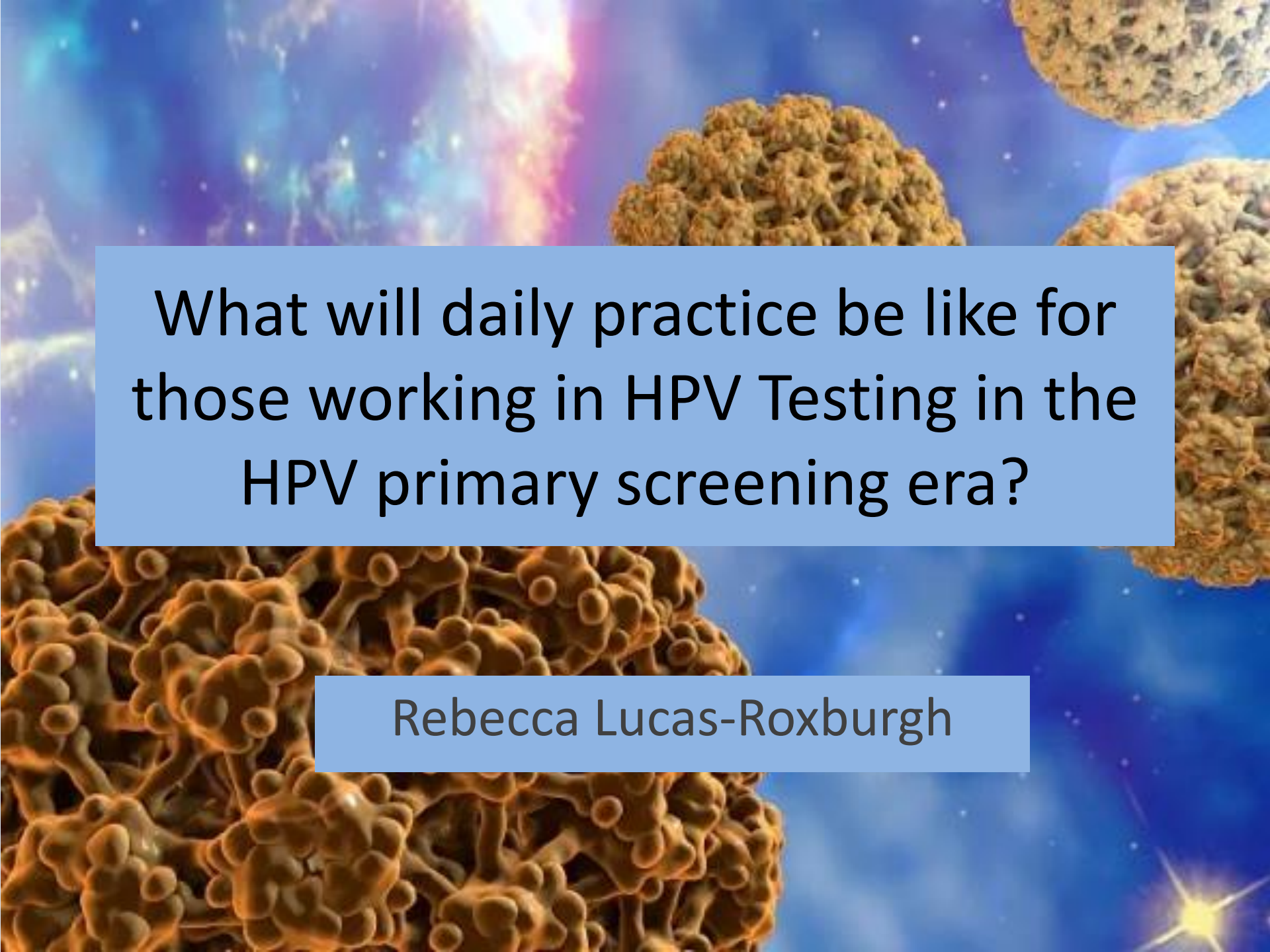
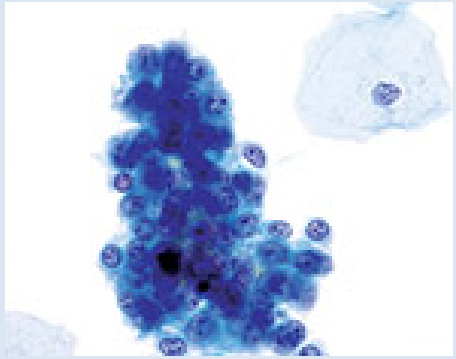
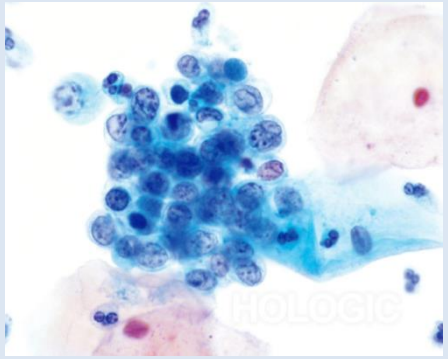
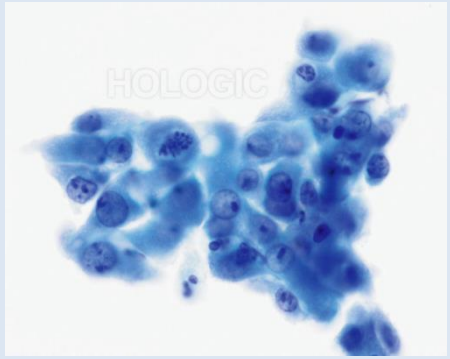
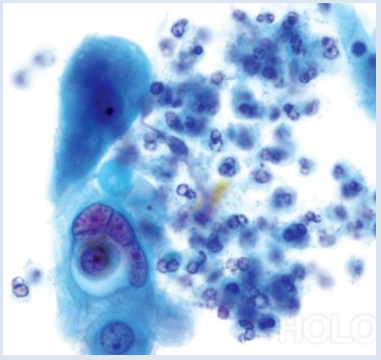


