Pathways to Cancer Prevention

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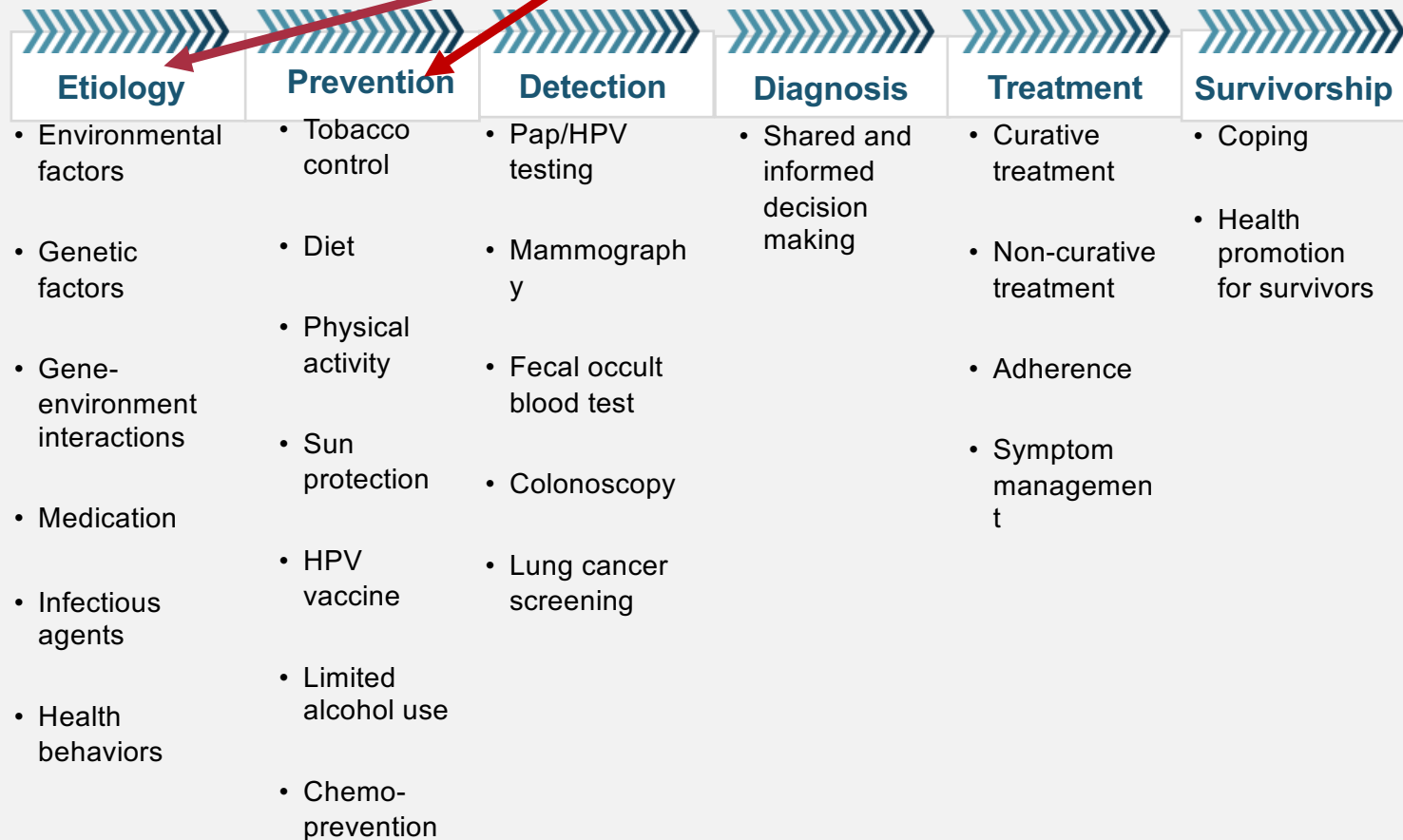
www.sehn.org

Collaborative on Health and Environment

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THE CANCER CONTROL CONTINUUM (NCI)

TODAY'S FOCUS

Etiology	Prevention	Detection	Diagnosis	Treatment	Survivorship
• Environmental factors	• Tobacco control	• Pap/HPV testing	• Shared and informed decision making	• Curative treatment	• Coping
• Genetic factors	• Diet	• Mammography		• Non-curative treatment	• Health promotion for survivors
• Gene-environment interactions	• Physical activity	• Fecal occult blood test		• Adherence	
• Medication	• Sun protection	• Colonoscopy		• Symptom management	
• Infectious agents	• HPV vaccine	• Lung cancer screening			
• Health behaviors	• Limited alcohol use				
	• Chemo-prevention				

Adapted from David B. Abrams, Brown University School of Medicine

Etiology: Causes of cancer

- More than 100 kinds of cancer; causes vary

- What do we mean by "cause"?

