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Pack years of smoking exposure

- Non-smoker
- Evidence of simple accumulation of risk with pack years
- Evidence of a sensitive period effect with timing of puberty conditional on pack years

FIG. 3

RR of breast cancer

- 1.0
- 1.5
- 2.5
- 3.5
- 2.5

Puberty

Time
FIG. 4

**Physical environment**: material conditions, infectious agents, radiation, climate
Indoor/outdoor environmental pollutants, medical intervention, assisted technology

**Social environment**: family, friends, neighbourhood, schools, occupation, workplace, retirement, health care

Lifelong learning & socialisation

Lifetime lifestyles & psychosocial stress

Biomarkers of exposure & effect

1. **Cognitive & emotional development**
   - Cognitive & emotional development
   - Physical growth & maturation

2. **CNS integrity/neurodegeneration**
   - Homeostatic (dys)regulation
   - Body composition & change
   - Energetics capacity/consumption
   - Reproductive function

3. Early decrements in ageing phenotypes & structure/function of related physiological systems e.g. CVD & respiratory systems

4. Cognitive & physical capability
   - Age-dependent chronic diseases & disorders

5. Emotional health, Participation

**Internal environment**

**External environment**

Markers of exposure

Biomarkers of exposure & effect

F1 F2 F3 F4 F5

Conception Pre-natal Pre-pubertal Pubertal Maturity Senescence
FIG. 5

- **Structural reserve**
- **Compensatory reserve (intrinsic)**
- **Adaptations (extrinsic)**

Responses to external exposure or age-related pathology.