Centro di Riferimento Oncologico – Aviano (PN), Italy
IRCCS, National Cancer Institute

Screening history of invasive cervical cancer cases in Friuli Venezia Giulia Region - Italy -

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Background

- Cervical cancer screening through Papanicolau (Pap) smear, allow the identification of pre-invasive lesions that can be adequately treated:

  →reduced incidence and mortality rates for invasive cervical cancer (up to 80%)

Background

- Since 1999: Organized Cervical Screening (OCS) in Friuli Venezia Giulia (FVG), Northeast Italy
  - Whole region coverage
  - Target population: women aged 25-64 years
  - Personal invitation letter
  - A free Pap-smear, every 3 years

In 2005:

- 90% coverage of target population
- 55% compliance with the screening

Background

- FVG is one of Italian regions with the highest practice of Pap-smear (National Institute of Statistics survey, 2004-2005)
  - 86% of women aged ≥25 years, receive at least one Pap-smear in their life
  - 64% of women living in Northeast Italy perform opportunistic (i.e., left to women's initiative) Pap-smears

Rationale

- Why do women still develop invasive cervical cancer (ICC) in FVG, despite the existence of an OCS and the widespread use of opportunistic screening?
  - ICC std (EU pop) incidence rates x100,000:
    - 8.7 in 1999-2003
    - 6.7 in 2004-2005

- Feasibility: FVG region has both OCS and Cancer Registry covering the whole area

Objectives

1. To assess screening history of women diagnosed with ICC

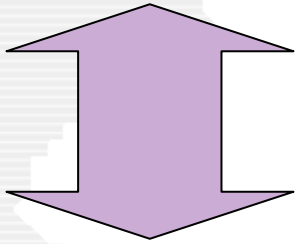
   →In order to identify flaws undermining prevention

2. To evaluate associations between screening history and women/tumor characteristics

3. To estimate survival according to screening history

Material and Methods

- 438 women with ICC, diagnosed between 1999 and 2005 (FVG Cancer Registry)



(by anonymous regional identification codes)

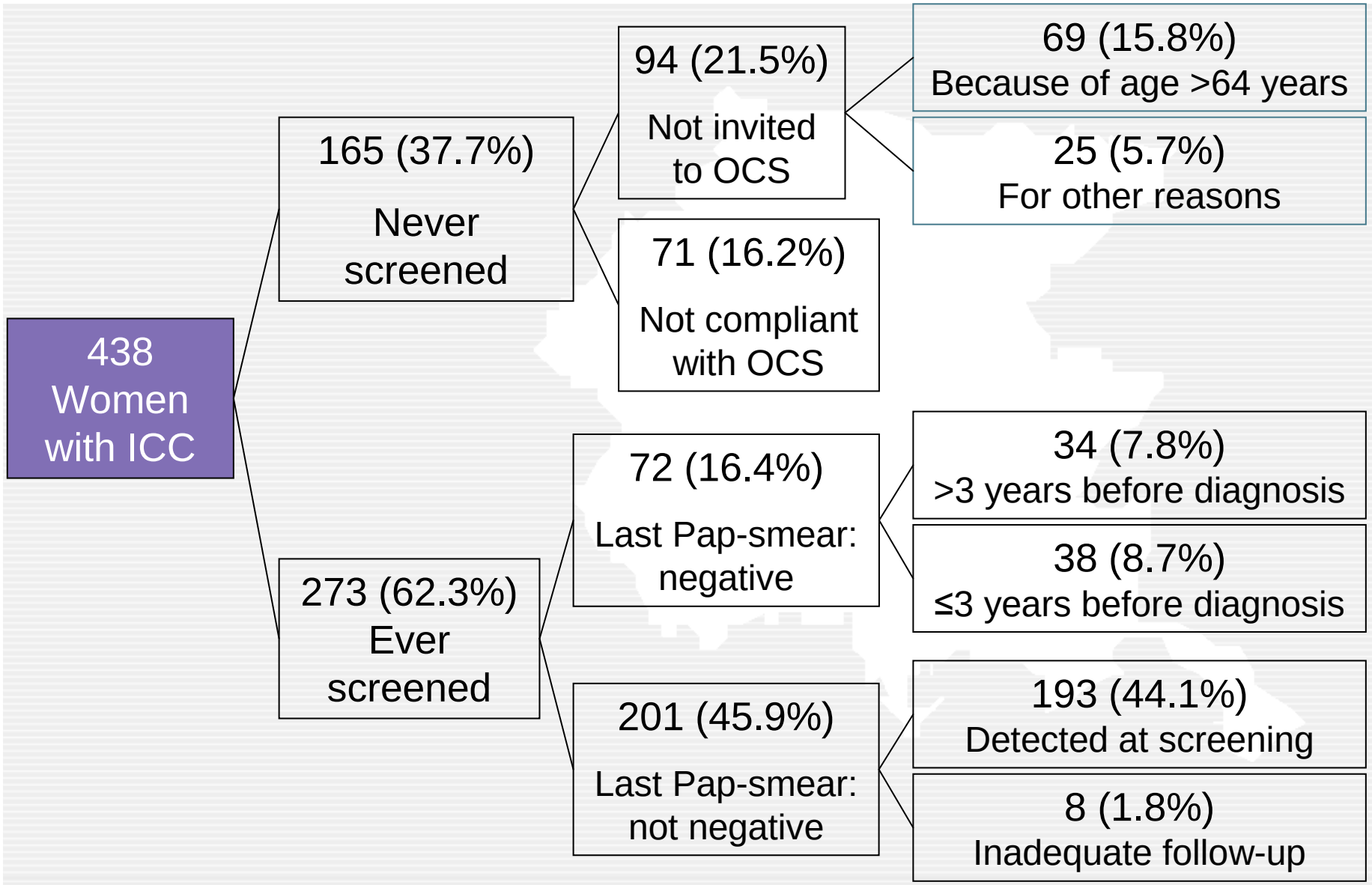
  - Pathological Archives: cytological (e.g., Pap-smear dates and results) and histological information (e.g., tumor stage and histology)
  - OCS database: invitation and compliance with OCS (e.g., invitation dates, reasons of non invitation)

