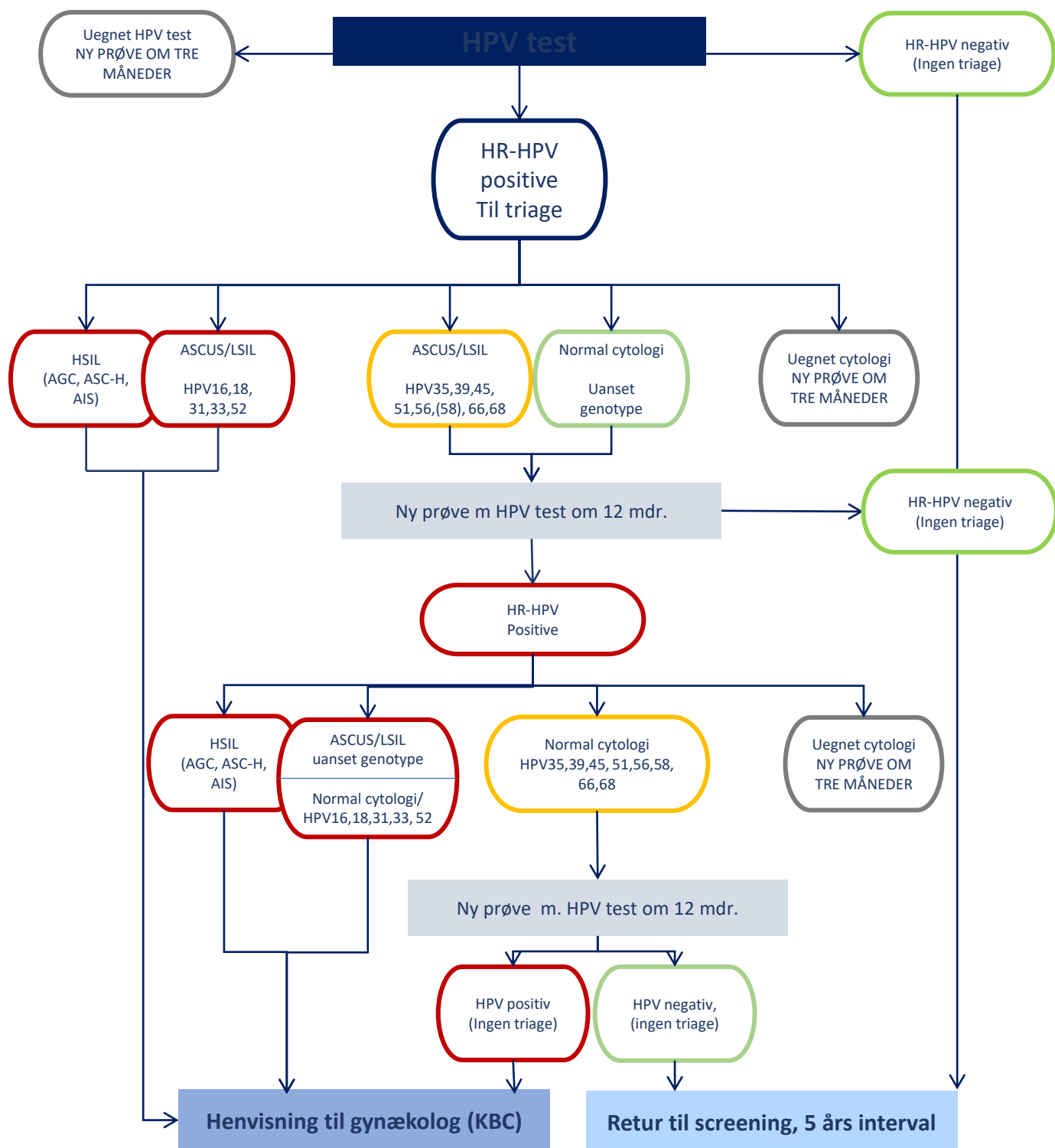
Screening for Livmoderhalskræft - 2018 Retningslinjer

Oversigt screeningsalgoritmer



HPV screening : 30-59 år.

Triage: Cytologi og udvidet genotypning



Note: Det er ikke alle HPV platforme der kan skelne mellem HPV 33 og HPV 58. I de tilfælde vil HPV 58 i praksis blive henvist til gynækolog.

