BC Cancer Agency
CARE + RESEARCH
An agency of the Provincial Health Services Authority

Primary HPV Testing in a Canadian Organized Cervical Cancer Screening Program

A Randomized Controlled Trial

(funded by the Canadian Institutes of Health Research)

ISRCTN79347302

HPV FOCAL Study

BC Cancer Agency
CARE + RESEARCH
An agency of the Provincial Health Services Authority

PROVINCIAL Health Services AUTHORITY
Province-wide solutions. Better health.

BC Centre for Disease Control
AN AGENCY OF THE PROVINCIAL HEALTH SERVICES AUTHORITY

UBC

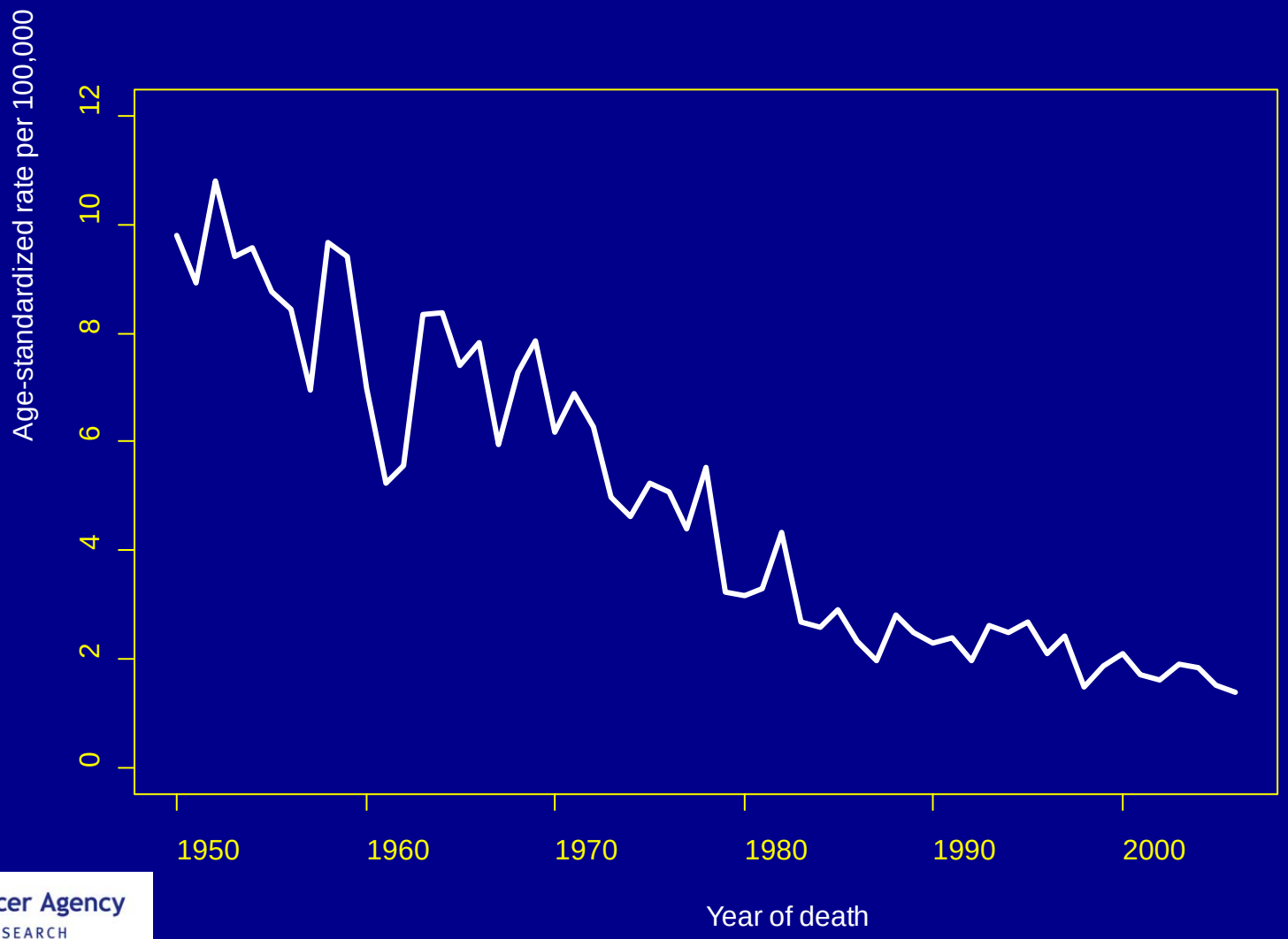
McGill

CIHR IRSC

Pap Smear Screening: The BC Experience

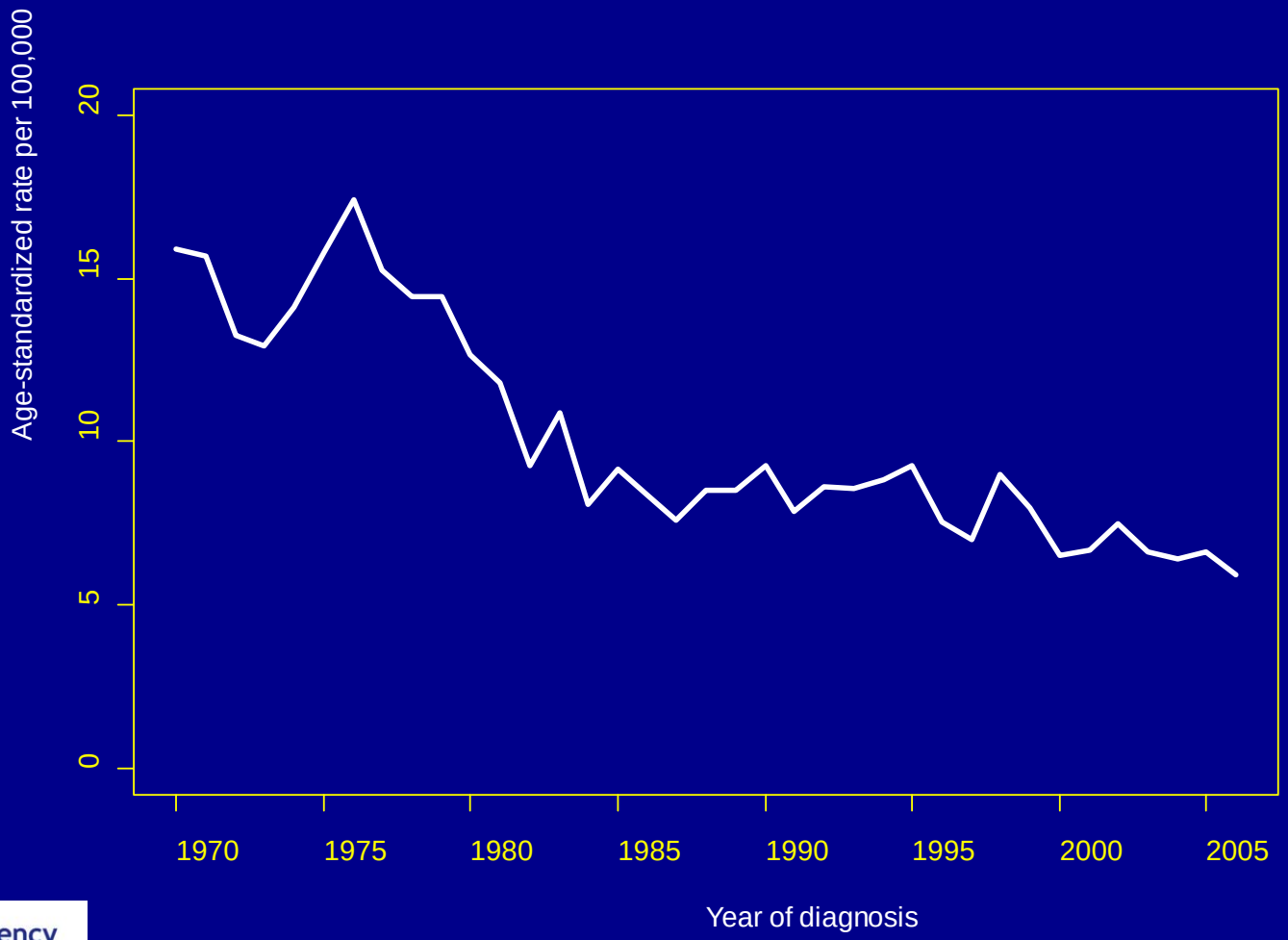
- Pap smear testing commenced in British Columbia (BC) in 1949
- Single Computer Database for all Pap Smears since 1983 – linked to Cancer Registry
- Single Cytology Laboratory for all BC (1.52 million women aged 20-69)
- Interprets ~550,000 smears annually.