Material and Methods

Women with ICC were classified as:

- **Never screened** (i.e., women without any information about Pap-smears)
  - Not invited to OCS
  - Invited but not compliant with OCS
- **Ever screened** (inside or outside OCS)
  - Last NEGATIVE Pap-smear
  - Last POSITIVE or inadequate Pap-smear
    - Detected at screening
    - Inadequate follow-up (diagnosis >1.5 years after abnormal Pap-smear)

Results – screening history



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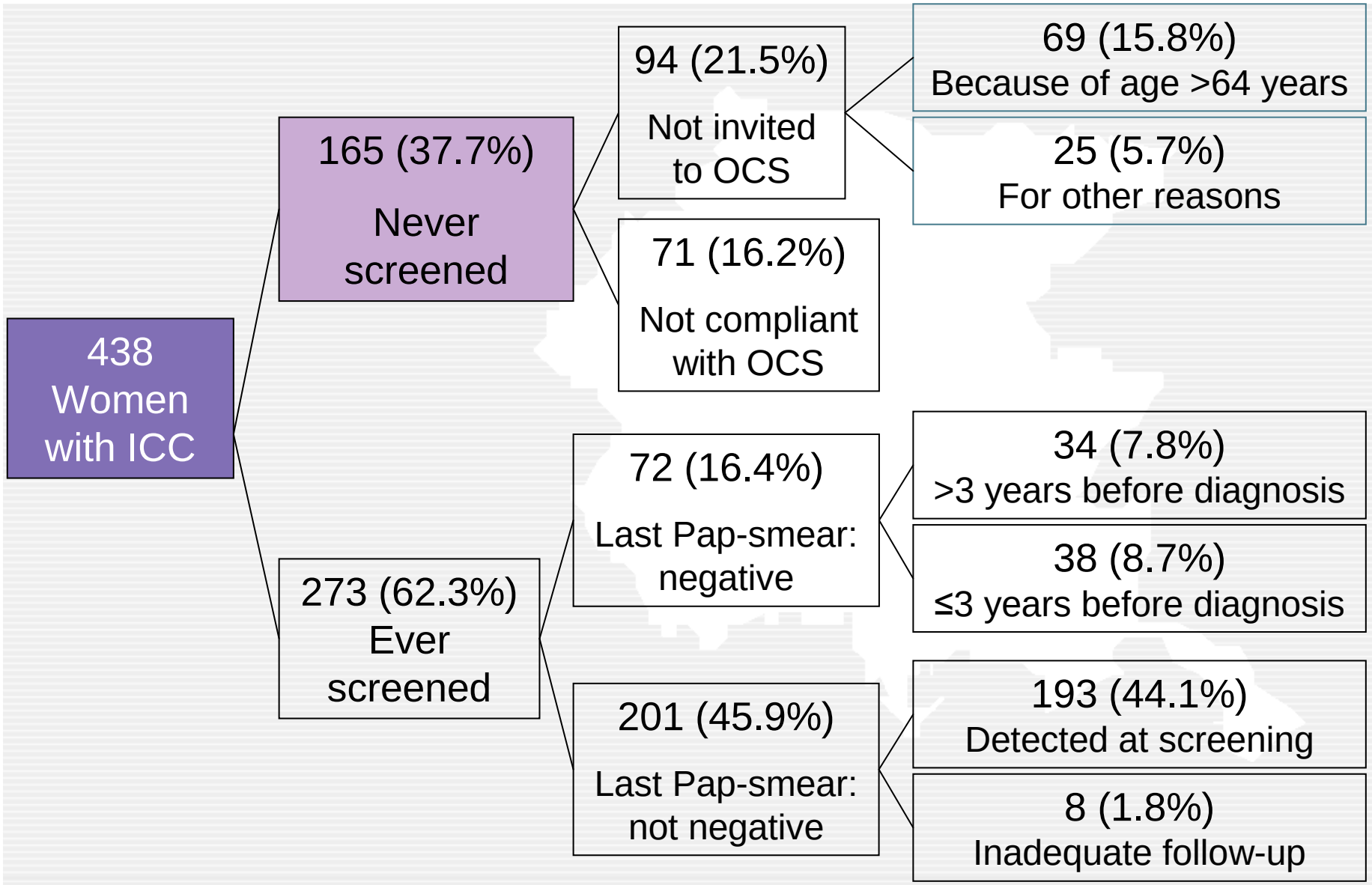

