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FIG. 2

Unique search 1 results (n=1209)
Results identified by searches 1 and 2 (n=204)
Unique search 2 results (n=2722)

Year of publication of 4 selected works
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
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

**Internal environment**

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

**External environment**

Markers of exposure

**Biomarkers of exposure & effect**

F1, F2, F3, F4, F5

Conception, Prenatal, Pre-pubertal, Pubertal, Maturity, Senescence
FIG. 5

responses to external exposure or age-related pathology

Level of physiological function

Years of life

Structural reserve
Compensatory reserve (intrinsic)
Adaptations (extrinsic)