

# Understanding patients' life stories: a life course approach to the aetiology of Head and Neck Cancer

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# TINKER, TAILOR, FARMER, SAILOR

We can intuitively guess how these people started their life, and how they reached here and where they will go....

But evidence to support those intuitions are is still being collected.



# Presentation outline

- ❑ Definition of life course epidemiology
- ❑ Development of life course approach
- ❑ Presentation of the HeNCe life study

# Introduction to life course epidemiology

**What is life course epidemiology?**

How does it differ from conventional risk factor epidemiology?



# Defining life course epidemiology

*A conceptual framework.....Not a study design*

“The study of long-term effects on chronic disease risk of physical and social exposures during gestation, childhood, adolescence, young adulthood and later adult life” (Kuh & Ben-Shlomo, 2004).

It takes into consideration the importance of:

- 1) time (duration)
- 2) timing



# Why has life course epidemiology arisen?

- ❑ Dissatisfaction with conventional adult life style models of risk
  - ❑ Poor predictors of individual risk
  - ❑ Inability to fully explain geographical, temporal and social variations
- ❑ Natural history studies of children showing tracking of conventional risk factors
- ❑ The rise of early life influence on disease aethiology

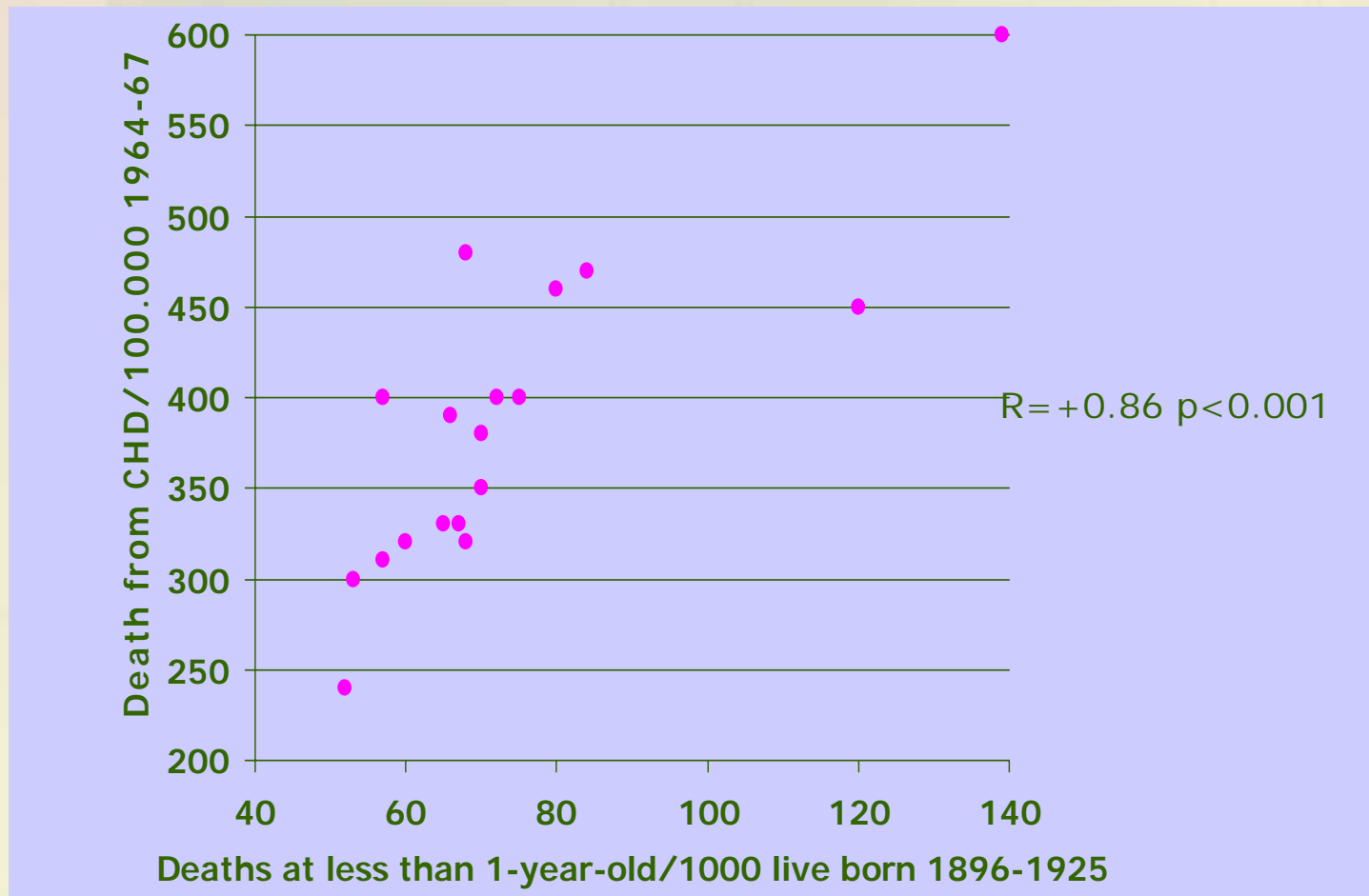


# Development of the biological programming hypothesis

- Forsdahl (1977) showed strong correlations between death rates during the 1970's from coronary heart disease and infant mortality around the time of birth of these same individuals. who died in the 1970's.



## Correlation between infant mortality rates during 1896-1925 and CHD-related mortality in 40 to 69 yr old men during 1964-67, in Finland





# Development of the biological programming hypothesis

- ❑ **Ecological studies** (Williams et al., 1979; Barker & Osmond, 1986; 1987; Barker et al., 1989)
- ❑ **Height and mortality** (Marmot et al., 1978; Notkola et al., 1985; Peck et al., 1992)
- ❑ **Historical cohort studies**

# Biological programming

Organ development in utero (*as indexed by e.g., birth weight*) and during infancy determines maximum function during adulthood (*Barker 1998*).