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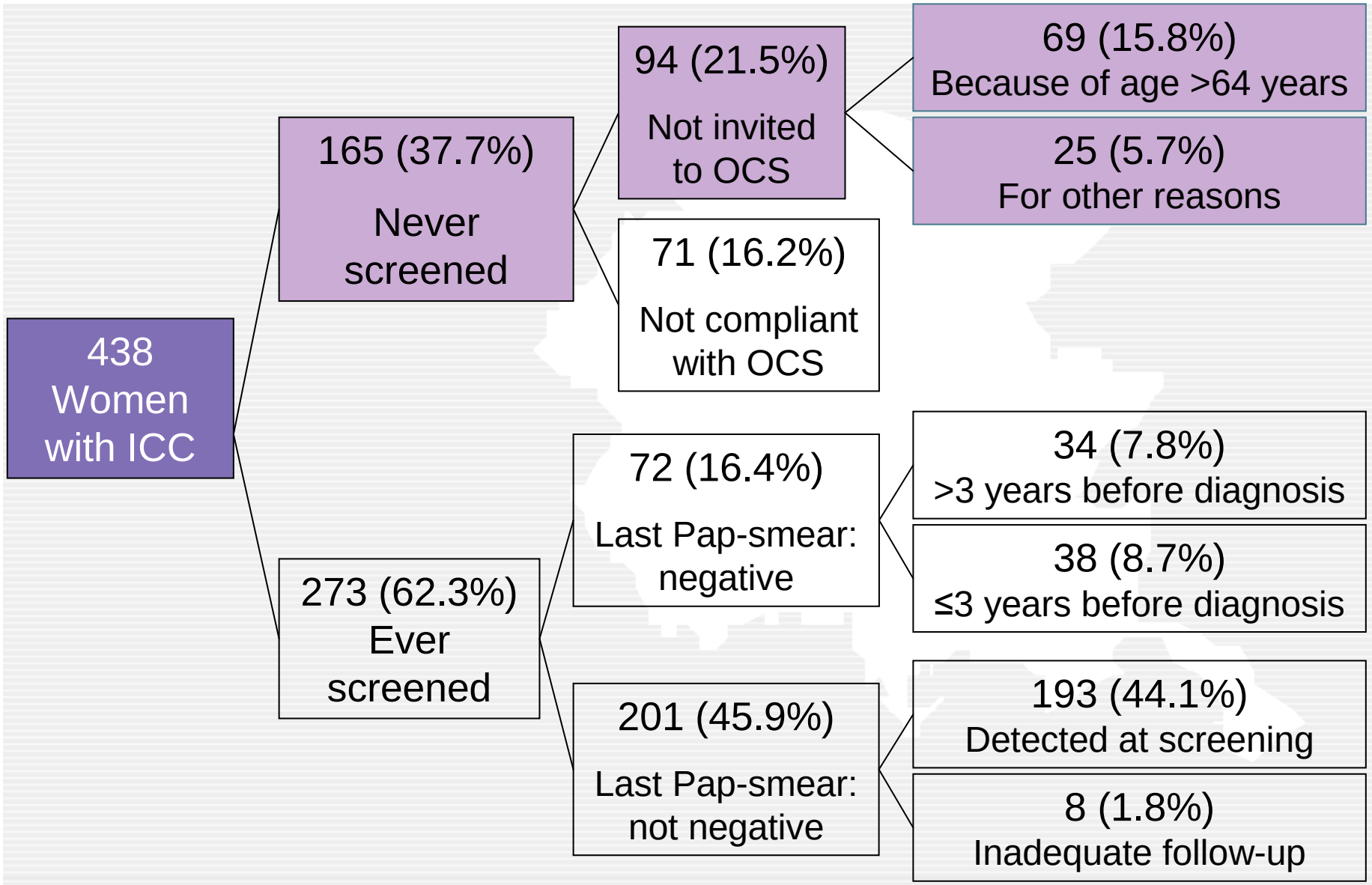