What will daily practice be like for those working in HPV Testing in the HPV primary screening era?

Rebecca Lucas-Roxburgh

Cervical screening with cytology

- NCSP established in 1991 as a coordinated national programme
- Significant reduction in cervical cancer incidence and mortality since then
- However cytology is a highly interpretive test and suffers from low sensitivity

HPV as a primary test

- Advantages:
  - Higher sensitivity than cytology for pre-cancerous lesions
  - Higher negative predictive values
  - Can safely have longer screening intervals
- The Athena trial:
  - One in four women who are HPV 16 positive will have cervical disease within three years
  - Nearly 1 in 7 women with normal Pap cytology who were HPV 16 positive actually had high-grade cervical disease that was missed by cytology.
  - Sensitivity for CIN3 of
    - cytology – 53%,
    - HPV primary – 92%

Who's already done it

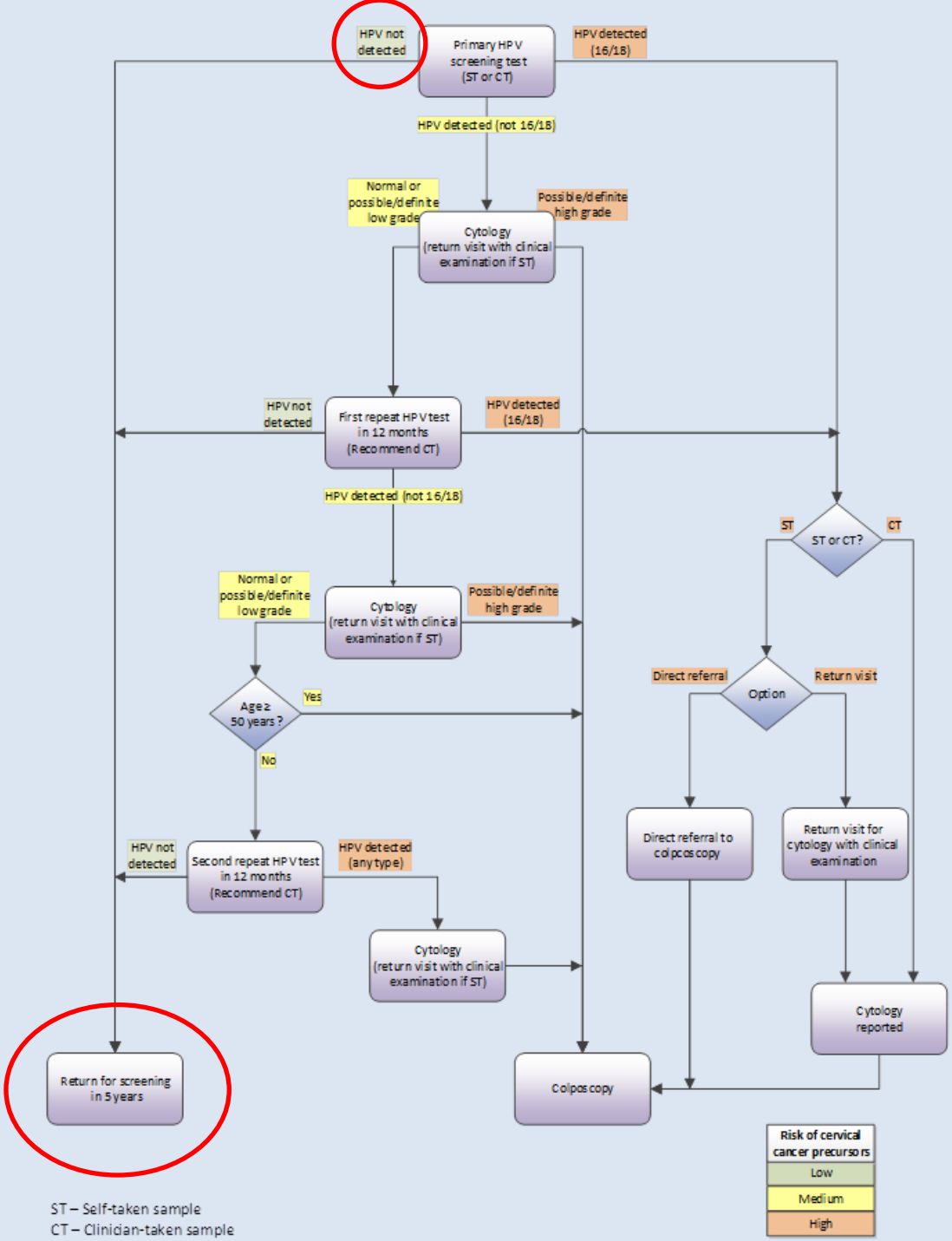
- Australia
  - Changed December 1, 2017
  - 5 yearly HPV test replaced 2 yearly smear
  - 25-74 age range
- England
  - Changed December 2019
  - 25-64 age range
  - 3 yearly HPV test for 25-49 year olds, 5 yearly for 50-64 year olds
- Scotland
  - Changed March, 2020
  - 5 yearly HPV test
  - 25-64 age range
- Netherlands
  - Changed January 2017
  - 5 yearly HPV test
  - 30-60 age range

