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INSTITUT NATIONAL DE SANTÉ PUBLIQUE DU QUÉBEC
Centre d'expertise et de référence

BREAST CANCER PHENOTYPES, AGGRESSIVENESS AND MAMMOGRAPHY SENSITIVITY

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BiESP
BUREAU D'INFORMATION ET D'ÉTUDES EN SANTÉ DES POPULATIONS

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Quebec breast cancer screening program

- Started in 1998
- Women 50-69 years
- Bi-annual bilateral two view mammography
- Participation rate of 58%
- 340 000 screening mammography yearly

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Interval cancers

- BCSP accuracy ➔ Mammography sensitivity
- Sensitivity metric ➔ Interval/screened detected ca
  - Screened detected ➔ca detected at screens
  - Interval cancers ➔ca diagnosed between screens
- Quebec BCSP ➔ 8.1 Interval Ca /10 000 women-y
- Interval ca biologically distinct from screened detected?

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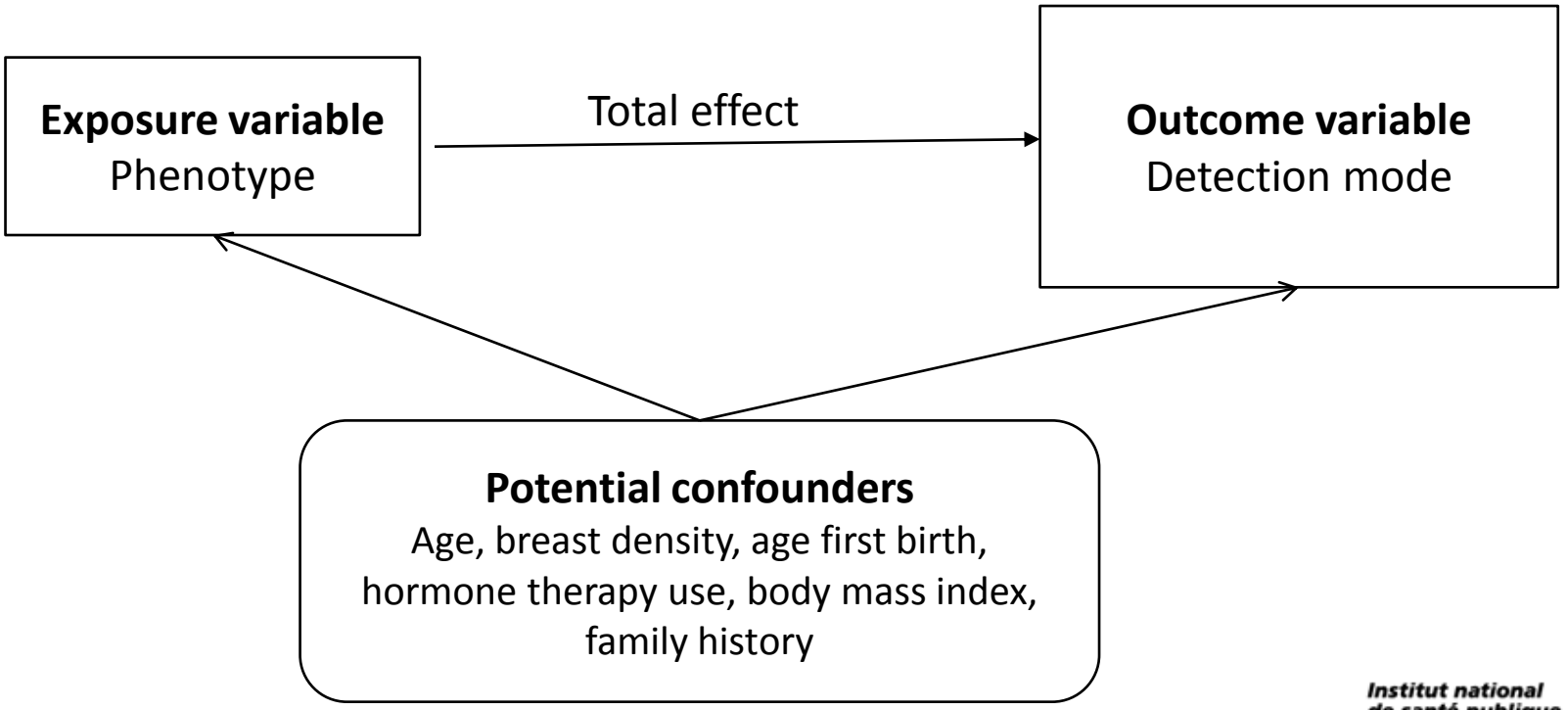
Biological characteristics of interval cancers