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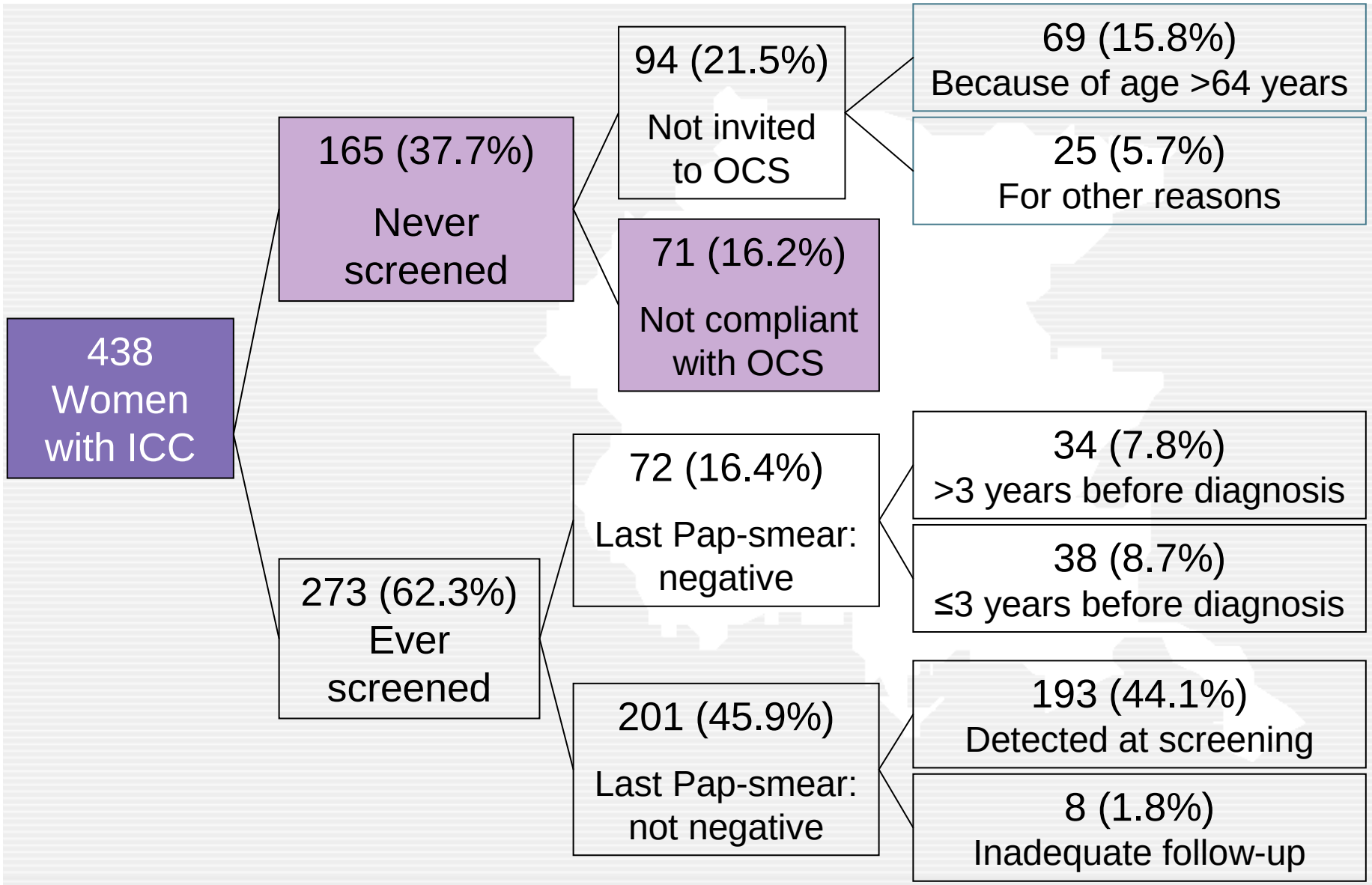