In New Zealand

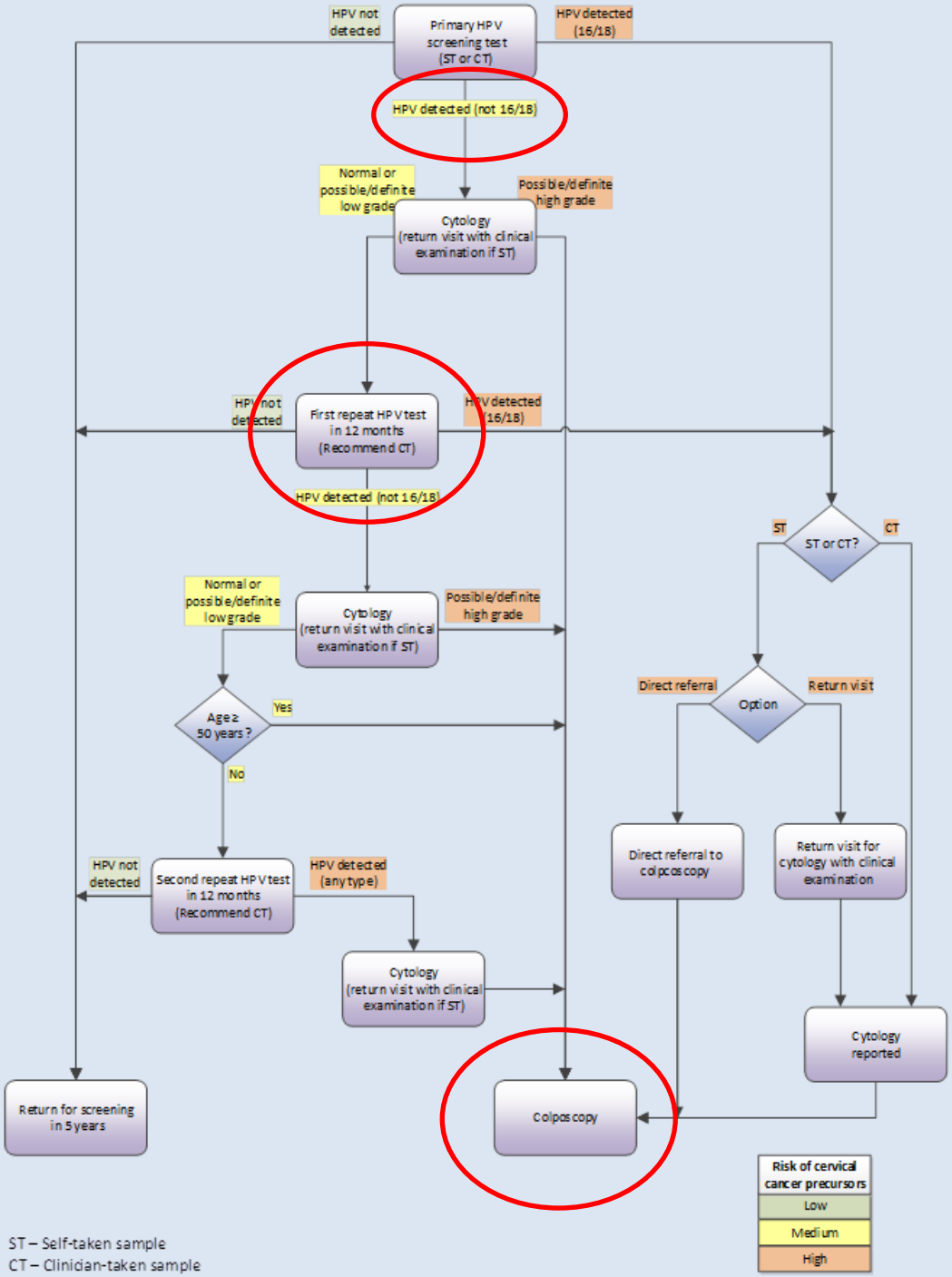
- HPV tests have been used since 2010 in addition to cytology under certain criteria.
- Much anticipated change to come in 2023
- Work already completed
  - Register
  - Public consultation
  - Development of screening algorithms