- Aggressiveness biomarkers
  - **Higher grade**
- Phenotype
  - **Estrogens receptor (ER) -**
  - **Progesterone receptor (PR) -**
  - **Human epidermal growth receptor 2 (HER2) +**
  - Molecular subtypes:
    - Luminal A ((ER+ or PR +) and HER2 -)
    - Luminal B ((ER + or PR +) and HER2 +)
    - HER2 enriched ((ER- and PR -) and HER2 +)
    - **Triple negative (ER- and PR – and HER2 -)**

Study objectives

First objective



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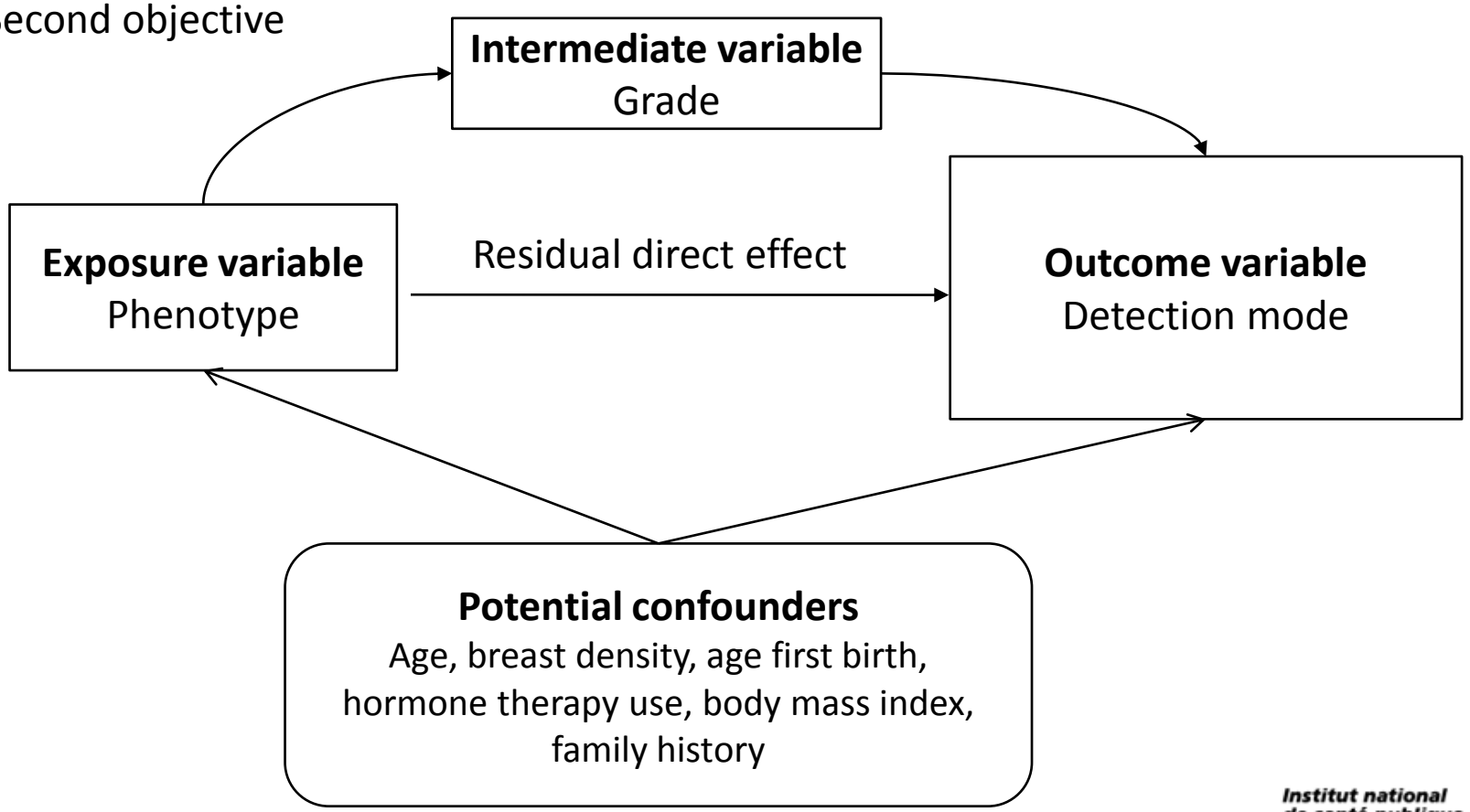
Study objectives