BC Cervical Cancer Mortality: 1950-2006



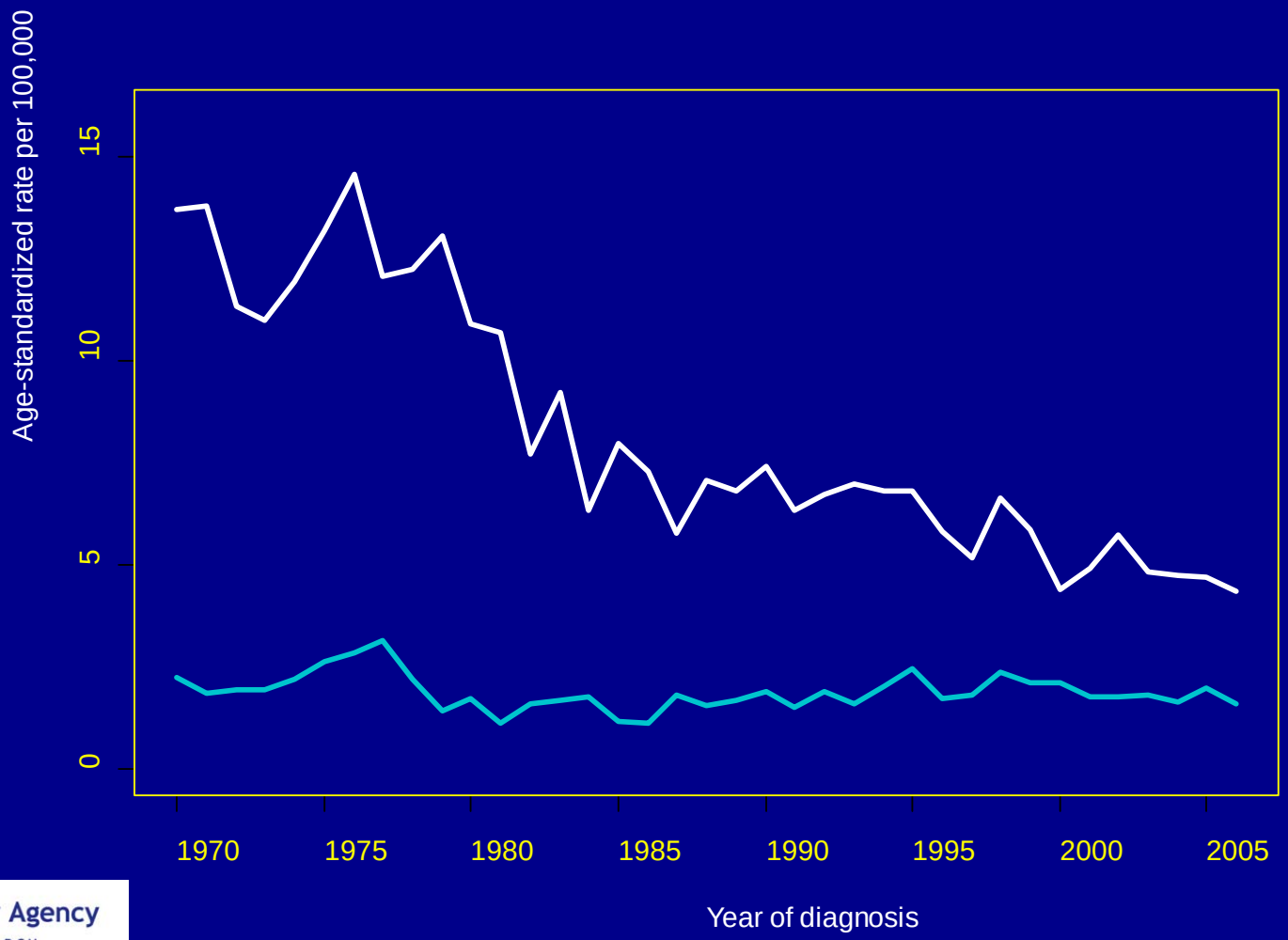
BC Cancer Agency
CARE + RESEARCH
An agency of the Provincial Health Services Authority