The testing process

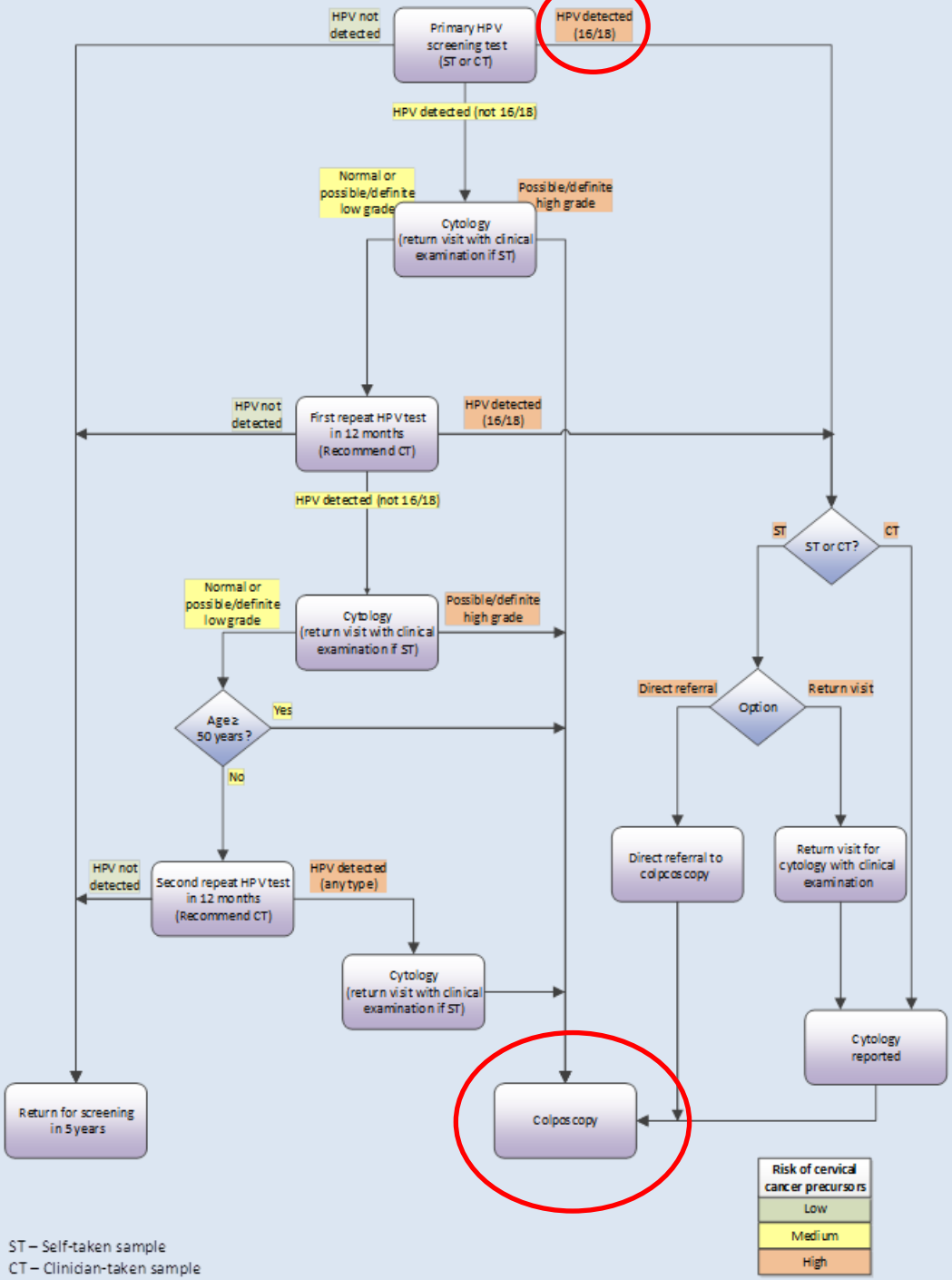
- Actual testing of samples only a small part of the process.
- Patient management forms a significant part of the screening process.
- Lab results inform clinicians what happens next – colposcopy referrals, routine repeats, further testing etc



The proposed screening process



The proposed screening process



The proposed screening process

Examples of when cytology needed

- In addition to reflex testing on HPV positive samples, cytology required:
  - In symptomatic women
  - In the test of cure process
  - If previous cytology unsatisfactory (cytology only, not HPV test required)
  - Cytology alone may be required to follow up on HPV detected swab samples (additional HPV tests not required)

HPV testing

- Requirements
- Similarities
- Turn around times
- Sample types
- Self sampling
- Numbers and positivity rates
- Reporting results

Requirements

- Section 5 requirements:

"A lead HPV testing scientist who is a medical laboratory scientist with a post-graduate degree in molecular science and a minimum of five years full-time (or equivalent) post-qualification experience in molecular science including a minimum of two years of experience in diagnostic molecular testing".

Similarities

- Testing process
- Leaky samples
- QA programmes
- Environmental testing

Turn Around Times

- Currently at 15 days for HrHPV tests (98%)
- Will be 3 days (100% in 3 days)
- HPV and cytology to be reported together
- Turn around time for reflex cytology testing:
  - 100% in 10 days (same for cytology only)

Sample types

- Clinician collected and self-collected
- More important:

LBC versus Swab

Sample types continued

- LBC samples
  - Collected by a clinician during a speculum exam

- Swab samples
  - Can be either:
    - self collected, or
    - clinician collected (no speculum exam required)

Self sampling workflow

- Likely dry swab received by lab
- Re-suspension required
  - Manual step
  - Could be time consuming depending on numbers of swab samples received.