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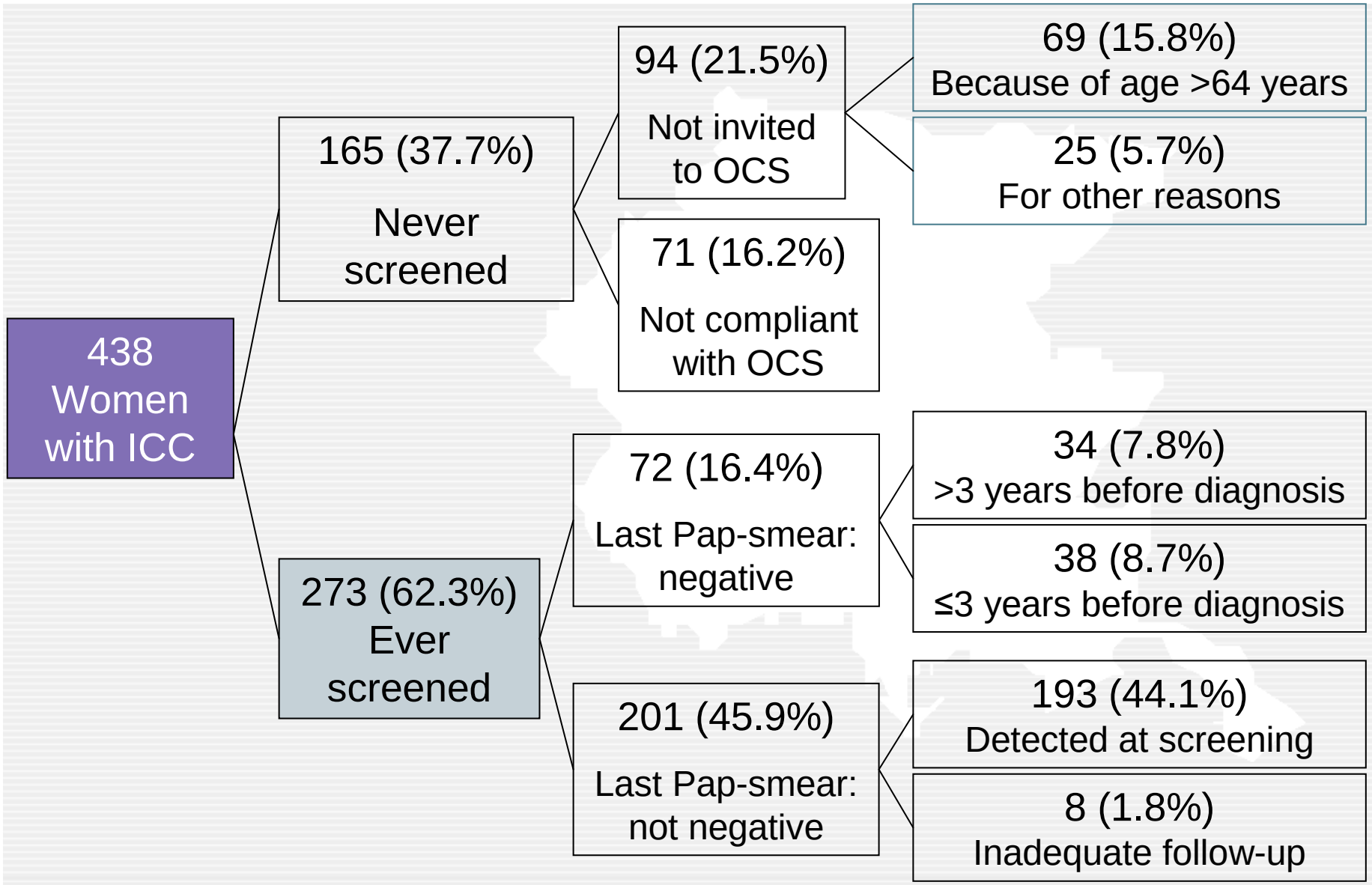

