An Introduction to Endocrine Disrupting Chemicals

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Disclosures / Conflicts of Interest

- My spouse is employed by CVS Health
- My work is funded by the National Institutes of Health, the Allen Family Foundation, the Great Neck Breast Cancer Coalition, and the Cornell Douglas Foundation.
- I have received travel reimbursements from NGOs, industry, and academic organizations to speak about endocrine disrupting chemicals

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Objectives

1) Explain endocrine disrupting chemicals (EDCs)

2) Examine endocrine disease trends

3) Apply the principles of endocrinology to the study and understanding of EDCs

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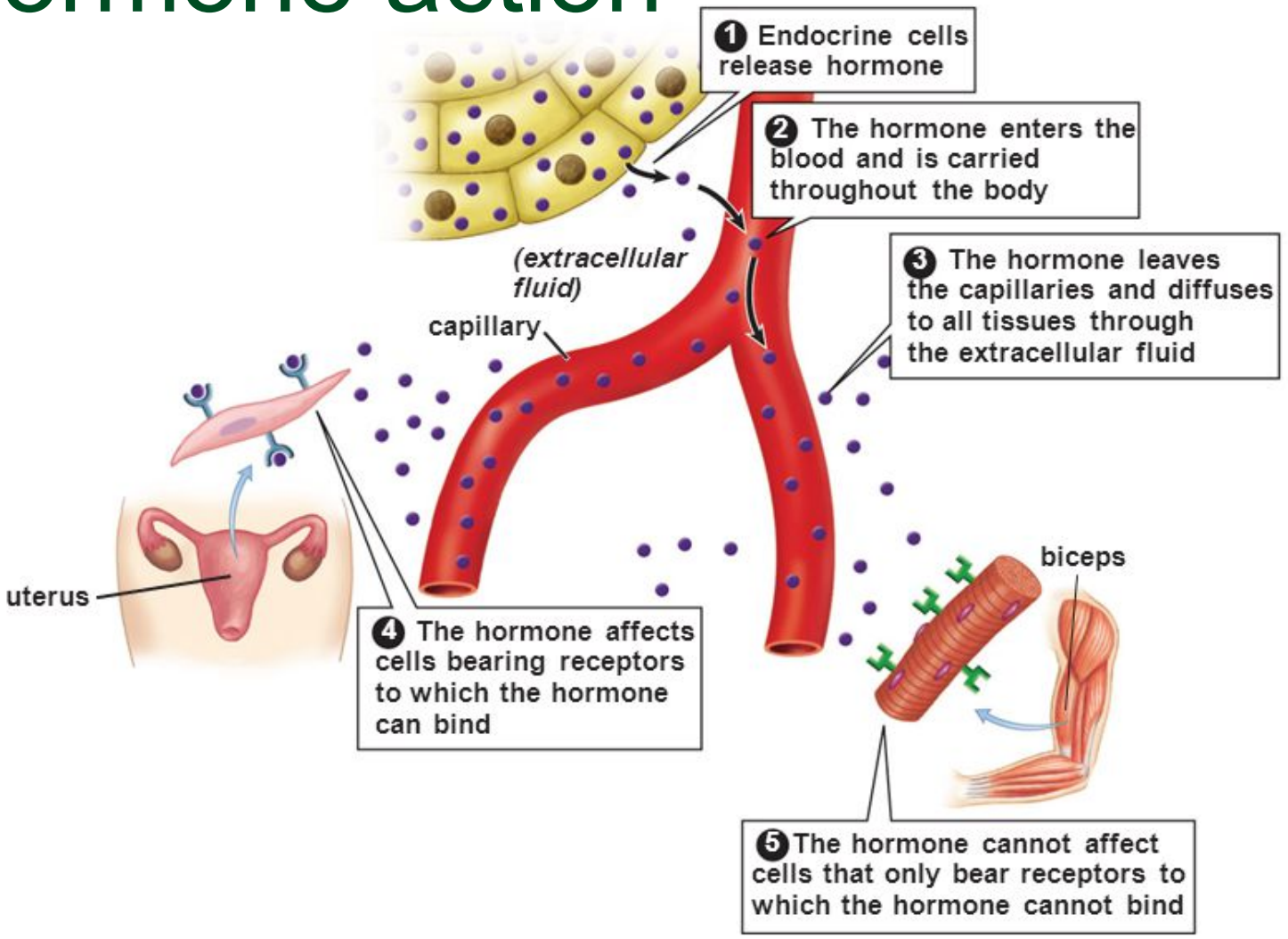
What are Endocrine Disrupting Chemicals (EDCs)?