Numbers

- Currently labs process around 31,000 HPV tests per year.
- With HPV primary screening:

Test	Currently	With HPV primary
Cytology	430,000	80,000
HPV	31,000	425,000

Current use of HPV testing

- Test of cure
  - For women with previous High grade lesions
- Triage
  - For women aged >30 with ASCUS/Low grade
- Patient management tool / colposcopy request

Current positivity rates

- Triage test
  - 22.3% for women with ASC-US results, and 59.4% for women with LSIL results
- Colposcopy requested
  - No data available but generally a high percentage
- Test of cure
  - Not covered by monitoring report but generally lower than that seen for triage testing

Expected positivity rates

- Types 16/18
  - Approximately 2% positive in the first few years after transition,
  - Approximately 3% around five years after the transition
  - Percentage expected to decrease after that.
- Other high risk HPV types
  - Approximately 6% positive for non-16/18 HrHPV in the first few years after transition,
  - Approximately 7% around five years after transition

Cytology results

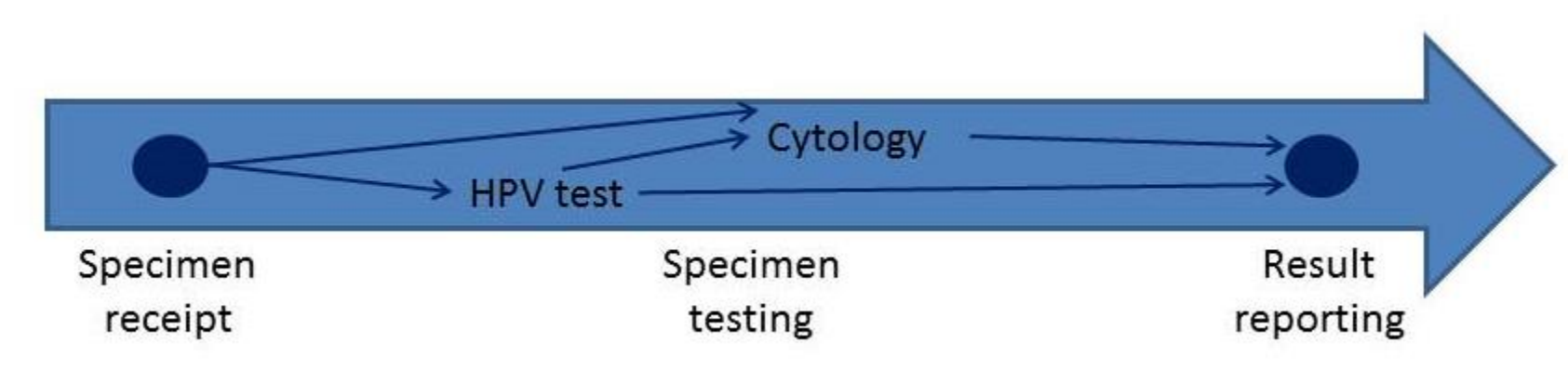
Consist of three components:

1. Specimen adequacy
   - Satisfactory or unsatisfactory
2. Interpretation
   - Normal / abnormal + other findings
3. Recall
   - When to return for next screen

Molecular / cytology roles

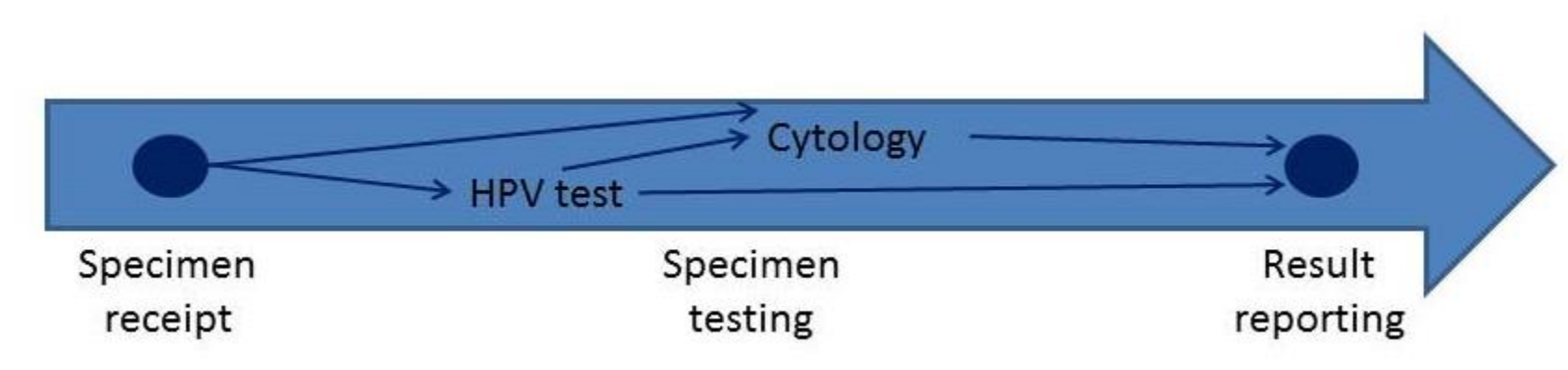
- Molecular and cytology departments will likely work much more closely after the transition.
- Input from cyto-scientists / cyto-technicians will be important for sample management in the lab.
- Key decision points are at the beginning and end of the testing process.