Forkortelser:

ASCUS: Atypisk pladeepitel af ukendt betydning

LSIL: Let grad af pladeepitelforandring

ASC-H: Atypiske pladeepitelceller, muligt HSIL

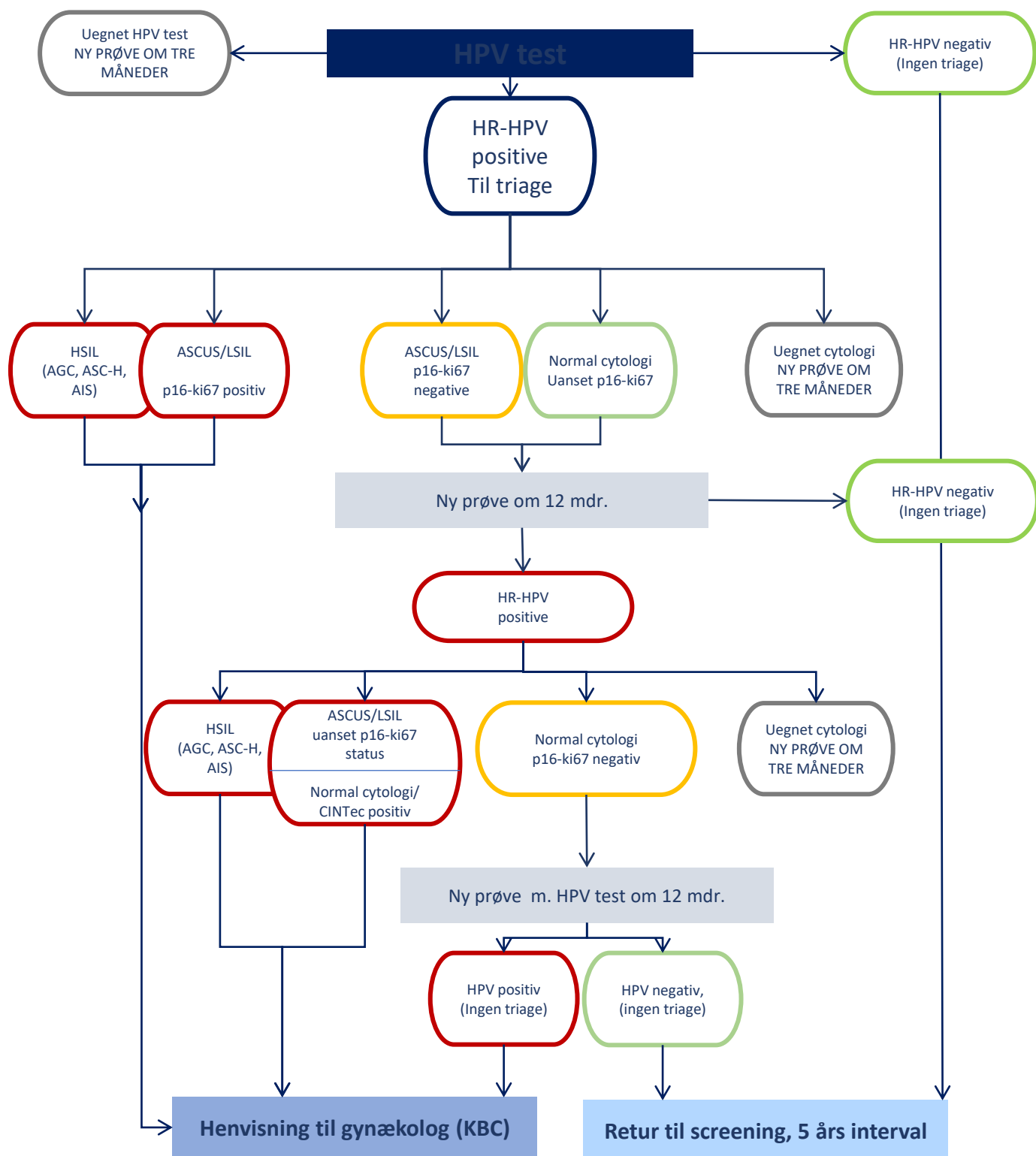
AGC: Atypiske cylinderepitelceller

AIS: Adenokarcinom in situ

HSIL: Svær grad af pladeepitelforandring

HPV screening: 30-59 år.