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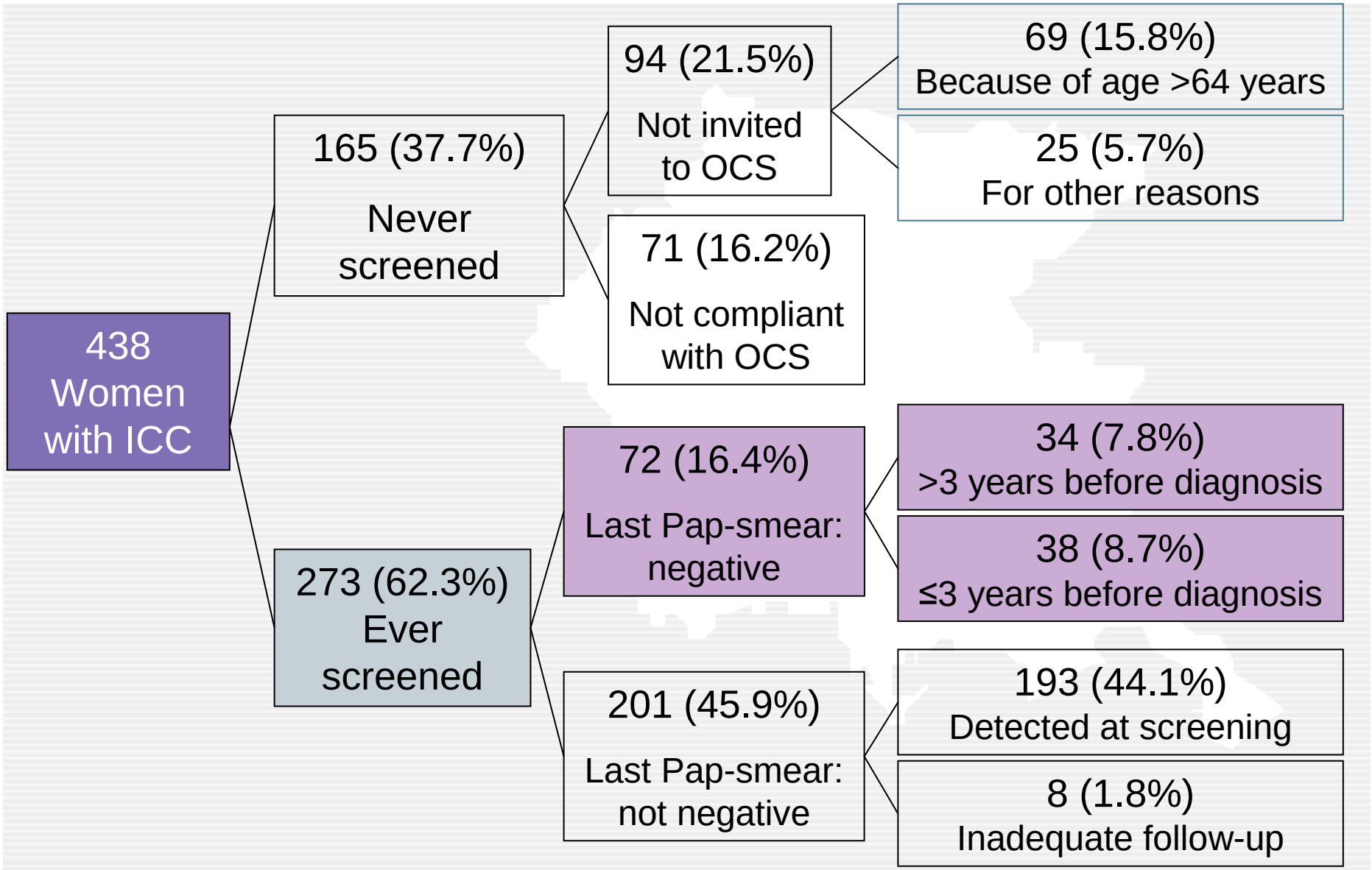