Cytology input



- At registration
  - Which samples need HPV / cytology or both
  - For example: Test of Cure, previous unsatisfactory cytology, symptomatic women.

Cytology input



- At reporting
  - Patient recalls can be complex
  - Dependent on many factors including patient age, previous results, which HPV type/s detected etc

The screening register

- There will be a new / updated register introduced
- Stores information on:
  - Test results: Cytology, histology, and HrHPV
  - Recall recommendations
  - Other events eg. pregnancy

An example history

Screening History

Event Date	Event	Lab ID	Specimen ID	Site Code	Specimen Type	Adequacy	Rec	Interpretation Codes	Grade
30-NOV-20	HrHPV	PN	200015388120 3600		RHAMP			Not Detected	
30-NOV-20	CYT	PN	200015388123 7500	R	L	S1	R1	OT1	N
30-AUG-18	HrHPV	PN	180033465720 3600		RHAMP			Not Detected	
30-AUG-18	CYT	PN	180033465723 7500	R	L	S1	R13		N
28-MAR-18	HrHPV	PN	180024781220 3600		RHAMP			Not Detected	
28-MAR-18	CYT	PN	180024781223 7500	R	L	S1	R9	ASL	L
11-MAY-17	CYT	PN	170006325623 7500	R	L	S1	R8		N
04-OCT-16	HIST	PN	H25928/16621 200	T83	P11461	SAT		M74008	H
24-AUG-16	HIST	PN	H23893/16621 200	T83	P11481	SAT		M76700, M74008	H
13-JUL-16	CYT	PN	160020163623 7500	R	L	S1	R9	HS1	H
03-JAN-15	PREG								
27-JUN-12	CYT	PN	120009955201 237500	R	L	S1	R1		N
26-FEB-09	CYT	PN	0900045766	R	O	S1	R1		N
15-NOV-07	HIST	PN	07H16494	T83200	B	SAT		M60000	N
15-NOV-07	CYT	PN	0700211200	R	P	S1	R13	None	N
05-APR-07	HIST	PN	07H05650	T83200	B	SAT		M73000	N
05-APR-07	CYT	PN	0700054140	R	P	S1	R13	None	N
10-OCT-06	CYT	PN	0600171807	R	P	S1	R9	LS	L
07-APR-06	CYT	PN	0600058663	R	P	S1	R5	LS	L

An example history

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07-APR-06	CYT	PN	0600058663	R	P	S1	R5	LS	L

Vaccination in New Zealand

- A National HPV vaccination programme commenced in New Zealand in 2008.
- When introduced, the quadrivalent HPV vaccine was offered to young women born in 1990 and 1991.
- In 2009, the HPV vaccination programme was extended to girls and young women born from 1992 onwards.
- From 2017 nine-valent vaccine offered
- Vaccine now free to all aged 9-26

Vaccination continued

- Vaccination coverage in 2017 was approximately 70% for boys and girls aged 12 years.
- The impact of vaccination on screening outcomes is being seen in the 25-29 year old cohort.
- Initial 12 year old cohort now aged ~25 and entering screening

Vaccination continued

- Those vaccinated from 2008 – 2016 have protection against 16/18 only.
- Those vaccinated from 2017 onwards (now aged ~17) have protection against an additional 5 HrHPV types
- Effects of vaccination will increase over time as cohorts reach screening age.

Future directions

- Decreased screening due to vaccination
- Methylation
- Extended genotyping
- Point of care testing