## Examples

- ❑ Pancreatic development – adult diabetes
- ❑ Kidney development – adult hypertension
- ❑ Lung development – adult COPD



# Challenges

- ❑ The effect of childhood and adulthood socioeconomic circumstances on adult health (Power et al., 1999; Davey Smith et al., 1997, Poulton et al., 2002);
- ❑ People who experience deprivation in early life are also, in general, those who suffer deprivation throughout their lives (Ben-Scholomo & Davey-Smith, 1991);
- ❑ Studies showing the potentially modifying influences of experiences occurring later in life (Davey Smith 2002).



# Life course epidemiology



# Life Course Models

- Critical periods
- Accumulation
- Pathways



# Critical periods

Extends the idea of biological programming to include:

## Childhood

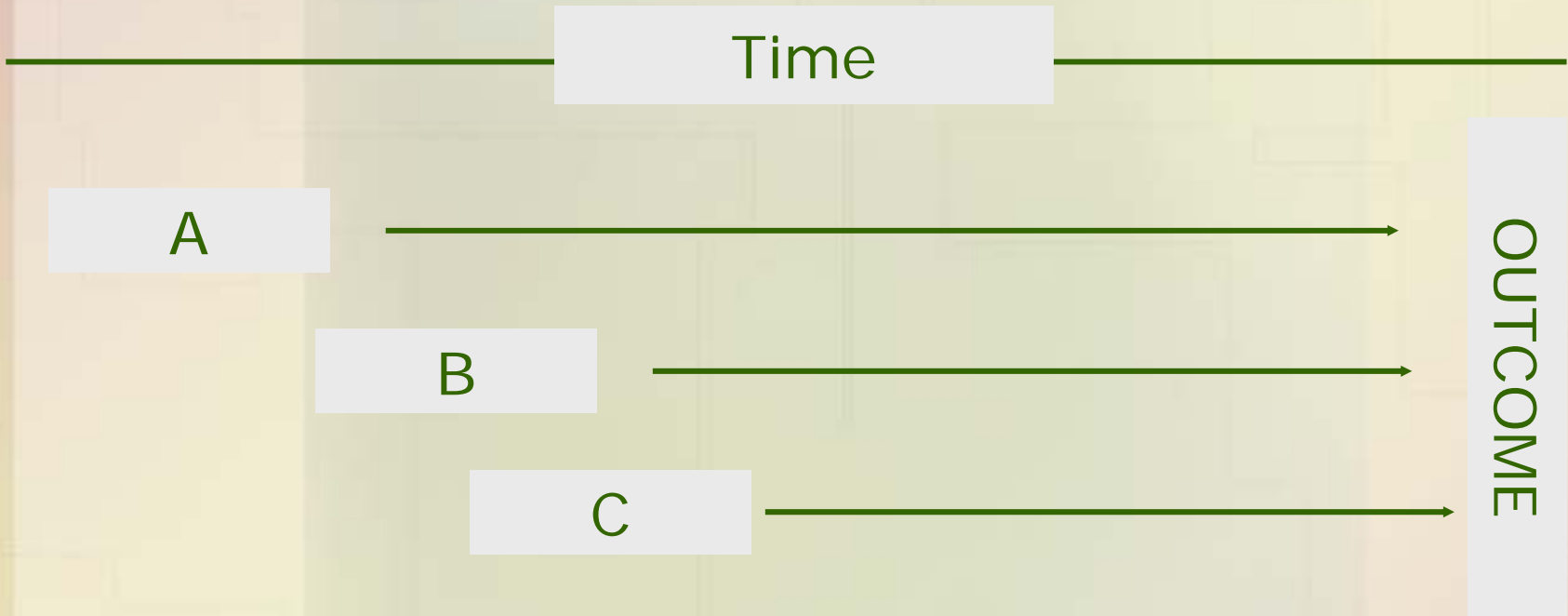
- Exposure to HPV infection at a younger age may increase the risk of developing cervical cancer (Lynch & Davey Smith, 2004);

## Social development

- Key social transitions (Bartley et al., 1997)