EDCs are exogenous chemicals or chemical mixtures that interfere in some way with hormone action.

Hormone action



- Synthesis
- Secretion
- Transport
- Binding
- Action
- Elimination

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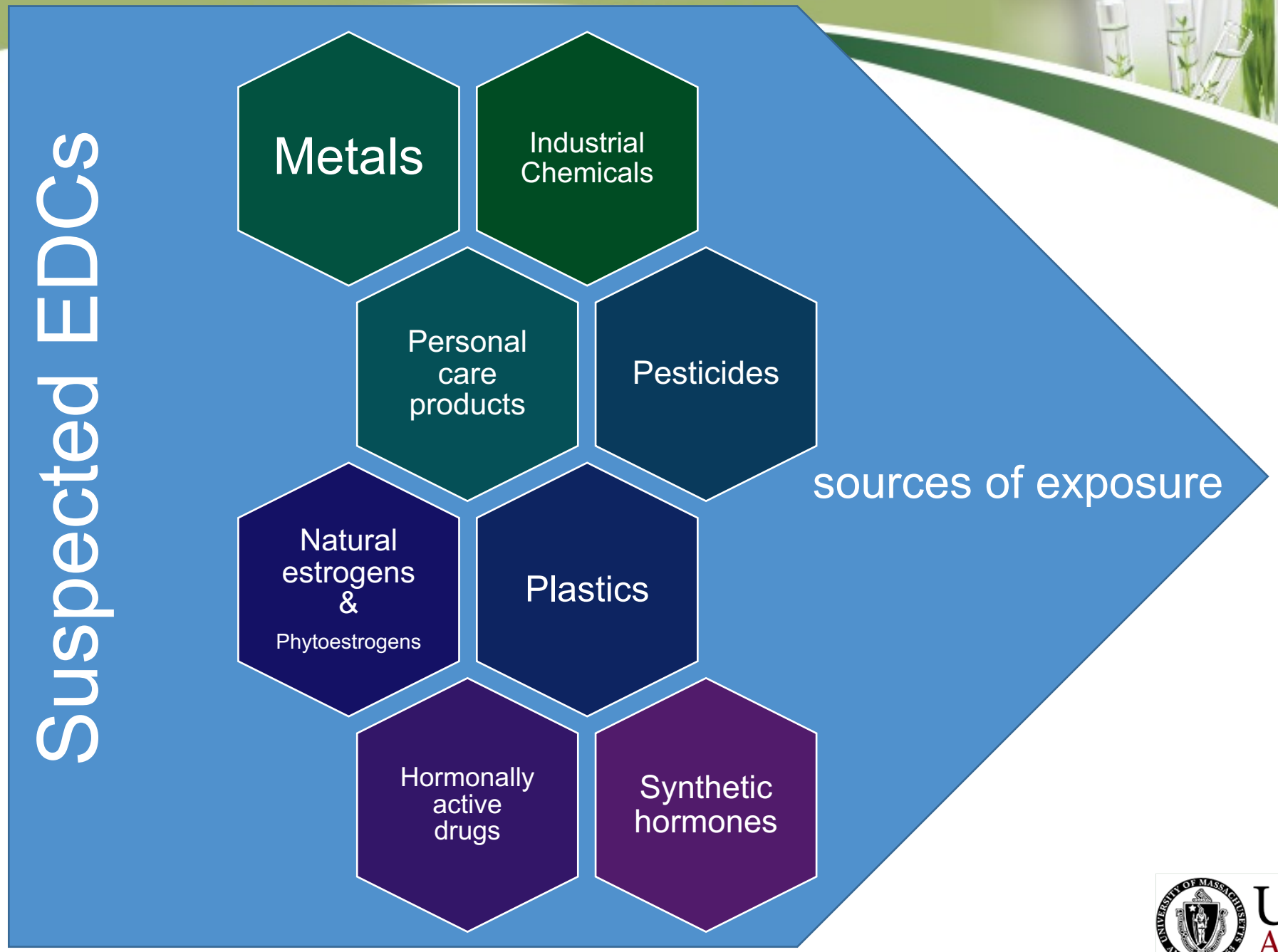