BC Cervical Cancer Incidence: 1970-2006



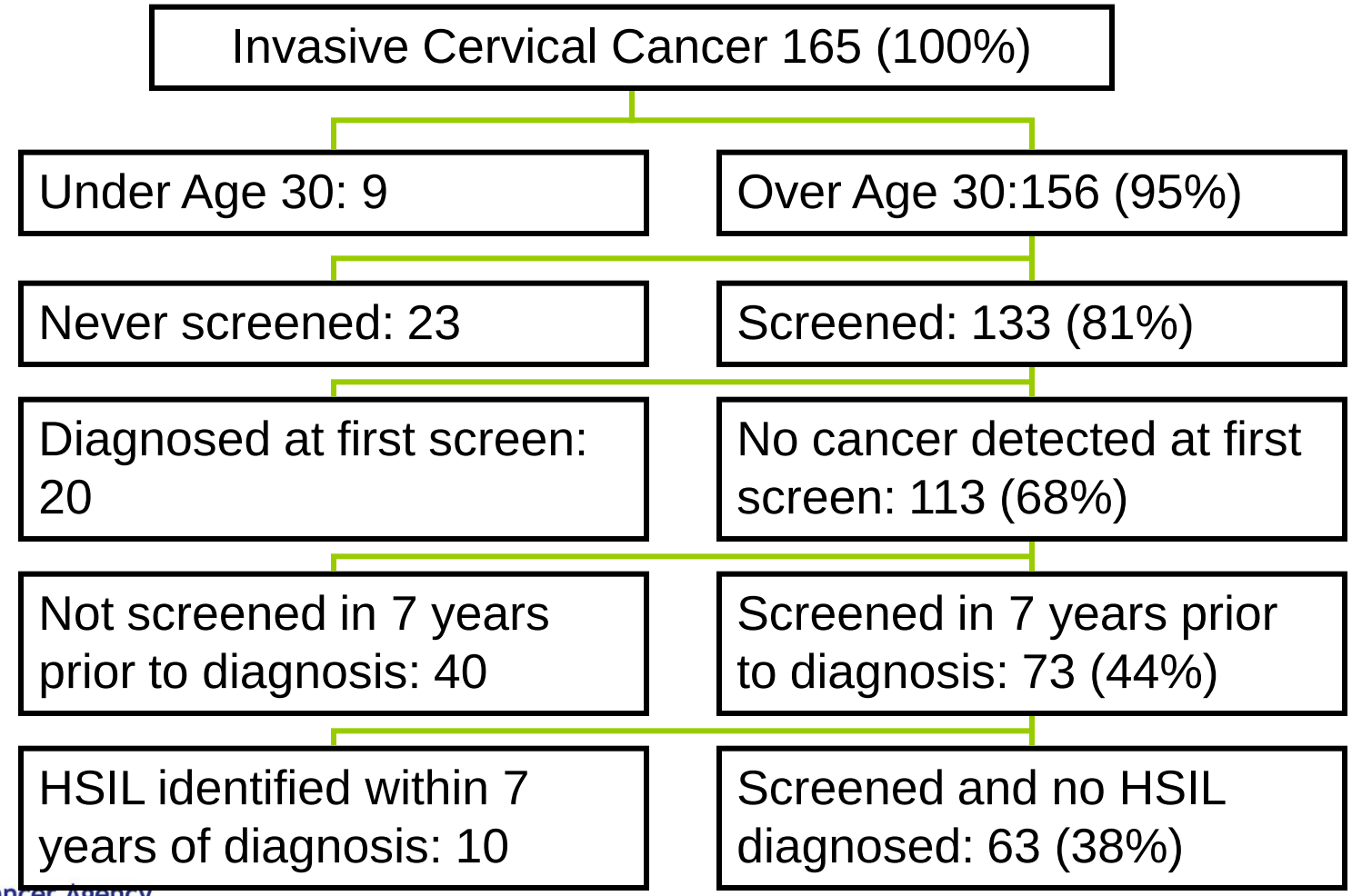
BC Cancer Agency
CARE + RESEARCH
An agency of the Provincial Health Services Authority

BC Cervical Cancer Incidence by Histology: 1970-2006



BC Cancer Agency
CARE + RESEARCH
An agency of the Provincial Health Services Authority

Analysis of Cervical Cancer Cases (failures) for BC in 2002



FOCAL Trial Objectives

To establish the efficacy of HPV DNA testing as a stand-alone screening test, followed by cytology triage (LBC) for HPV positive women

:

- Appropriate screening interval for HPV negative women
- Cost-effectiveness of HPV testing for primary screening within the context of an organized Canadian cervical cancer screening program

Trial Arms

Control Arm –Initial LBC sample: Cytology testing. Negatives screened again in 2 years (cytology testing) and 4 years (HPV and Cytology testing)

Intervention Arm-Initial LBC sample: HPV DNA Testing (cytology triage of HPV positives). HPV negative women screened again in 4 years (HPV and cytology testing, to compare to Control arm at 4 years)

Safety-Check Arm – Initial LBC sample: HPV DNA testing (cytology triage of HPV positives). HPV negative women screened again in 2 years (with cytology, to compare to Control arm at 2 years)

Methods

Initially blinded, randomized controlled, three arm trial

- Sample size:11,000 per arm - 33,000 total
- Population: women aged 25 to 65 years of age. Two centres: Vancouver & Victoria
- Initial screen followed by second or third screening round (depending on arm) (2-4 yr participation)