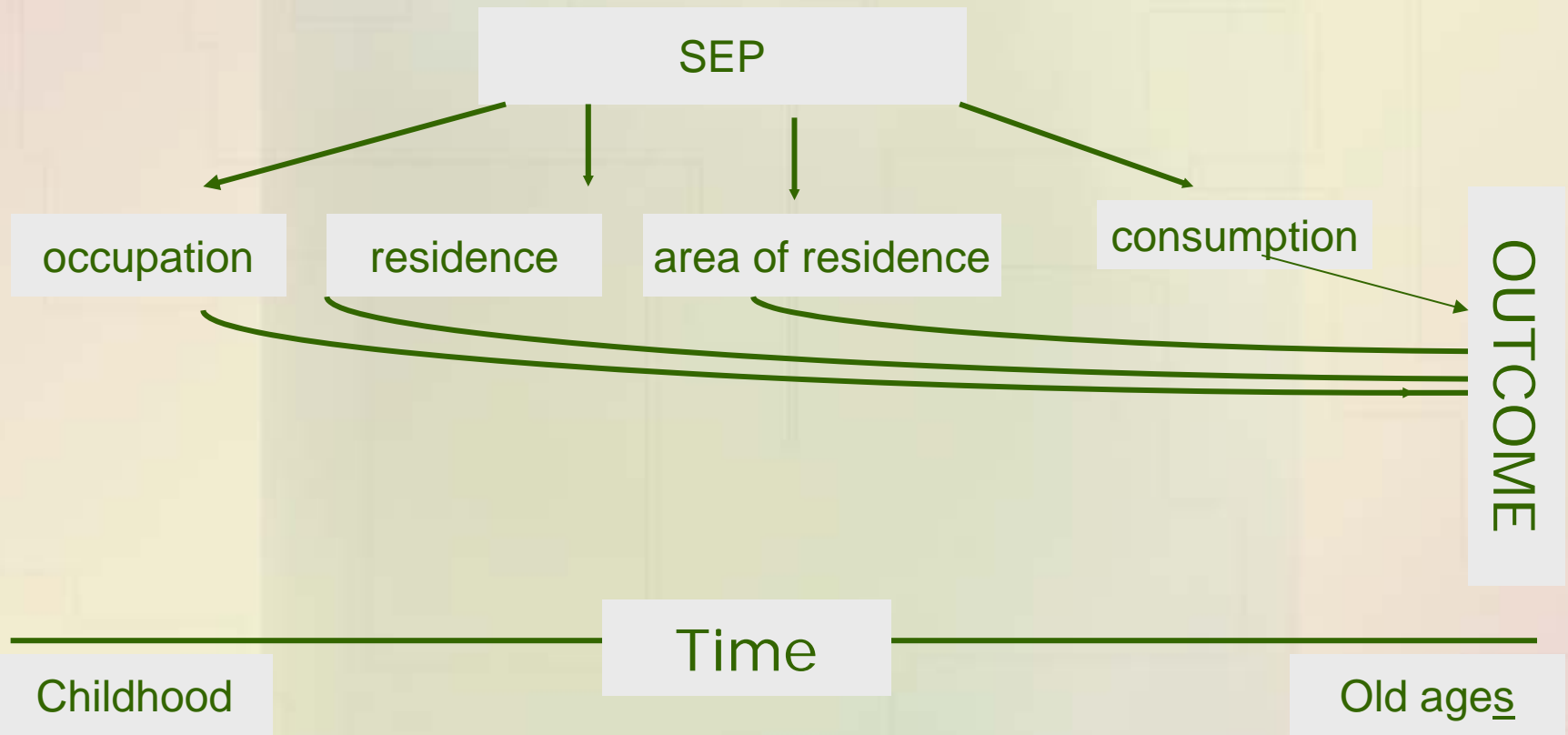
# Accumulation models



(Ben-Shlomo & Kuh 2002)