- Most cancers arise from a collection of multiple factors, not exposure to single agents. Multi-causality. "Causal webs"

Rothman's Sufficient Causal Model

A cause is not a single component, but a minimal set of conditions or events that produces the outcome in an individual person. Interactions among component causes are a primary feature

One sufficient causal "pie" for lung cancer
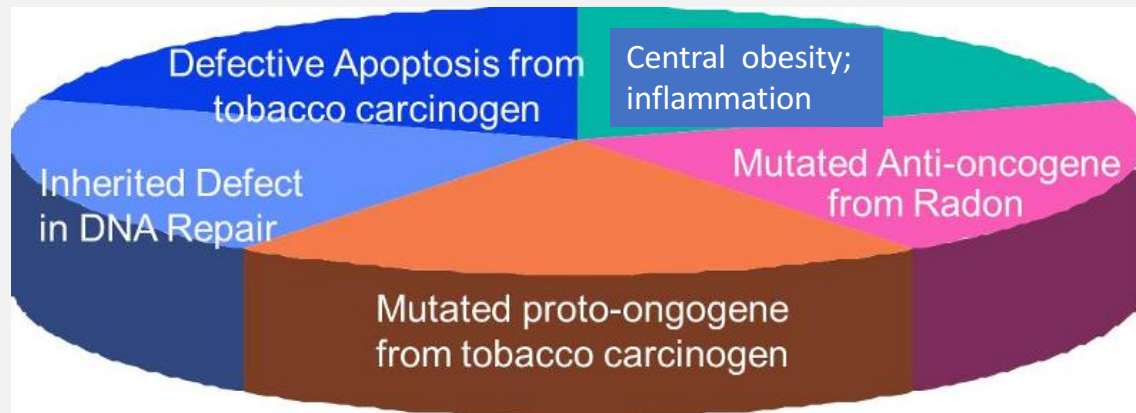
Which causal pathway <u>combinations</u> are sufficient to result in cancer development over time? What are the implications for cancer prevention? "Intercepting" cancer before "sufficiency" is completed?

Sufficient Causal Model
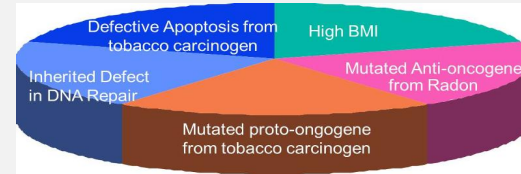
- More than one collection of risk factors can cause a particular kind of cancer
- Combinations of other component causes can also be sufficient; i.e., various sufficient causes for lung cancer
- Tobacco is important but, what else? Proportion of never-smokers among patients with NSCLC increasing 1990-2013. (Pelosof, 2017)

Criteria air pollutants; diesel exhaust; dozens of hazardous air pollutants; industrial chemicals, metals; asbestos; silica; radon; radiation; etc.
        (IARC; Field, Clin Chest Med, 2012)

Interactions among causal risk factors, over the life course, make it very difficult to determine valid population attributable fractions for many kinds of cancer

Etiology

- A common list of cancer risk factors: Tobacco, diet, obesity, infectious agents, reproductive factors and hormones, ionizing radiation, genetics, alcohol, UV light, pharmaceuticals

- What's missing? Why?

- Candidates:
  - Environmental and workplace chemicals linked to cancer; Chemicals in consumer products
  - Neighborhood- and community-level variables, including pollutants in air, water, food; some communities have dramatically higher exposures (e.g. St. John the Baptist Parish in La.; communities with cancer risk from air carcinogens 50 X the national average
  - Non-ionizing radiation (cell phones, etc.)