Triage : Cytologi og p16-ki67



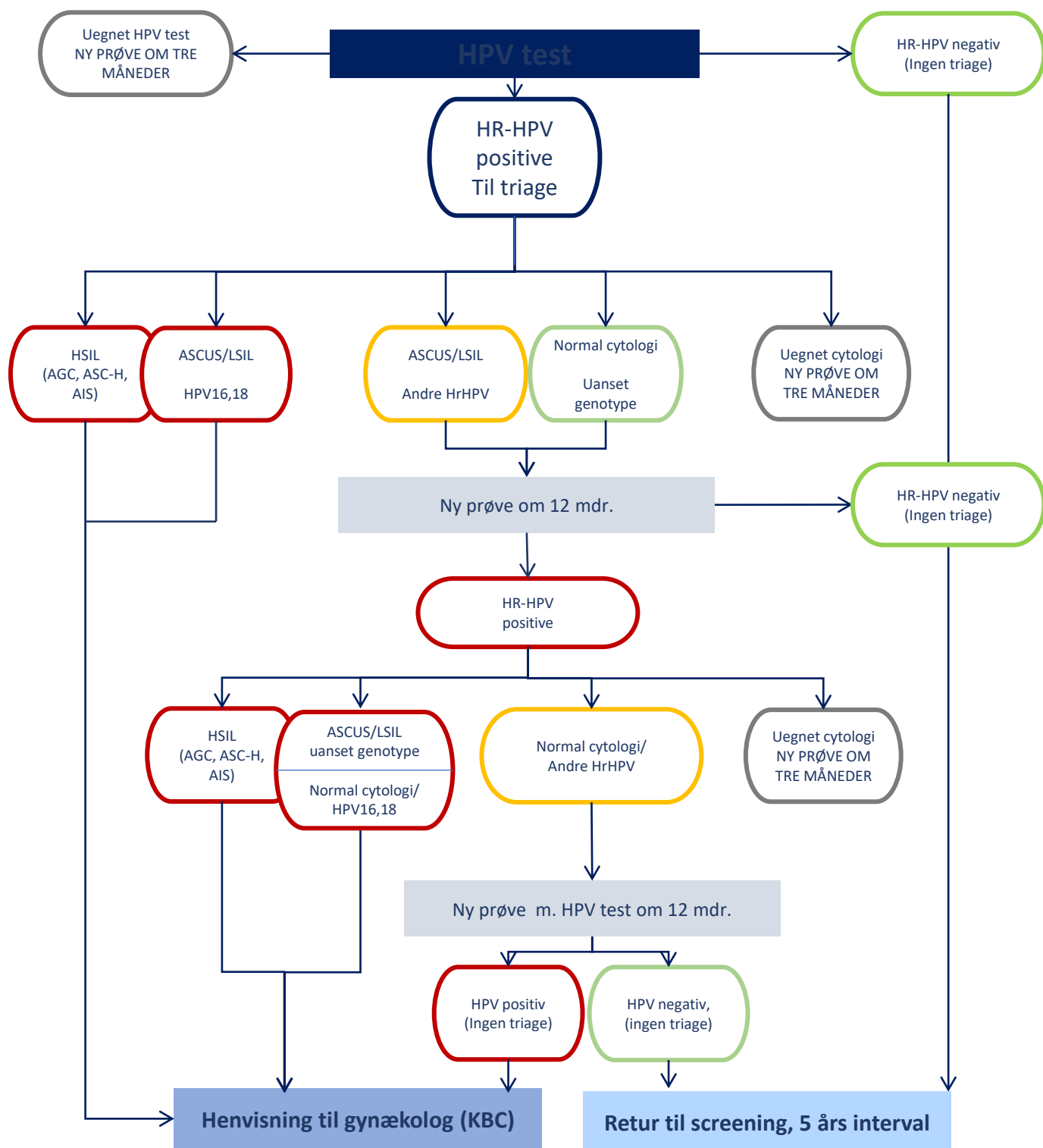
Forkortelser:

ASCUS: Atypisk pladeepitel af ukendt betydning
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AGC: Atypiske cylinderepitelceller
 AIS: Adenokarcinom in situ
 HSIL: Svær grad af pladeepitelforandring

HPV screening: 30-59 år.