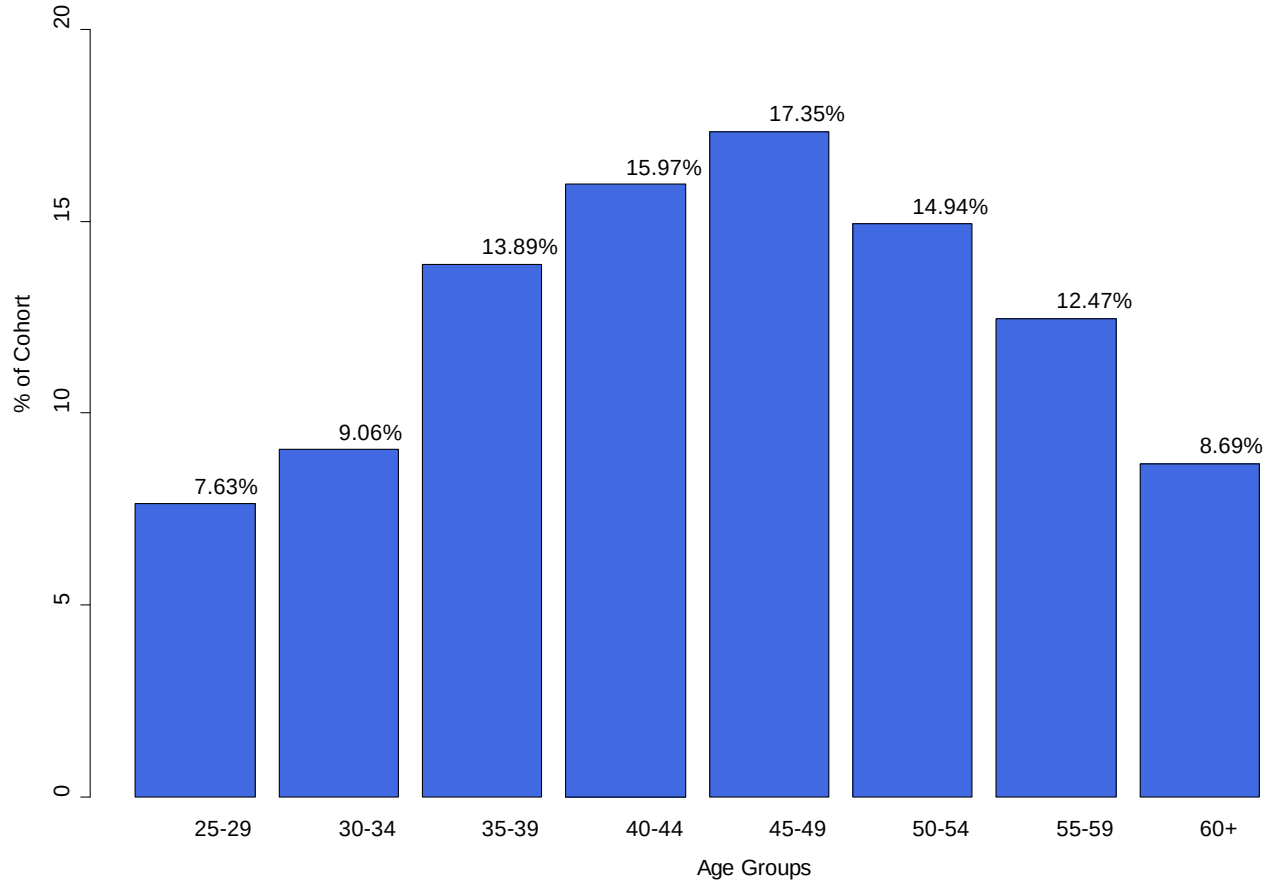
Trial Organisation

- Study Centre in BC Cancer Agency which manages the Cytology Laboratory, Cervical Cancer Screening Program (CCSP) and Provincial Cancer Registry.
- Family Physicians (FP) participating in trial were recruited through the CCSP
- Patients are individually consented by FP's supported by study centre

Important Trial Design Elements

- LBC collection utilized for cytology and HPV assessment
- All testing based on a single specimen (no patient recall)
- For subjects randomized to initial HPV with a positive result subsequent cytology interpretation is performed with knowledge of HPV status.
- Standardized colposcopy performed at 2 centres
- Blinded pathology interpretation
- Inclusion of a two year Safety-Check arm

Study Population - Age Distribution



BC Cancer Agency
CARE + RESEARCH
An agency of the Provincial Health Services Authority

Epidemiological Info (6305 FOCAL Participants)

- Mean age of study participant (in all arms): 46

<u>Top 3 Reported</u>

- (ethnicity): British 55%; Western European 16.3%; Other 14.7%
- : Married 65.4%; Single 14.2%; Divorced 9.8%
- : University Grad 47%; Trade certificate/College 30%; High school complete 14.3%

Other variables:

- Employment: 78.4% currently working
- Smoking History: Ever smoked 39.5%; Mean age started smoking: 16.5 yrs

  Still smoking: 18.7%
- Sexual History: Mean age of sexual debut 18.8 yrs

  Lifetime no. of male sexual partners: 2-5 (34.7%); 6-10 (23,1%); 1 (21.3%)