Second objective



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Study objectives

- Model build under two assumptions
  - No uncontrolled confounder of the “grade – detection mode” relation
  - No tumour phenotypes drift during tumour progression

Methods

- Women 50-71 years
- Who were Quebec BCSP participant
- With invasive breast cancer
- Diagnosed between 2003 and 2007
- At the Quebec City breast disease center
- 858 cases :
  - Screened detected → 596
  - Interval cancer→ 262

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Histological grade according to phenotype

Tumour phenotype	Grade I-II (n=643) %	Grade III (n=163) %	p-value
Estrogens receptor			<0.0001
Positive	95	46	
Negative	5	54	
Progesterone receptor			<0.0001
Positive	75	28	
Negative	25	72	
HER2 status			<0.0001
Negative	93	76	
Positive	7	24	
Tumour subtypes			<0.0001
Luminal A	88	33	
Luminal B	5	13	
HER2-enriched	2	11	
Triple-negative	3	41	
Unclassified	3	2	

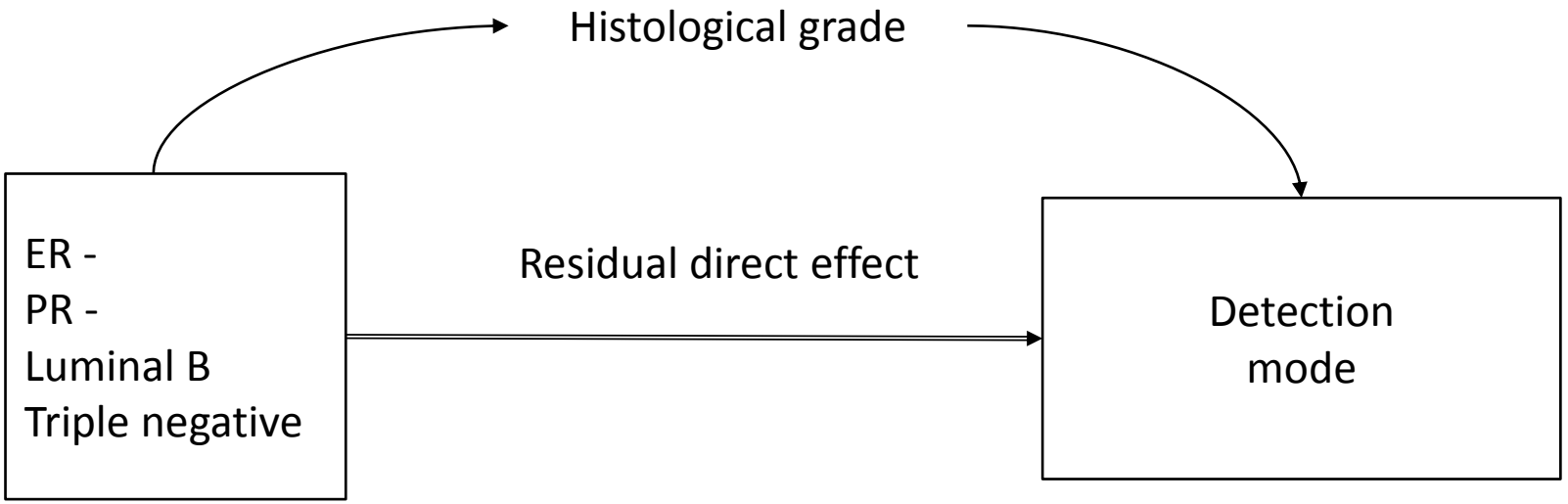
Mode of detection according to phenotype