Triage: Cytologi og standard genotypning



Forkortelser:

ASCUS: Atypisk pladeepitel af ukendt betydning

LSIL: Let grad af pladeepitelforandring

ASC-H: Atypiske pladeepitelceller, muligt HSIL

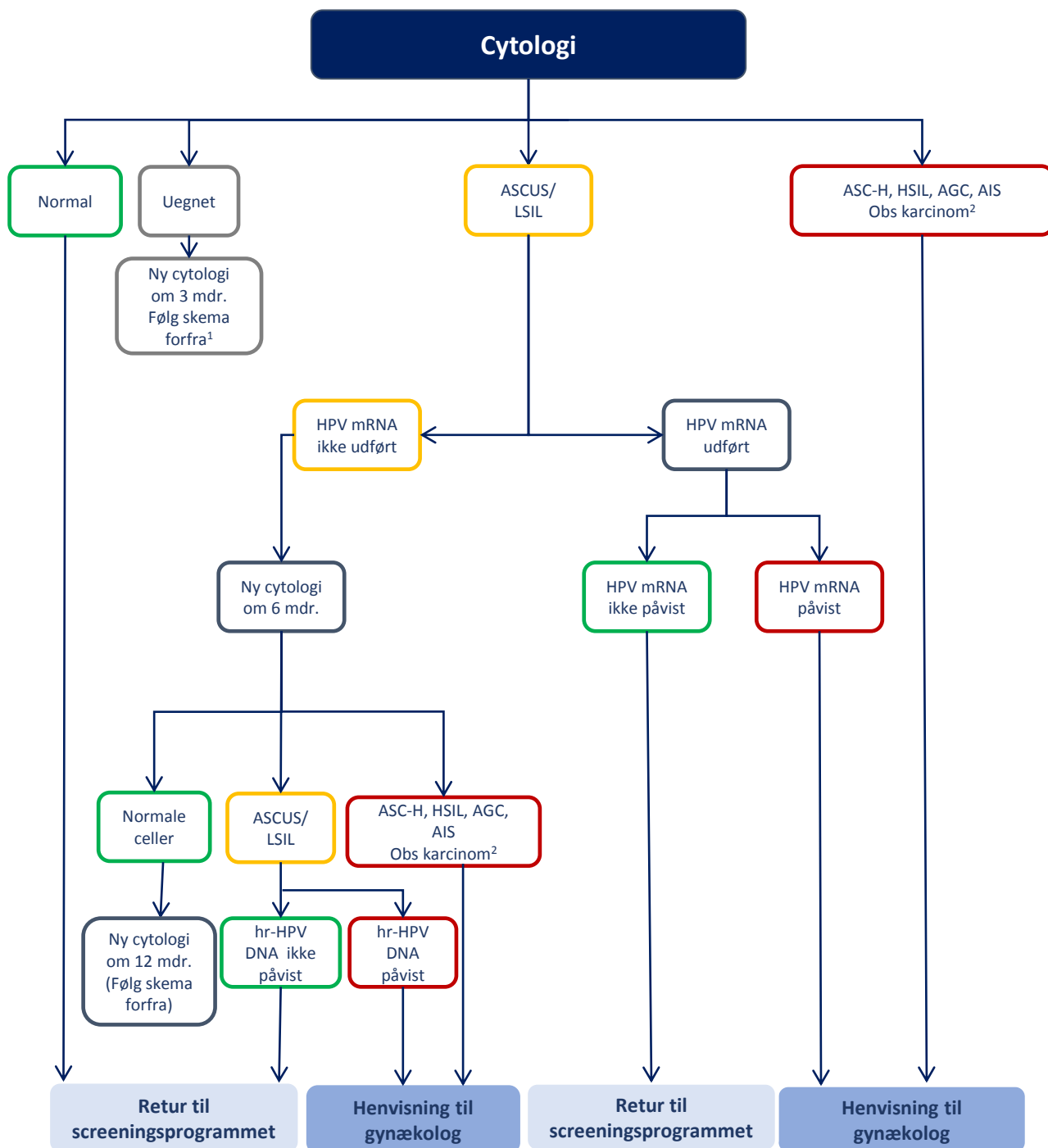
AGC: Atypiske cylinderepitelceller

AIS: Adenokarcinom in situ

HSIL: Svær grad af pladeepitelforandring

UDKAST

Bilag 3

**Noter:**

1: Ny prøve inden 3 mdr. og ved gentagen uegnet prøve tilrådes henvisning til gynækolog

2: Cytologi eller histologi fra livmoderhalsen med mistanke om carcinom skal medføre henvisning iht. kræftpakkeforløb
https://www.sst.dk/da/sygdom-og-behandling/kraeft/pakkeforloeb/~/_media/C2FFDC70A66949BCABF54F20C9F345FA.ashx