Initial Round – Screening Results

As of 7th March 2010, screen available for 11,838 subjects

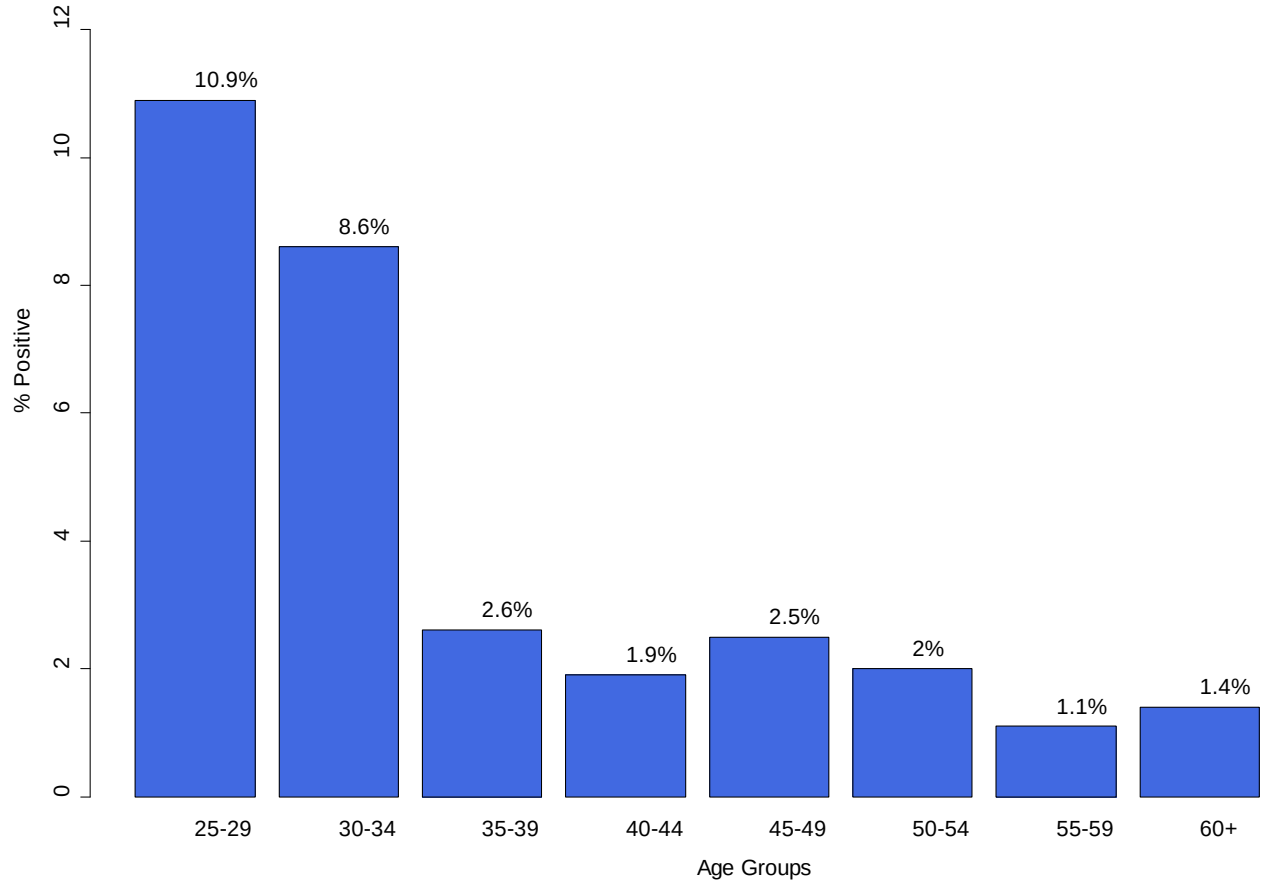
Control Arm:

- 3769/3938 (95.7%) cytology negative, 52 (1.3%) ASCUS with 39 HPV-
- Referred for colposcopy – 130 (3.3%)

Combined Intervention and Safety Check Arms:

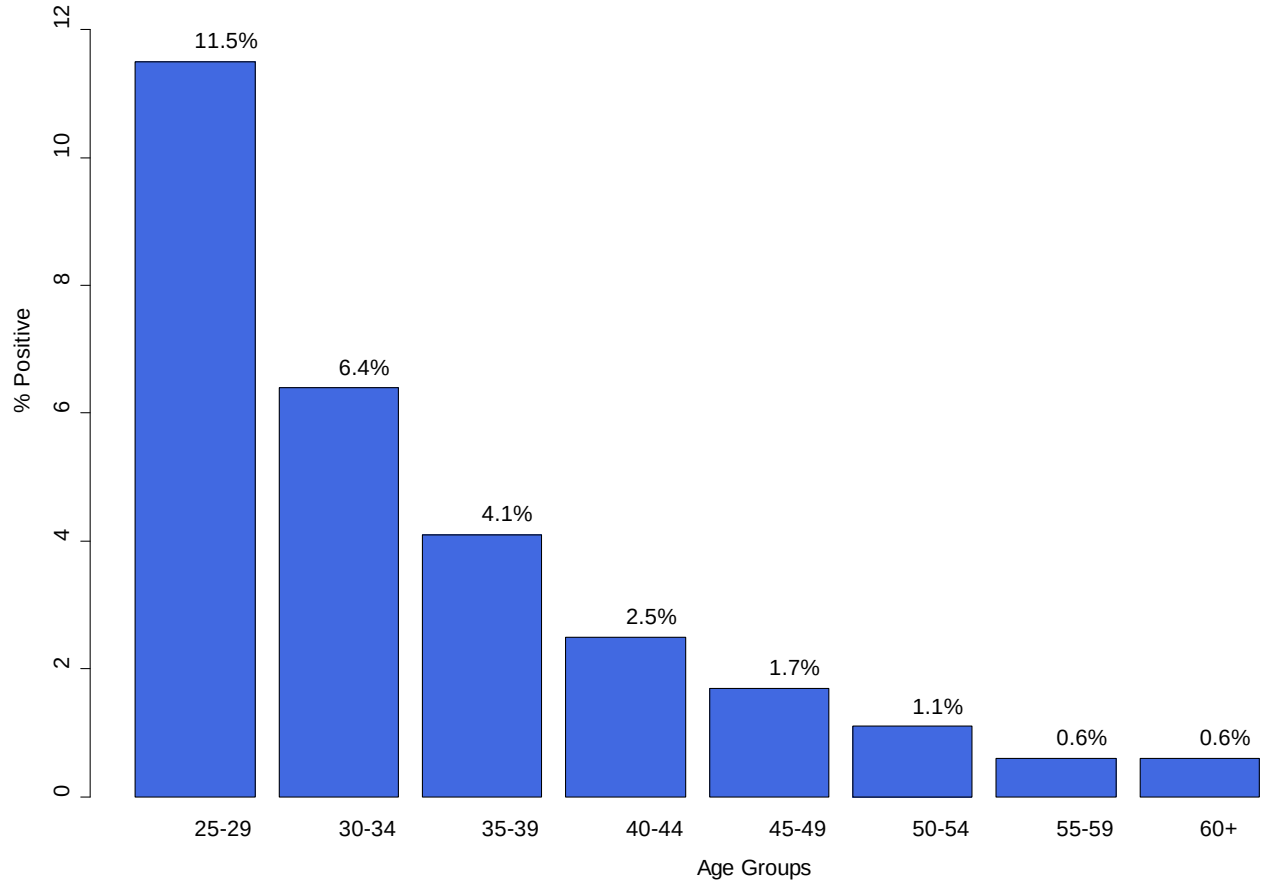
- 7290/7893 (92.4%) HPV DNA Neg, 365 (4.6%) with Negative Cytology
- Referred for colposcopy – 238 (3.0%)

Control Arm
- Screen Positivity Rates by Age



BC Cancer Agency
CARE + RESEARCH
An agency of the Provincial Health Services Authority

Combined Intervention/Safety Arms - Screen Positivity Rates by Age



BC Cancer Agency
CARE + RESEARCH
An agency of the Provincial Health Services Authority

Initial Round – Pathology Results

Control Arm:

- Results available on 112 subjects
- PPV's Cin3+: 12% (13), Cin2+: 32% (36)
- Estimated Cin3+ rate per subject: 3.8/1,000
- Estimated Cin2+ rate per subject: 10.6/1,000

Combined Intervention and Safety Check Arms:

- Results available on 213 subjects
- PPV's Cin3+: 18% (38), Cin2: 38% (81)
- Estimated Cin3+ rate per subject: 5.4/1,000
- Estimated Cin2+ rate per subject: 11.5/1,000