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Daily exposures to many of these chemicals are typically low – and often unsuspected

Bisphenols

Perchlorate

Benzophenones

PFAS

Parabens

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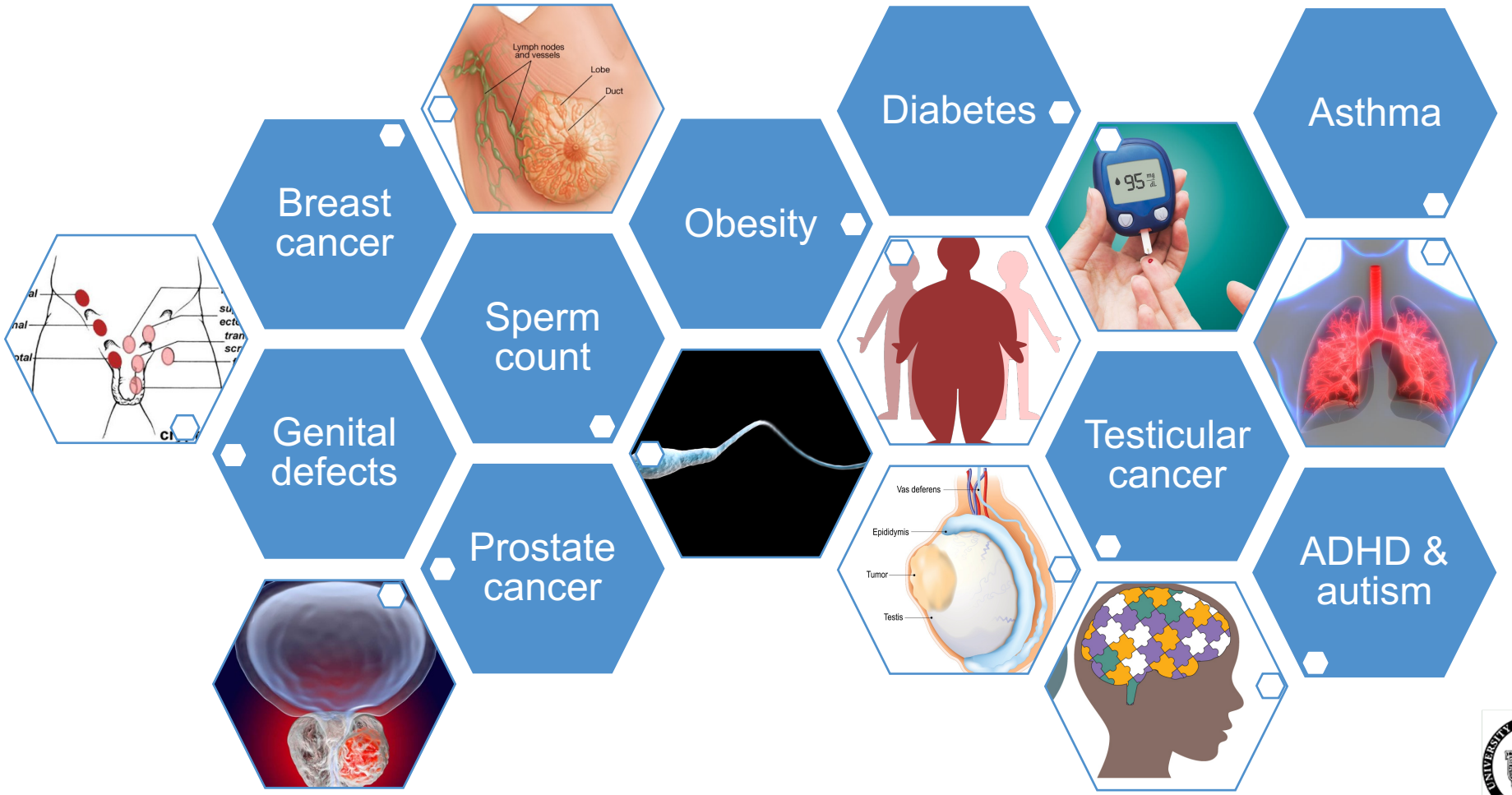
We often hear: “But we’ve all been exposed and we’re all fine!”