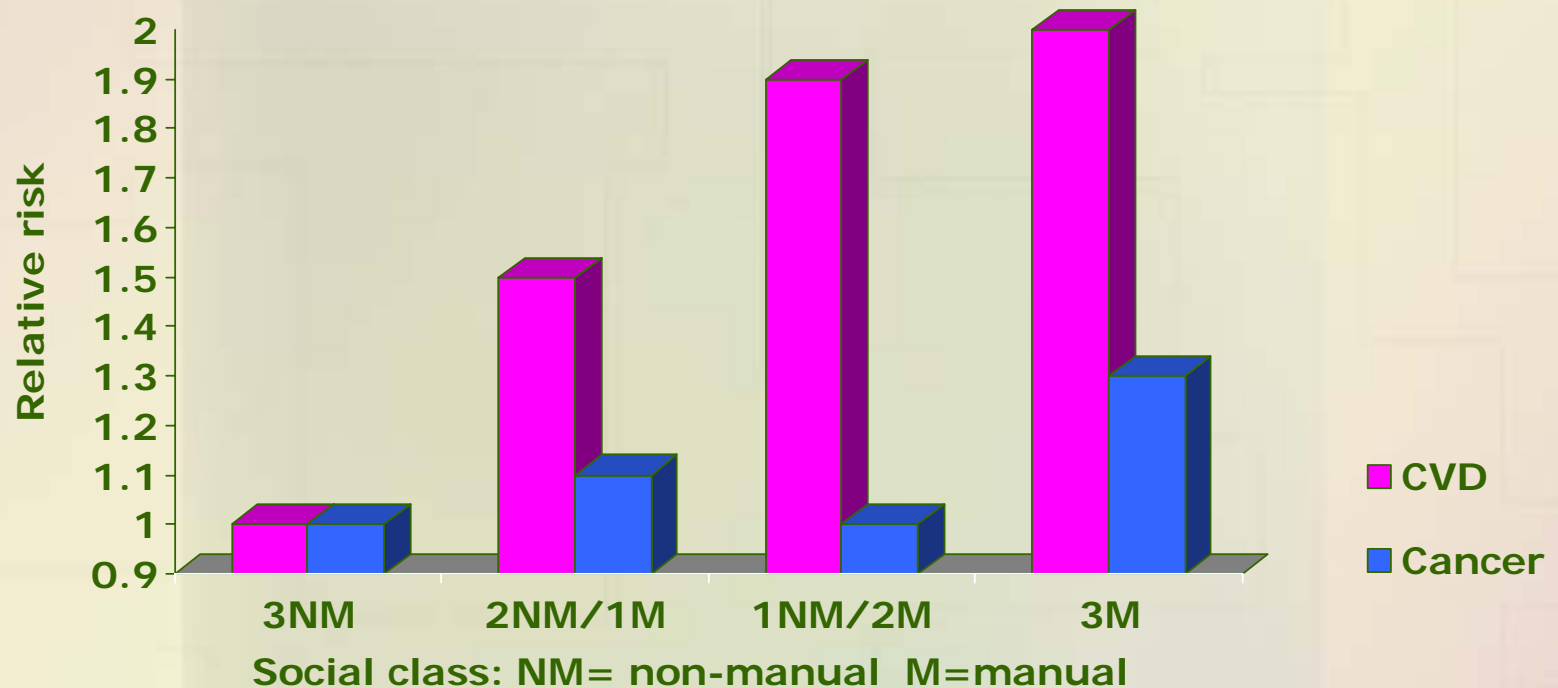


# Accumulation models





# CVD & cancer mortality and social class at different stages of the life course



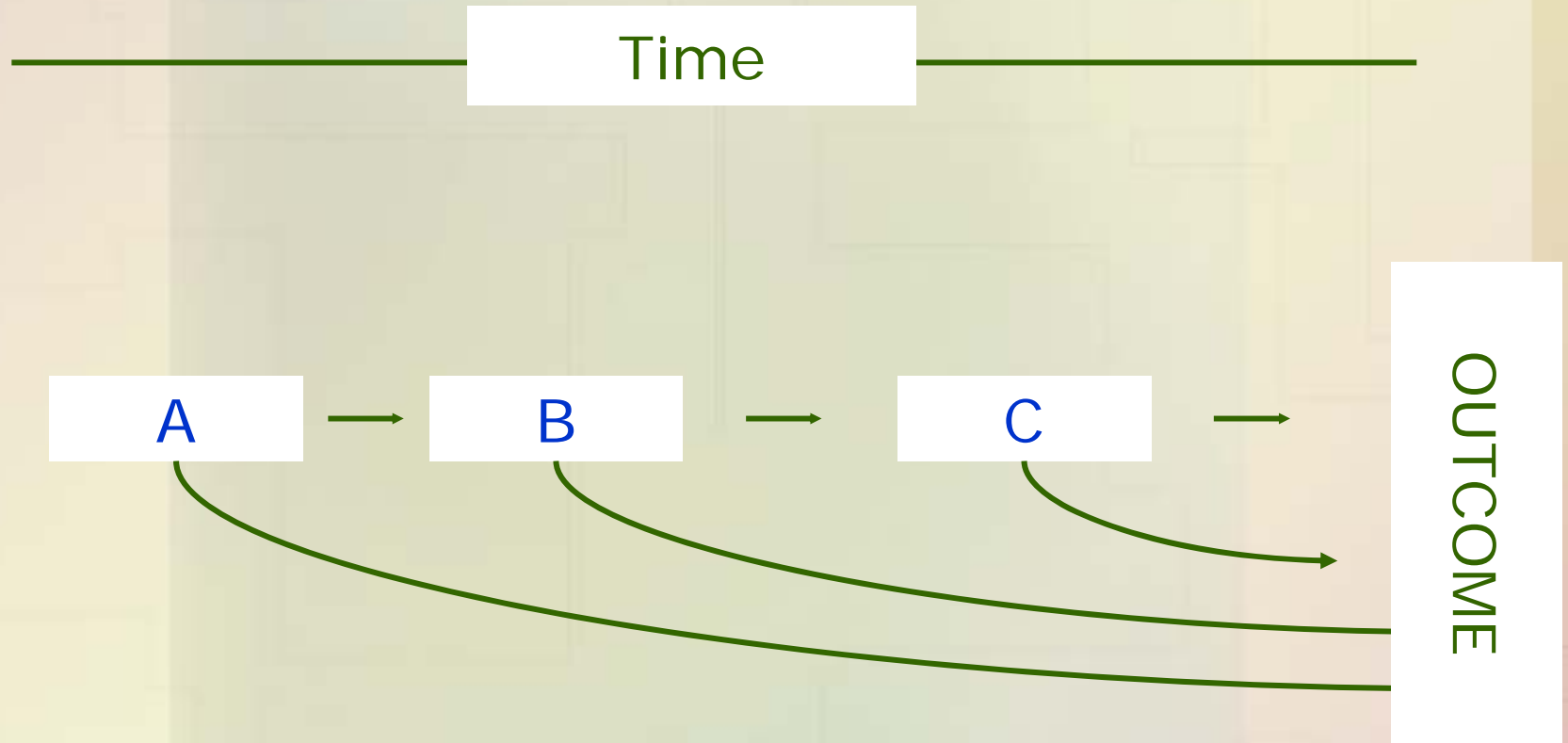
(Davey-Smith et al., 1997)



# Poor health at age 33 & cumulative SES (0-33yrs) 1958 birth British cohort



# Chain of risks or pathways



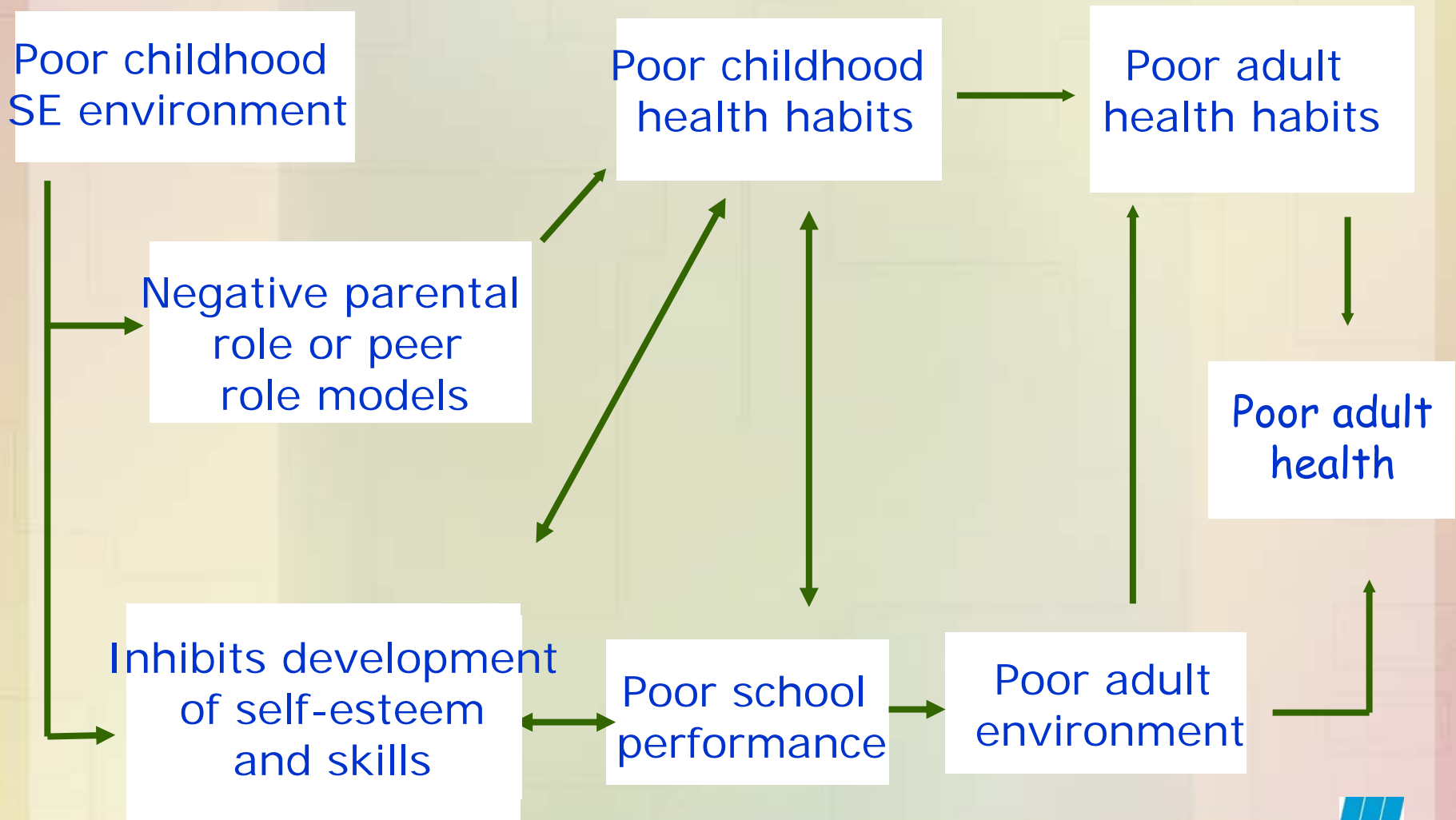
(Ben-Shlomo & Kuh 2002)