Key Characteristics of Carcinogens

Known human
carcinogens
have one or more of
these properties;

These are now
routinely integrated
into IARC's assessments
of potential carcinogens

Smith et al, EHP, 2016

**Table 2.** The KCs of human carcinogens (from (16))

Key characteristic
1. Is electrophilic or can be metabolically activated
2. Is genotoxic
3. Alters DNA repair or causes genomic instability
4. Induces epigenetic alterations
5. Induces oxidative stress
6. Induces chronic inflammation
7. Is immunosuppressive
8. Modulates receptor-mediated effects
9. Causes immortalization
10. Alters cell proliferation, cell death or nutrient supply

Exposome

Exposure to all <u>exogenous</u> environmental agents, socioeconomic conditions, lifestyle, and diet along with markers of <u>endogenous</u> processes across the life-time of an organism or community of interest.
(Wild, 2005)

Rationale:

- To balance the outsized emphasis on the genome with a comparable concept that encompasses the complexity of exposures
- To link external exposures to internal body burden, and internal body burden to biologic responses and disease outcomes.
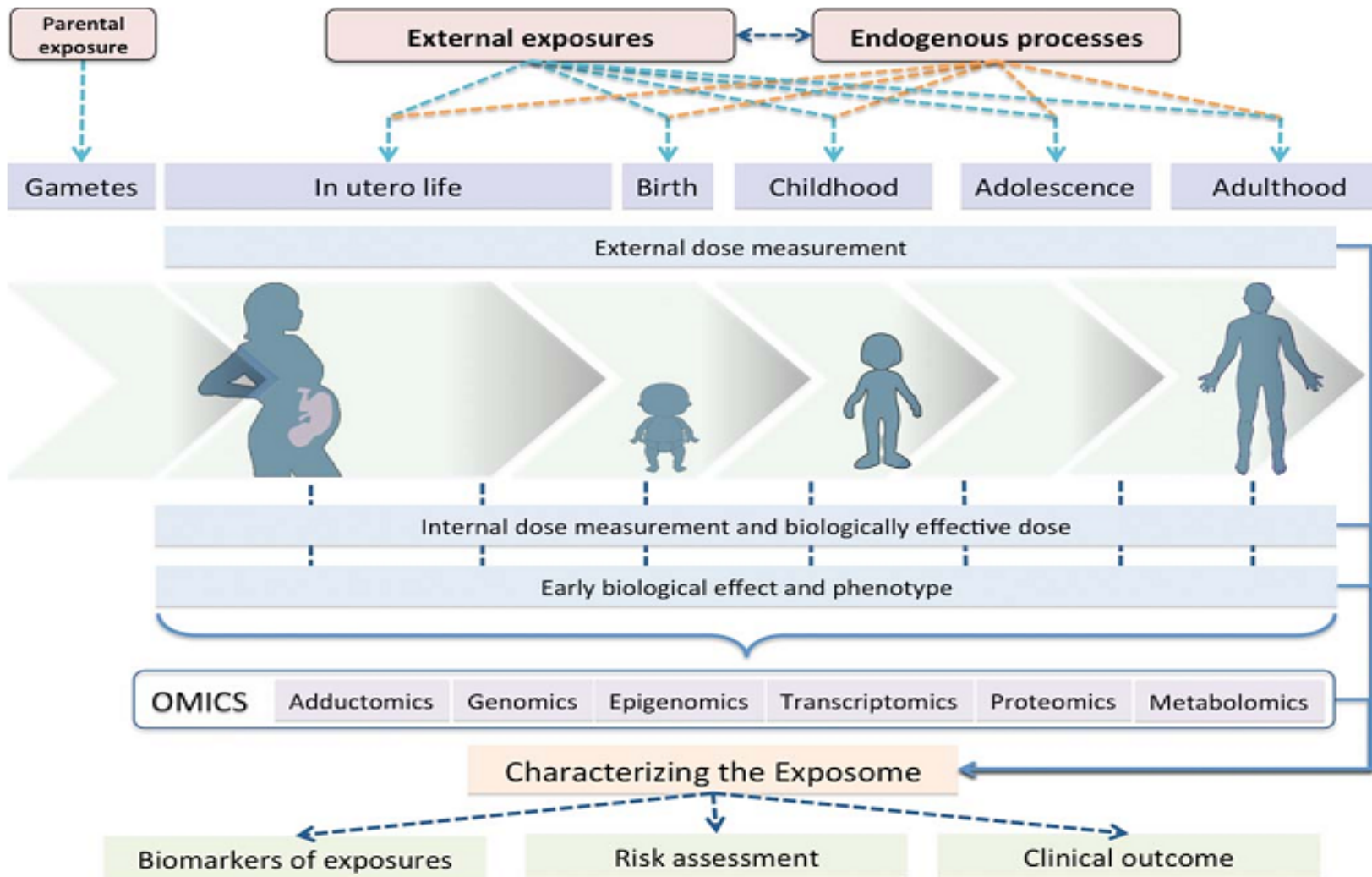
Wild, EMM, 2013

Public health exposome

A framework that helps identify and compare differential levels of exposure at critical life stages, personal health outcomes, and their contributions to health disparities at a population level

- Includes mediating and moderating factors at both the individual and population health levels.