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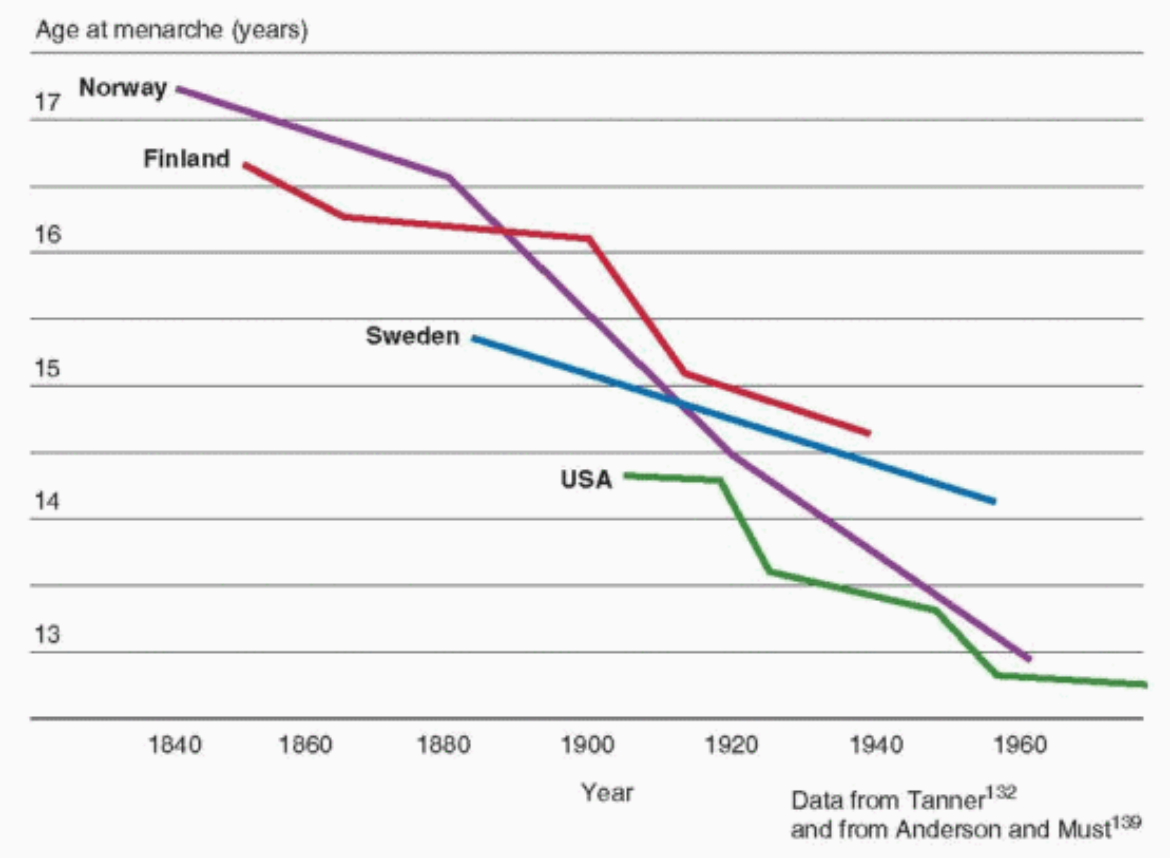
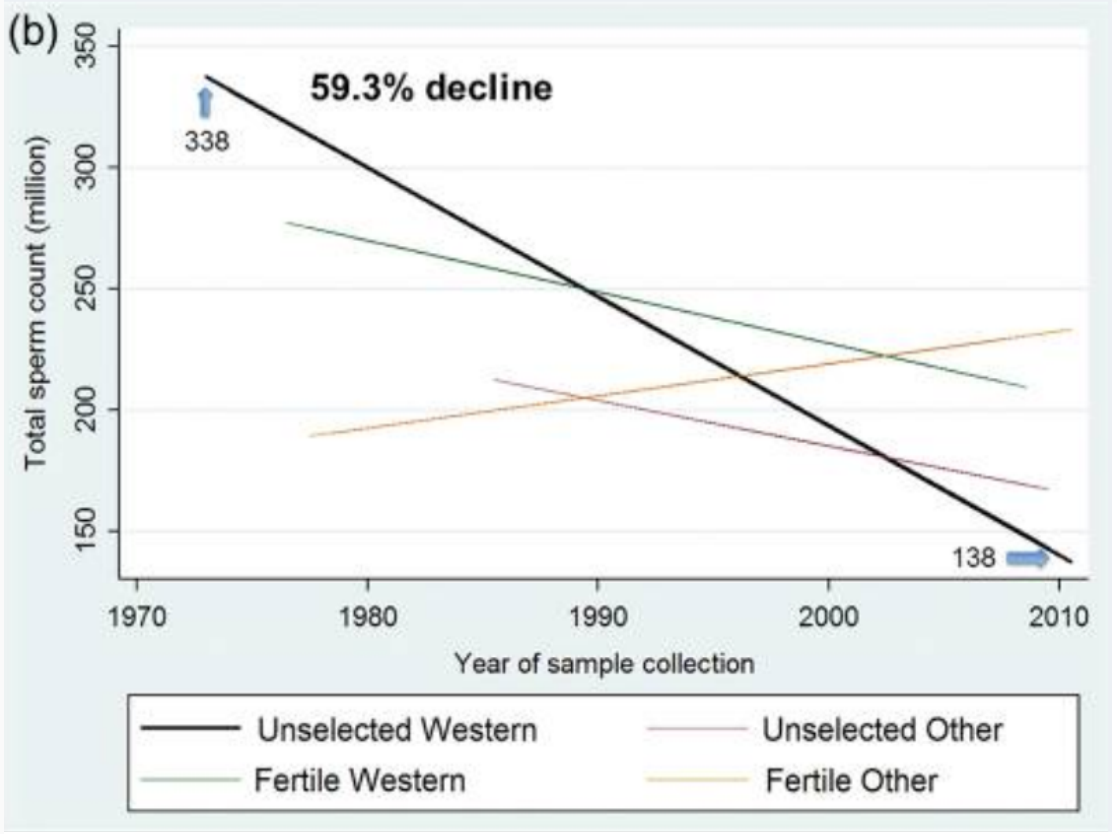
We are not fine