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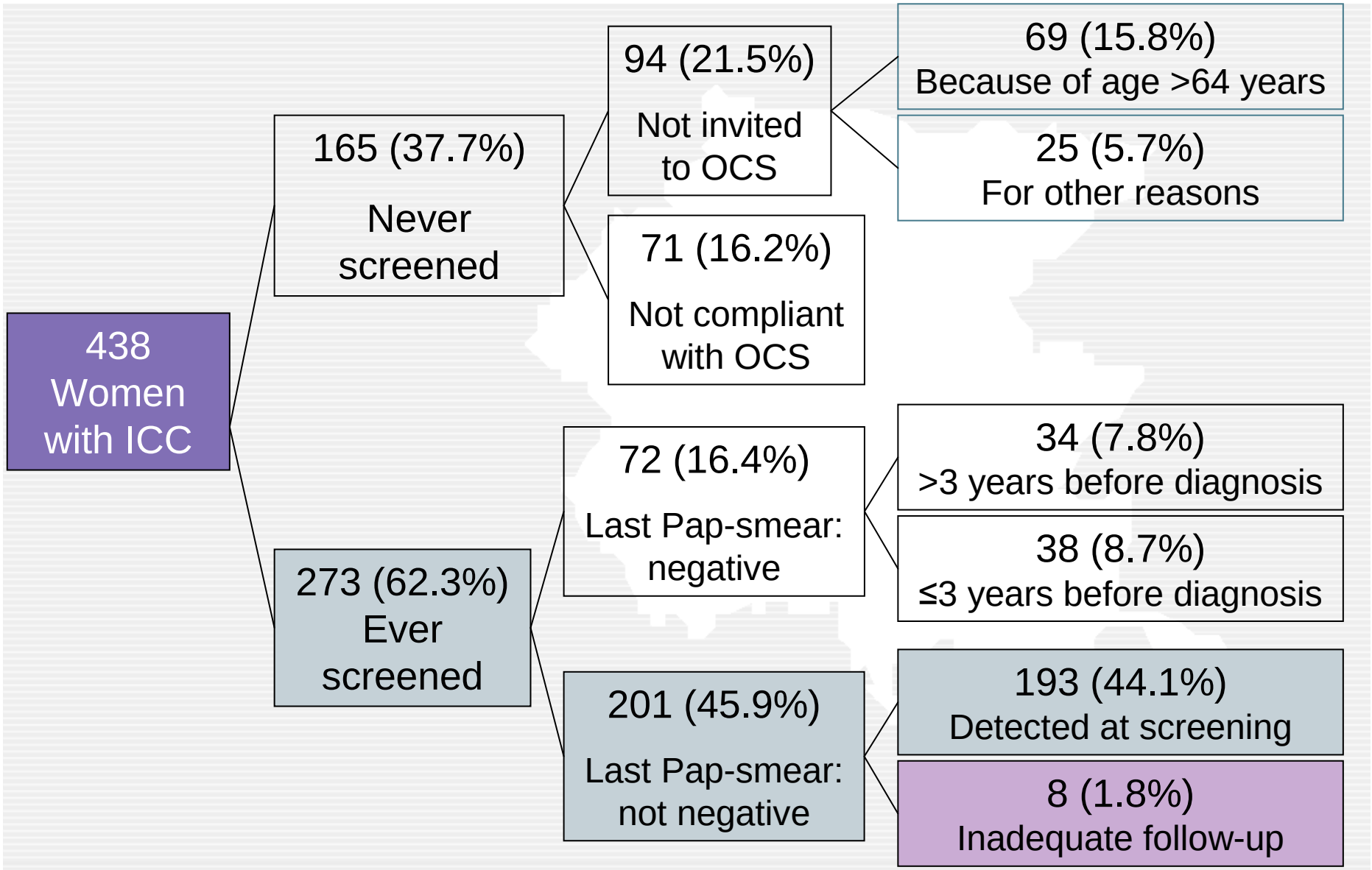