Tumour phenotype		Total effect OR (95% CI)*	Residual effect OR (95% CI)**
Estrogens receptor			
	Positive	1(Referent)	1(Referent)
	Negative	2.7 (1.8 – 3.9)	1.4 (0.8 – 2.3)
Progesterone receptor			
	Positive	1(Referent)	1(Referent)
	Negative	1.8 (1.3 – 2.5)	1.2 (0.8 – 1.7)
HER2 status			
	Negative	1(Referent)	1(Referent)
	Positive	2.4 (1.3 – 3.4)	1.6 (1.0 – 2.8)
Tumour subtypes			
	Luminal A	1(Referent)	1(Referent)
	Luminal B	1.8 (1.0 – 3.2)	1.4 (0.7 – 2.7)
	HER2-enriched	4.1 (2.0 – 8.5)	2.8 (1.2 – 6.5)
	Triple-negative	2.8 (1.7 – 4.4)	1.4 (0.8 – 2.6)
	Unclassified	2.0 (0.8 – 5.0)	1.5 (0.5 – 4.0)

* Adjusted for age at diagnosis, breast density, age at first birth, hormone therapy use, body mass index and family history.

** Adjusted for age at diagnosis, breast density, age at first birth, hormone therapy use, body mass index, family history as potential confounders and for grade as an intermediate variable.

How tumour phenotype affects mammography sensitivity?



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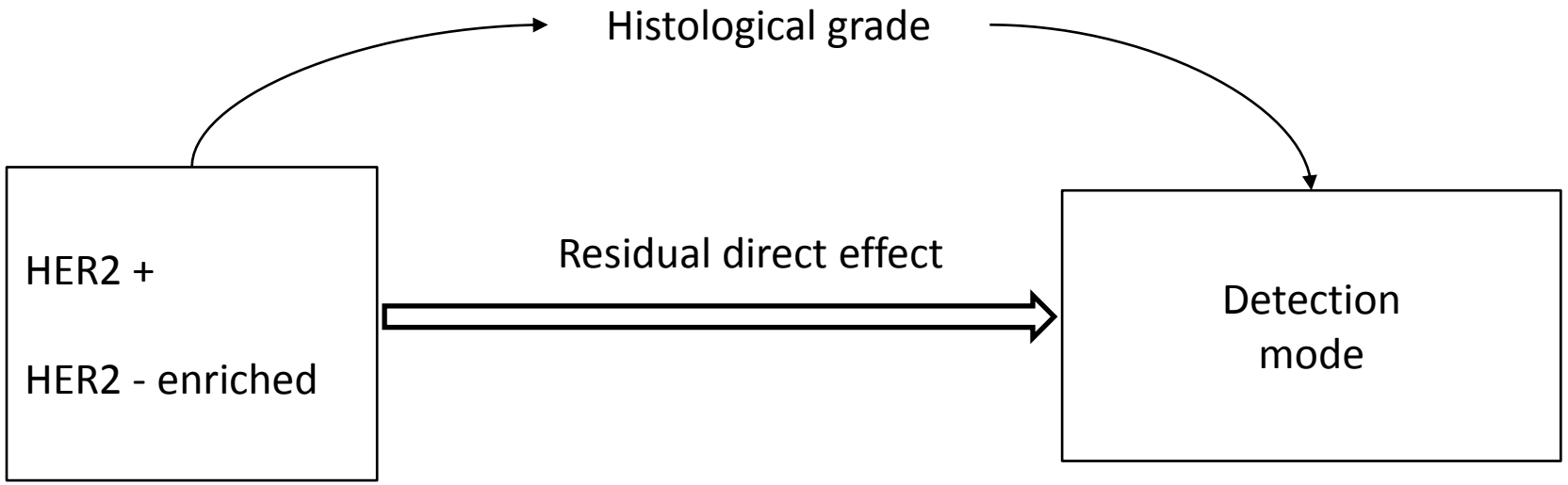

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Study strengths and limits

- Strengths
  - Relatively large sample size
  - Few missing data
  - Each molecular subtype analysed separately
  - Clear etiologic model
- Limits
  - Grade ≠ aggressiveness
  - No stratification for type of interval ca, breast density, histological type
  - Sensitivity odds ratios ≠ Sensitivity risk ratios

Conclusion

- Take into account molecular subtypes when assessing BCSP sensitivity
- Use grade as a surrogate to subtype
- Search for other etiologic pathways for HER2-enriched tumours
- Adapt BCSP