Left: Tanner, Anderson & Must
Right: Levine et al., Hum Reprod Update. (2017)

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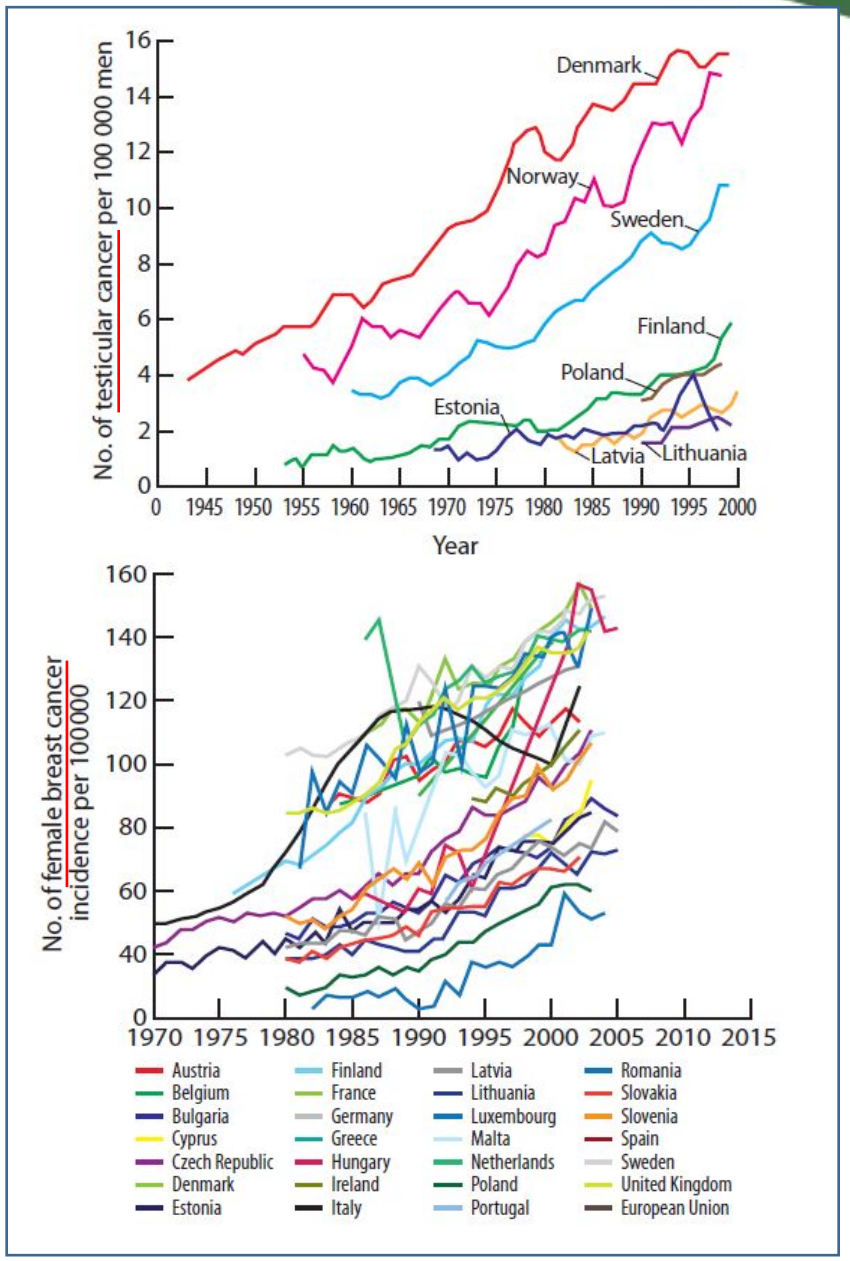
We are not fine



