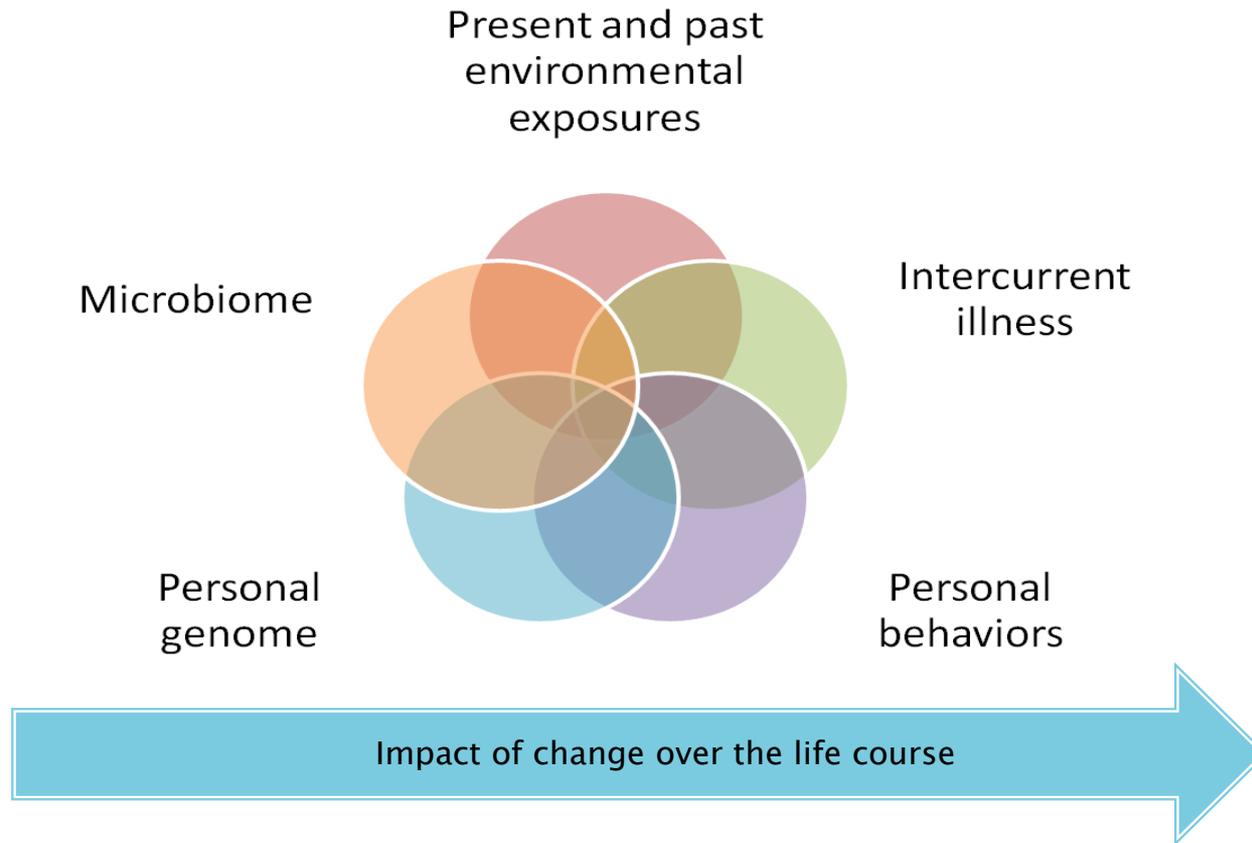


# Susceptibility to adverse effects from vaccines – from emerging science to policy

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# Susceptibility – occurrence of disease usually attributable to more than one cause



# Susceptibility to vaccine AEs

- ✓ Invasive viral disease in immunodeficient individuals
- ✓ Immune mediated
  - ✓ Egg and gelatin allergic people
  - ✓ Predisposition to adverse effects of smallpox vaccines (ICAM-1, CSF-3, IL-4)
  - ✓ Rechallenge
- ✓ Age and gender
- ✓ Hypothetical -- Metabolically vulnerable because they lack reserve
  - ✓ But note that some of these children have worse outcomes with the natural disease

# How should we think about genetics?

- ✓ Unusual for a specific genetic change to have the same manifestations in each individual
- ✓ The case of sickle cell disease
  - ✓ All cases have the same mutation but the clinical course is widely variable
- ✓ Understanding the full array of symptoms that patients have is critical

# How should we think about genetics?

## Why is this hard?

- ✓ The effect of ascertainment bias
  - ✓ Phenotype based ascertainment -- Usually use extreme cases to try to find genetic factors
  - ✓ Subsequent genotype based ascertainment usually reveals a broader array of phenotypes
  - ✓ Cystic fibrosis (CF) and medium chain acyl CoA dehydrogenase deficiency (MCAD) examples
- ✓ What about windows of vulnerability?
  - ✓ Changing expression over time

These questions of phenotypic variation, ascertainment bias, and changing impact over the life course arise no matter what the source of the susceptibility



# How do we define the impact of intervening exposures?

- ✓ The easy case
  - ✓ Immunodeficient people who develop invasive disease with vaccine virus
- ✓ What level of biological evidence is/should be required?
  - ✓ What is needed may depend on your purpose
  - ✓ Understanding biological mechanisms to understand or treat disease?
  - ✓ Compensation?