Forkortelser:

ASCUS: Atypisk pladeepitel af ukendt betydning

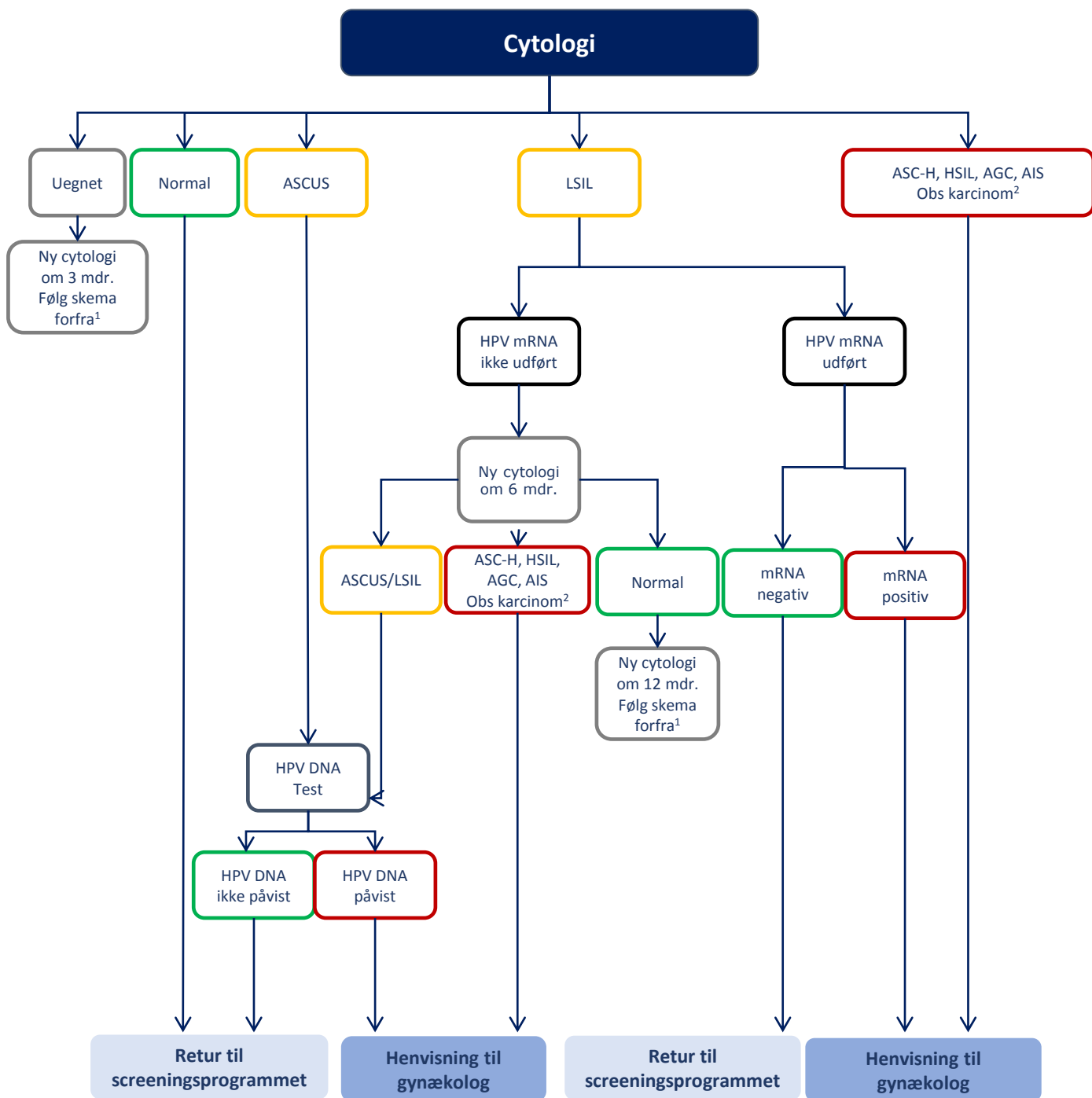
LSIL: Let grad af pladeepitelforandring

ASC-H: Atypiske pladeepitelceller, muligt HSIL

AGC: Atypiske cylinderepitelceller

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(<https://www.sst.dk/da/sygdom-og-behandling/kraeft/pakkeforloeb/~media/C2FFDC70A66949BCABF54F20C9F345FA.ashx>)

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