# Chain of risk or pathways

- It applies the dynamic concept of a “chain of circumstances” where the exposure to one factor is likely to be connected with exposure to other factors and these exposures are likely to accumulate over the life course (Kuh & Ben-Shlomo, 1997; Blane, 1999; Wadsworth, 1997)

# Chain of risk or pathways



# Life course: behavioural capital

- It is the accumulation of positive individual attribute such as social competence, self-esteem, decision making and problem solving skills, coping strategies, attitudes and values that help the individual remain resilient in times of adversity or take advantage of talent and opportunities.



# Life course: behavioural capital

- The stock of “behavioural capital” that individual’s accumulate will reflect in their education aspirations and achievements as well as their choice of health behaviour suggesting that both have common origins.

(Schooling & Kuh 2002)



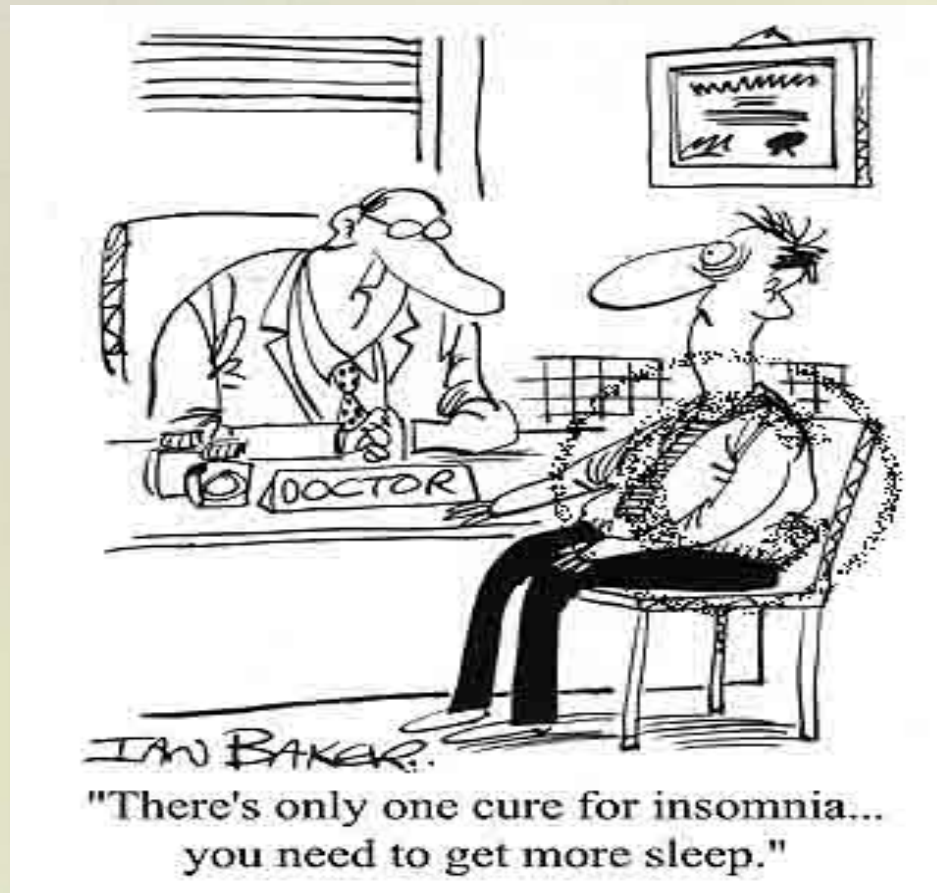
# Life course models

- ❑ It is empirically and conceptually difficult to disentangle (Kuh & Schloomo, 2004)
- ❑ They are not mutually exclusive, and a combination of all models may operate together (Kuh & Schloomo, 2004)





# Life course epidemiology: stating the obvious



But .....empirically complex.....