Results - Associations

Characteristics at diagnosis	No screening* (n=165)	Screening type: Opportunistic (n=141)		Organized (n=132)	
	No. (%)	No. (%)	OR (95% CI)°	No. (%)	OR (95% CI)
Age					
26-45	22 (13)	28 (20)	1*	61 (46)	1*
45-54	31 (19)	32 (22)	0.8 (0.4-1.7)	31 (24)	0.4 (0.2-0.7)
55-64	30 (18)	16 (11)	0.4 (0.2-1.0)	31 (24)	0.4 (0.2-0.8)
≥65	82 (50)	65 (46)	0.6 (0.3-1.2)	9 (7)	0.0 (0.0-0.1)
Tumor stage (FIGO)					
IA-microinvasive	18 (11)	27 (19)	1.0 (0.5-2.3)	61 (46)	1.9 (0.9-4.2)
IB	26 (16)	35 (25)	1*	40 (30)	1*
II	33 (33)	23 (16)	0.6 (0.3-1.2)	11 (8)	0.2 (0.1-0.7)
III-IV	55 (21)	34 (24)	0.5 (0.3-1.0)	17 (13)	0.3 (0.1-0.6)
χ^2 trend			*3.7 p=0.05*		*26.4 p<0.01*
Histologic type					
Squamous cells	126 (76)	101 (72)	1*	103 (78)	1*
Adenocarcinoma	27 (16)	27 (19)	1.4 (0.7-2.5)	27 (21)	1.5 (0.8-3.0)

° Odds ratio (OR) and 95% confidence intervals (CI) estimated with multinomial logistic regression models **adjusted for age**. *reference category.

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Results - Survival

Characteristic at diagnosis	Women No.	Deaths No. (%)	
	438	183 (42)	**HR (IC 95%)°**
Age (years)			
26-45	111	19 (17)	1*
45-54	94	23 (25)	0.8 (0.4-1.4)
55-64	77	35 (46)	1.6 (0.9-2.8)
≥65	156	106 (68)	2.5 (1.5-4.1)
Tumor stage (FIGO)			
IA- microinvasive	106	6 (6)	0.5 (0.2-1.4)
IB	101	15 (15)	1*
II	67	40 (60)	4.4 (2.4-8.1)
III-IV	106	84 (79)	11.1 (6.2-19.9)
χ^2 trend			*103.2 p<0.01*
Histologic type			
Squamous cells	330	125 (38)	1*
Adenocarcinoma	81	39 (48)	1.0 (0.7-1.5)
Screening type			
No screening	165	99 (60)	1*
Opportunistic	141	65 (46)	1.0 (0.8-1.5)
Organized	132	19 (14)	0.6 (0.3-0.95)

° Hazard ratios (OR) and 95% confidence intervals (CI) estimated with Cox regression models **adjusted for age, tumor stage, and histology**.
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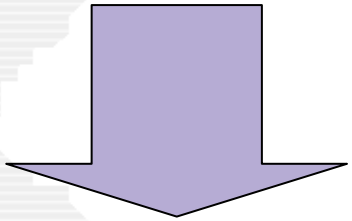
Discussion

Among women with ICC:

- 38% never screened
- 29% detected at FIRST Pap-smear



67% never screened before diagnosis of ICC

→Potentially preventable cancers

- Limit: unknown number of Pap-smears performed in the gynecologist's private practice (but estimates are low for FVG)

Discussion

OCS possible limitations:

- 28% of women with ICC never invited because older than 64 years

  → Is there need to extend target population?

- 16% of women with ICC not compliant with OCS

  → How to increase compliance?

- Among 132 women with ICC screened inside OCS:
  - 11% had a last NEGATIVE Pap-smear less than 3 years before diagnosis → false negatives?
  - 5% had a late diagnosis →inadequate follow-up?

Conclusions

- Women with ICC screened inside the organized program had a lower tumor staging and a better prognosis
  - What about pre-invasive cancers?
    - Limit: incomplete registration of pre-invasive cervical cancer (CIN3/In situ)
- In the end, it is recommended to increase compliance with organized screening programs

Thanks....

- Grant: Italian Association for Research on Cancer (AIRC)

for your attention