Juarez, Int. J. Environ. Res. Public Health 2014

General external exposures

- Chemical
  - Air, water, soil, food, consumer products
  - Built environment: home, work, school, community

- Social environment
  - Poverty, education, employment, segregation, discrimination, racism, adverse childhood experiences (ACEs), control in life and on the job, etc. (can directly or indirectly influence risk)
  - Access to resources and opportunities; measures of resilience

- Policy environment: Federal, state, local

Public health exposome conceptual model
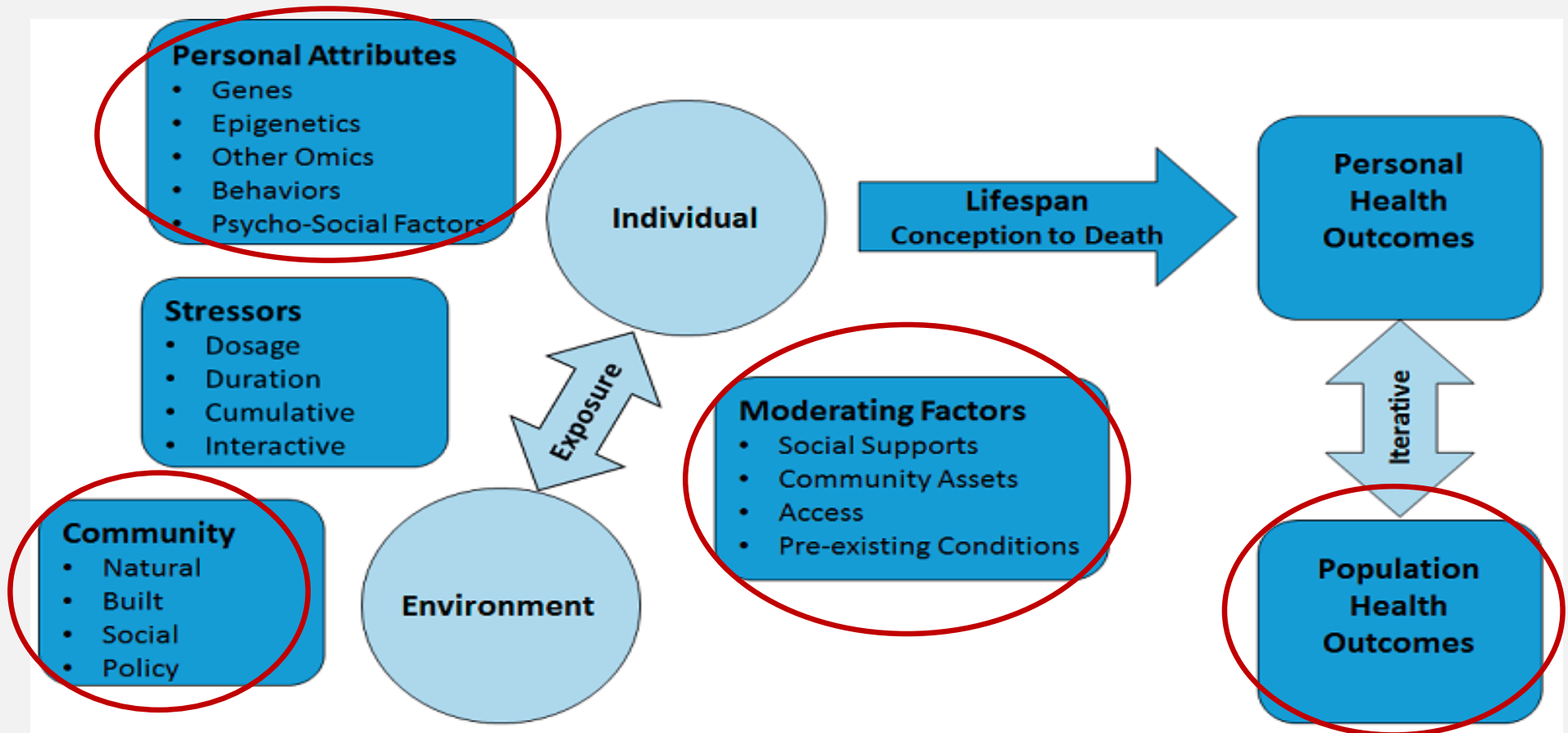
Juarez et al., 2014

Summary

- Unique combinations of exposure, susceptibility, resistance, and life history influence whether or not cancer develops.