# HeNCE life Study



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# HeNCe life study

(Head & Neck Cancer  
life course study)



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INRS-Institut Armand-Frappier

CENTRO DE TRATAMENTO E PESQUISA

HOSPITAL  
DO CANCER

A. C. CAMARGO

- An international multicentre study of the aetiology of head & neck cancer investigating biological, genetic, social and environment factors along the life course
  
- A collaboration of
  - McGill University & INRS-Institut Armand Frappier (Montreal, Canada)
  - Albert Einstein Hospital (New York, USA)
  - Hospital do Cancer (Sao Paulo, Brazil)
  - University of Western Cape (South Africa)
  - University of Tehran (Iran)
  - University St Andrews (UK)
  - Government Dental College (Kerala, India)



# Head & Neck (H&N) cancer

- ❑ About 615 000 new cases per year (IARC-WHO 2000)
- ❑ 5th most common cancer worldwide (IARC-WHO 2000)
- ❑ Makes up about 8% of cancers in the world
- ❑ Mouth 45%; Pharynx 32% and Larynx 25% (IARC-WHO 2000)
- ❑ Males incidence rates (per 100,000): 6.6 mouth; 5.4 pharynx; 5.7 larynx



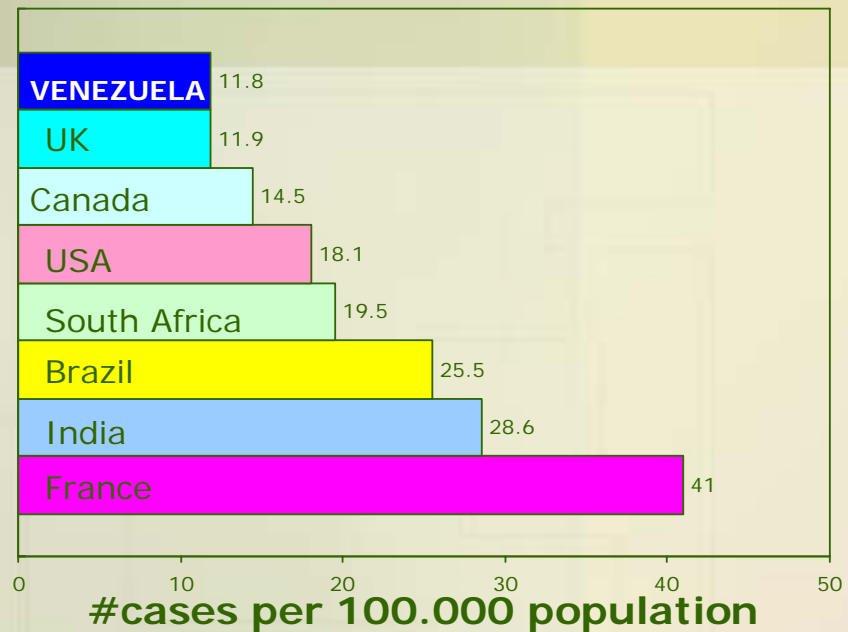
## H&N cancer

- ❑ Lack of knowledge on the aetiology of the disease.
- ❑ International variation in H&N cancer incidence rates does not follow the geographical distribution of its main risk factors.

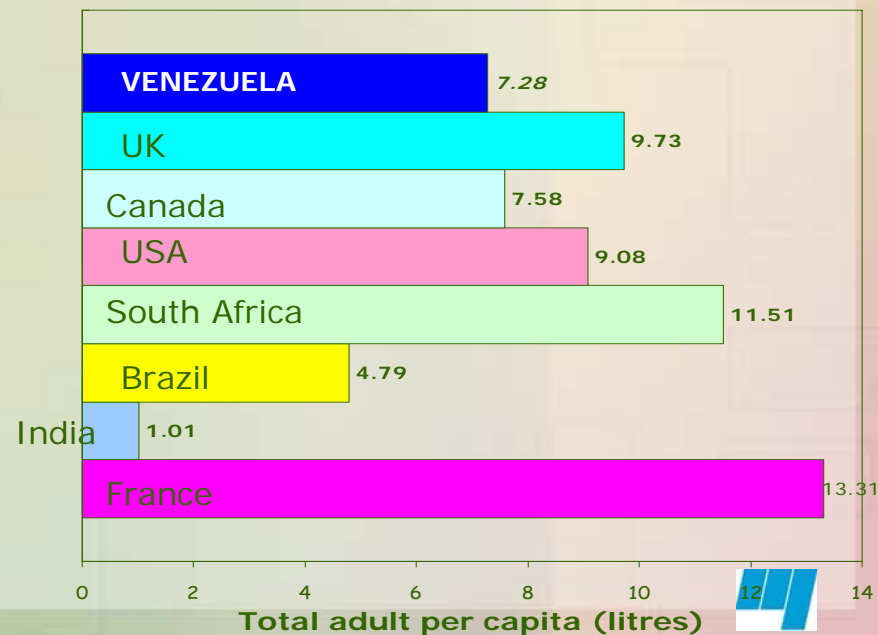
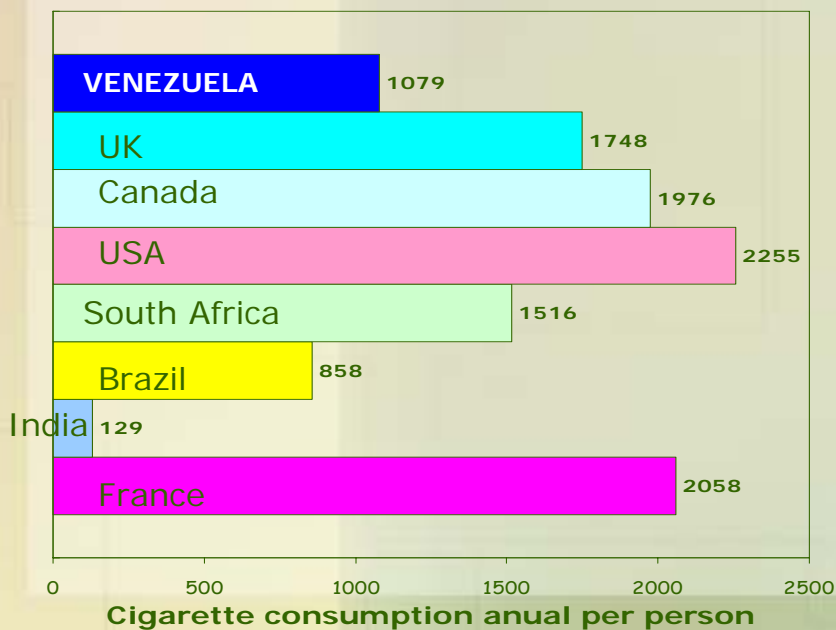


## Age-standardized international incidence of H&N cancer in males

Globocan, 2002



## Adult annual per capita cigarette & alcohol consumption in selected countries, (WHO, 2002)



# H&N cancer

- ❑ The overall incidence associated with H&N cancer is rising in some populations (Landis et al., 1999).
- ❑ 5-year survival rates have remained largely unchanged in the last 30 years, with overall survival of 53% (Greenle et al., 2001; Greenle et al., 2000).