Top: Richiardi et al., Cancer Epidem. Biomark. (2004);
Bottom: based on data from http://data.euro.who.int/hfadb/

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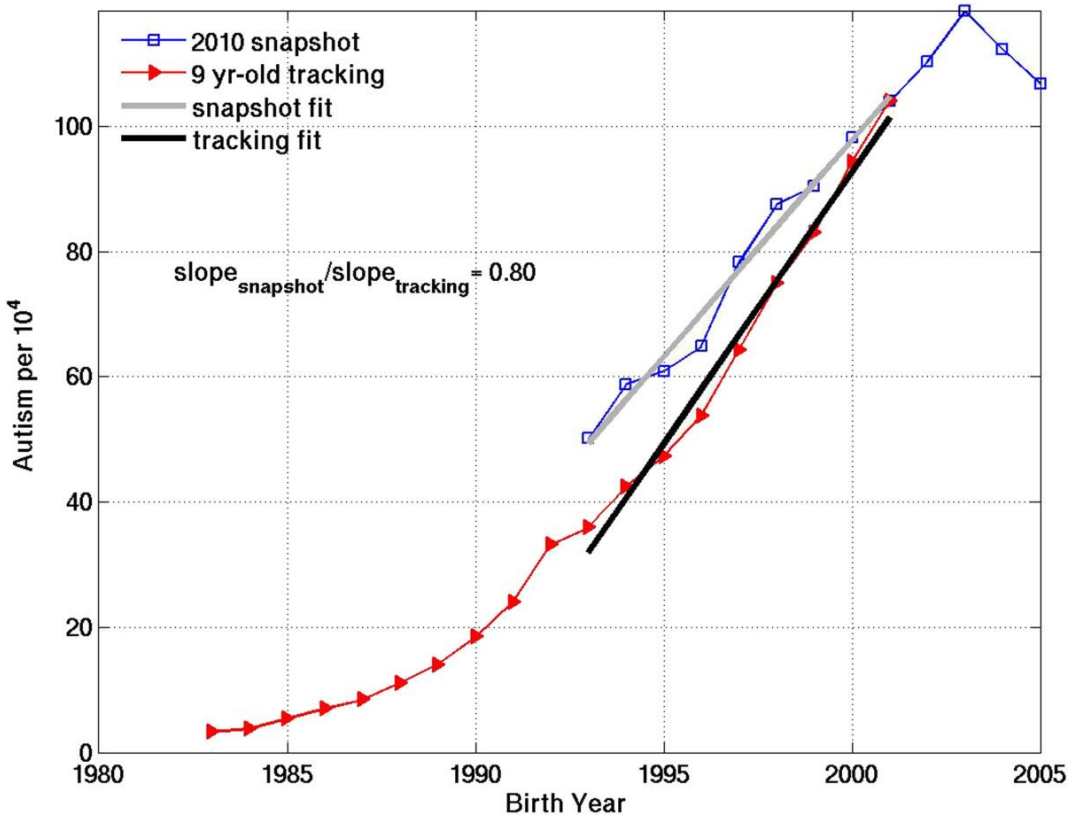