Current Trial Status

- Full recruitment expected by December 2011
- Final analysis anticipated 2016

FOCAL Trial Investigators and Collaborators

Vancouver

Dr. Kathy Ceballos

Dr. Andrew Coldman

Darrel Cook

Dr. Tom Ehlen

Dr. Mel Krajden

Dr. Ruth Martin

Wendy Mei

Dr. Gina Ogilvie

Dr. Stuart Peacock

Laurie Smith

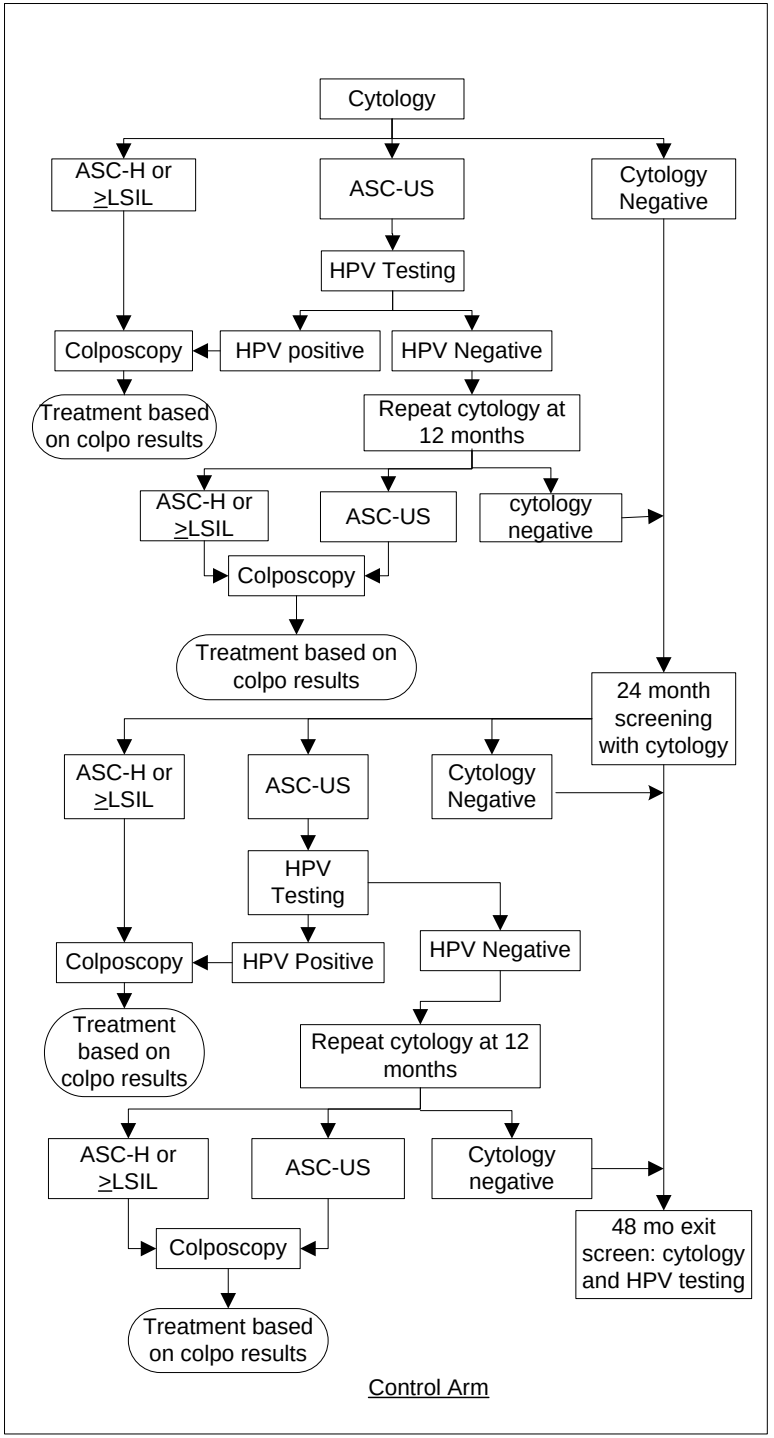
Dr. Gavin Stuart

Dr. Dirk van Niekerk

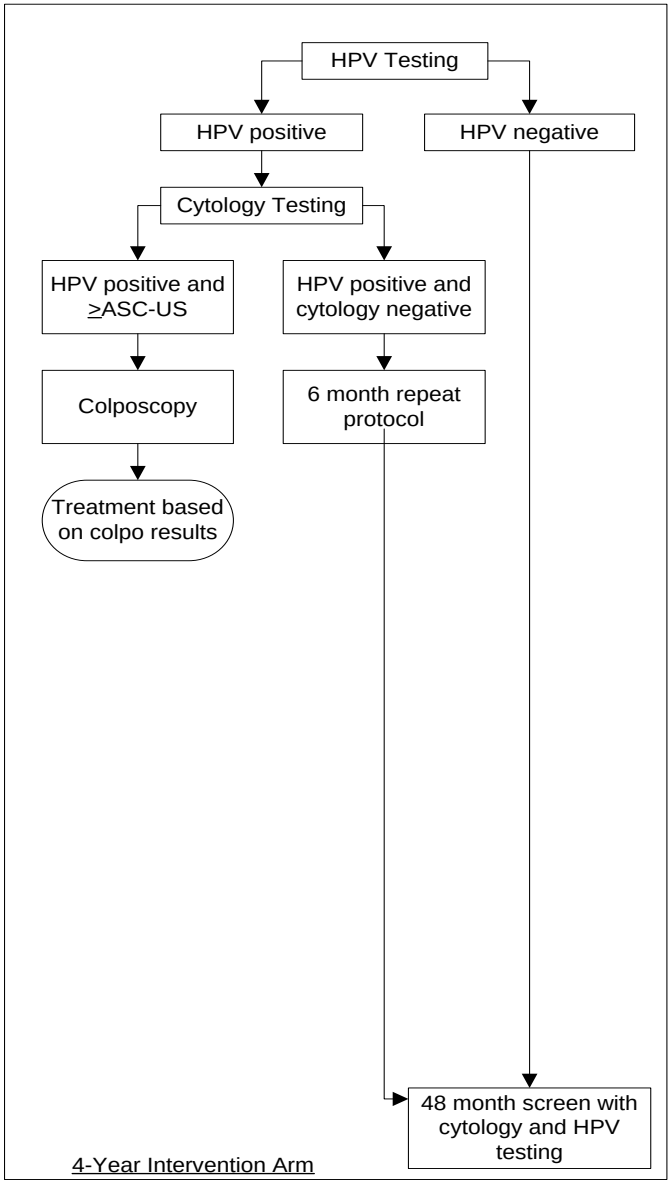
Montreal

Dr. Eduardo Franco

BC Cancer Agency
CARE + RESEARCH
An agency of the Provincial Health Services Authority



BC Cancer Agency
CARE + RESEARCH
An agency of the Provincial Health Services Authority



4-Year Intervention Arm