# The HeNCe Life Study



**Hospital based case control study in 5 different countries to investigate the aetiology of H&N cancer**

**Aim:** to investigate the interplay between socioeconomic and psychosocial environment at different life stages as it mediates:

- Onset of behavioral exposures
- HPV infection
- Interaction with genetic susceptibility



# The HeNce Life Course Framework

Genetic Susceptibility

Family history of cancer

SEP & family environment

Childhood behaviour



Childhood education

SEP & family environment

Adult life style & behaviour



Work environment

SEP & family environment

Adult life style & behaviour



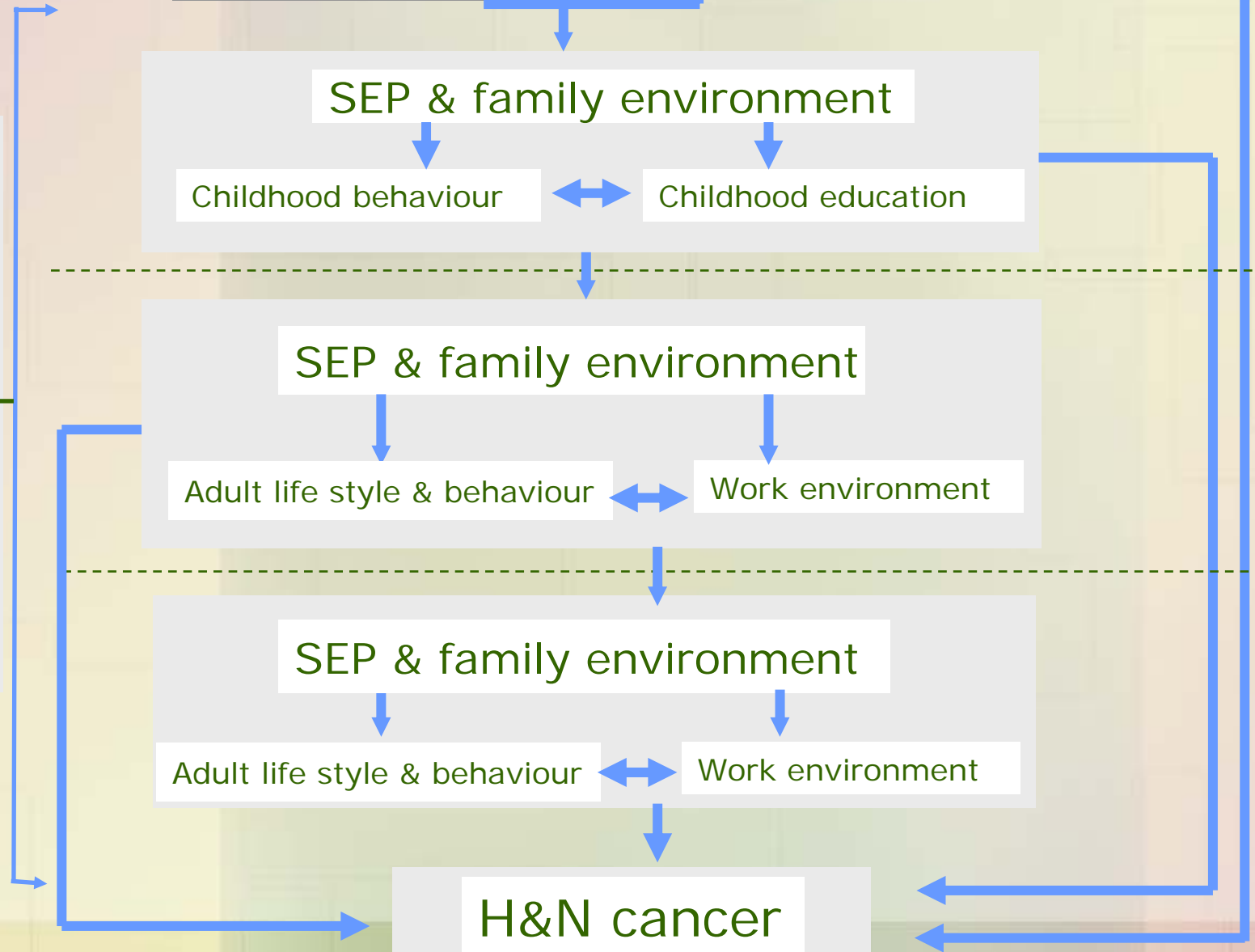
Work environment

H&N cancer

Childhood

Early adult life

Adult life



# Study design

- Hospital based case-control study with 560 cases and 560 matched (age and gender) controls from each country site

Exposure

Disease

?

?



# Sample selection

- ❑ Inclusion criteria
  - ❑ No history of cancer of any kind
  - ❑ No cognitive or mental disorders
  - ❑ Lives within a 50km radius of the hospital's area
  - ❑ Born in the country where the study is taking place
  - ❑ Speaks the country's mother tongue



## Definition of cases

Patients newly diagnosed with a histologically confirmed stage I to IV squamous cell carcinoma in the upper aerodigestive tract. This group includes cancer of the oral cavity (tongue, gum, floor of mouth, other mouth) oropharynx, hypopharynx and larynx



## Definition of controls

- ❑ Recruited from same hospital as the index cases or at a neighbouring general hospital with a similar catchment area.
- ❑ Recruited from a strictly defined list of non-chronic diseases unrelated to tobacco and alcohol habits.
- ❑ No single diagnostic group will contribute to more than 20% of the total sample.
- ❑ Matched to cases by gender, language and age ( $\pm 5$ years).