- It is impossible to know how these components add up to a specific proportion of the total cancer burden. Furthermore, "it is not necessary to propose a hierarchy or play one component cause off against another, fostering competition rather than collaboration". (Clapp, et al)

Summary

An exposome framework:

Explicitly acknowledges that multiple, multi-level chemical and non-chemical stressors, over the life course, influence cancer risk in individuals and populations
(a quintessential "mixture" problem)

Moves us away from an overwhelming emphasis on individual behavioral change and adds programs and policies that also address workplace, school, community and societal level contributions to risk
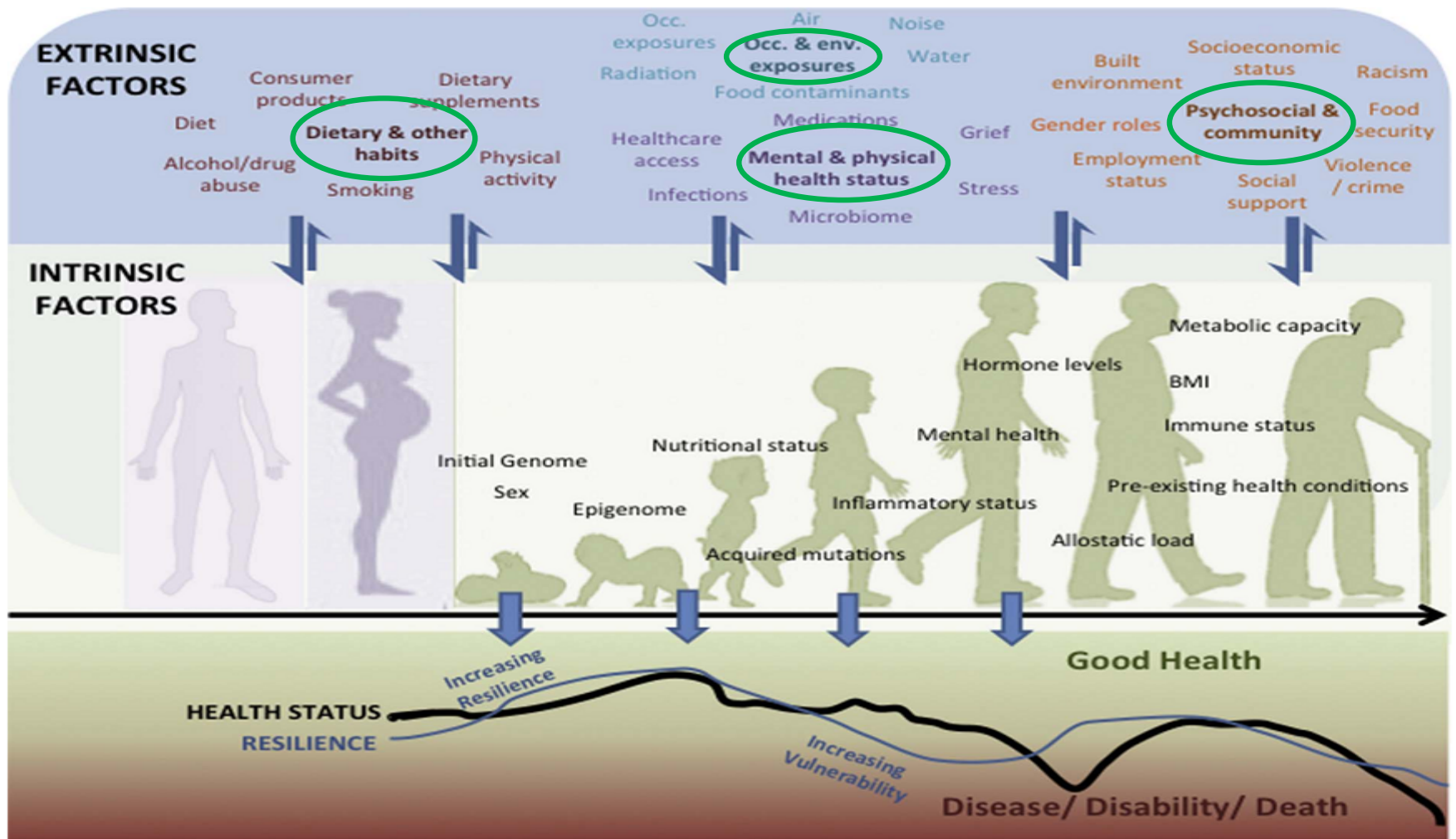
Moving from G x E to I x E (Individual, community, societal level variables) McHale; Mutat Res, 2018