# Data collection

- ❑ Structured interview using questionnaire and life grid during three time periods
  - ❑ Childhood: birth to 16 years old
  - ❑ Early adulthood: 17 to 30 years old
  - ❑ Adulthood: 31 years and over
- ❑ Medical records
- ❑ HPV testing
- ❑ Genetic polymorphisms



# The HeNCE Life interview technique

## The Use of the Life Grid & Questionnaire



# Life Grid

## Life grid:

- ❑ A tool to improve accuracy of recall
- ❑ Involves cross-referencing dates of changes of the behaviour or environment of interest
- ❑ Provides a better estimate of timing and the duration of events and behaviours at different stages of life.

## Events used for cross referencing:

- 1. Historical events:** Natural disaster, well known political or news event, end of war...
- 2. Personal life events:** Birth of child, marriage, graduation, death of parent, divorce, promotion .....



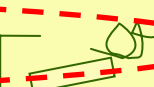






# The Training Video I:



# The Life Grid: Linking Life Events, Behaviours and Change

Other	Housing	Yr	Age	Education/Jobs	Habits
		1934	0		
			5		
End of WW2		1944	10		Started smoking
Death of Father			15		
Married		1954	20		
1 <sup>st</sup> child/63			25		①
JK death/63					
Expo 67		1964	30	Unemployed	 ++

# The Questionnaire

## Childhood

(0-16 years of age)

## Early adulthood

(17-30 years of age)

## Later Adulthood

(30 years to date of dx)

Medical History (childhood and adulthood)

Education

Employment

Housing and residential environment

Alcohol consumption habits

Smoking habits

Oral health

Sexual behaviour

Family history of Cancer

Parental relationship during childhood

Social Support

Life events (childhood & adulthood)

Dietary Habits

Quality of life (Brazilian & Indian sites)

# The Training Video II:



# Implementation across sites

❑ International sites will use country specific events

❑ Examples:

- ❑ Brazil: Military dictatorship started
- ❑ Canada: Ice storm
- ❑ *South Africa*: end of apartheid
- ❑ *India*: Mahatma Gandhi assassinated in New Delhi.



# Quality assurance & control

- ❑ Data collection procedures
  - ❑ guidelines for the interview and DVD
- ❑ Highly trained personnel
- ❑ Monitor performance of the personnel using meaningful criteria
  - ❑ interviews in different sites will be recorded and compared against a gold standard.
- ❑ Repeat studies
  - ❑ 10% of the whole sample will be re-interviewed to test for reliability.
  - ❑ a sub-sample of participants' siblings within same age range as the study's participants will be interviewed to check for accuracy of the information collected.
  - ❑ A sub-sample of participants will be re-interviewed using the life grid and without the life grid.



# Results from repeat studies

	<b>Interview using the life grid</b>	<b>Interview without life grid</b>
<b>Smoking</b>	0.82	0.76
<b>Alcohol</b>	0.75	0.72
<b># addresses/childhood</b>	0.71	0.60
<b># addresses/early adulthood</b>	0.78	0.75
<b># addresses/later adulthood</b>	0.80	0.80
<b>#unemployment</b>	0.85	0.72
<b>#Jobs</b>	0.85	0.74



# Benefits of the use of the life grid

- ❑ Improves accuracy with which events are remembered and the duration of these events
- ❑ Releases details from memory by linking different information from the same period of life
- ❑ Provides an interactive interview (maintains interest throughout the 1.5-2 hour interview)





## Pilot studies

- ❑ Brazil: 3 pilot studies (first country)
- ❑ Canada 2 pilot studies
- ❑ South Africa: 1 pilot study
- ❑ Iran: feasibility study and pilot study
- ❑ India: pilot study



## Conclusions: pilot studies

- ❑ In general, the pilot studies confirmed the feasibility of the methodology, although some minor modifications had to be made to the structure of the interview.

### ❑ Variations for different cultural settings:

#### *Examples:*

- ❑ In Brazil, the use of chimarrao (a special kind of herbal tea)
- ❑ Variations in dietary intake
- ❑ Sensitivity to sexual activity questions
- ❑ Heating systems in Canada



## Conclusions from pilot studies cont....

- ❑ The time required for the interview was realistic with the majority of the subjects finding it adequate.
- ❑ Acceptance rates were good
- ❑ Subjects were interested in the process of discussing their life and life events.



# Where we are today.....

- ❑ Studies have begun in Canada, Brazil and South Africa
- ❑ Feasibility/Pilot work is currently underway in Iran and India
- ❑ The questionnaire has been tested in French, Portuguese, Persian, and English. Malayalan version to be tested soon



## Summary and Implications

- ❑ The life course framework can be used to efficiently investigate complex associations.
- ❑ Data on life course exposures may be difficult to obtain when using a retrospective design. However, the combination of the life course interview technique with a strict quality control and assurance protocol, may provide data with acceptable levels of measurements errors.



# Summary and Implications

- ❑ The use of the life course framework allows a comprehensive understanding of the main exposures that may lead to H&N cancers.
- ❑ The dynamic and multi-dimensional nature of the quality of life concepts demonstrates that it is well fitted for life course studies



# Summary and Implications

Data from the Brazilian site the life course exposures and quality of life outcomes will soon be available to test.



# The HeNCe Life Team



**Canada:** Paul Allison, Eduardo Franco, Jennifer O'Loughlin, Francois Coutlee, Christine Gurekian;

**S. Africa:** Ratilal Laloo

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**India:** Gopal Netuveli, Ipe Verghese;

**UK:** Gerry Humphries, Amanda Sacker;

**Iran:** Batoul Shariati

**Brazil:** Luis Paulo Kowalski, Maria Paula Curado, Julia Mariko;



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- Canadian Institutes of Health Research
- Medical Research Council of South Africa
- AC Camargo Cancer Hospital
- University of the Western Cape



"It is better to know the patient who has the disease, than it is to know the disease which the patient has." (Hippocrates)

THANK YOU