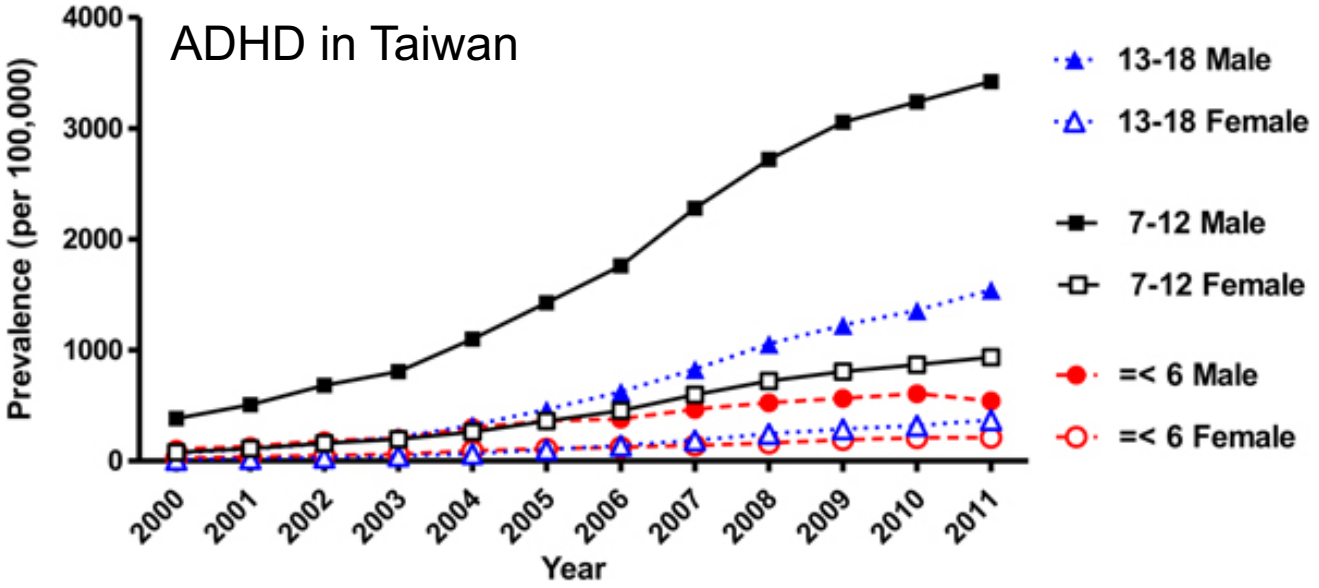
We are not fine





Left: Nevison, Environ Health (2014);
Right: Wang et al., Epidemiol & Psychiatry (2017)

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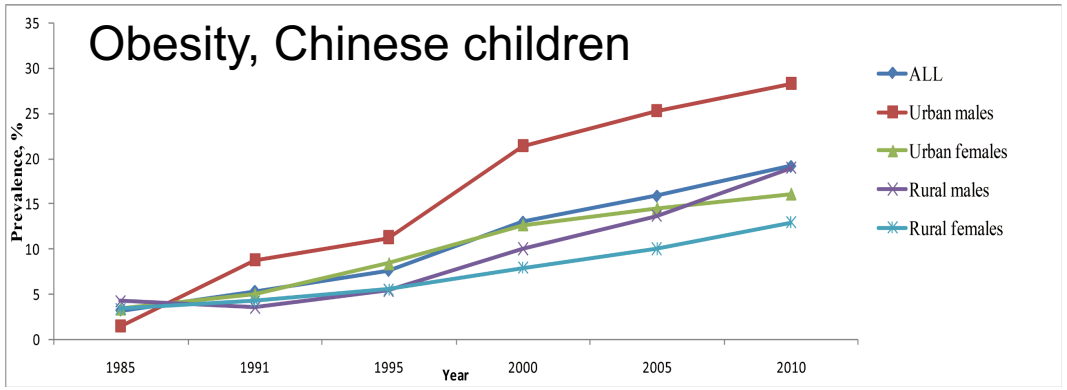
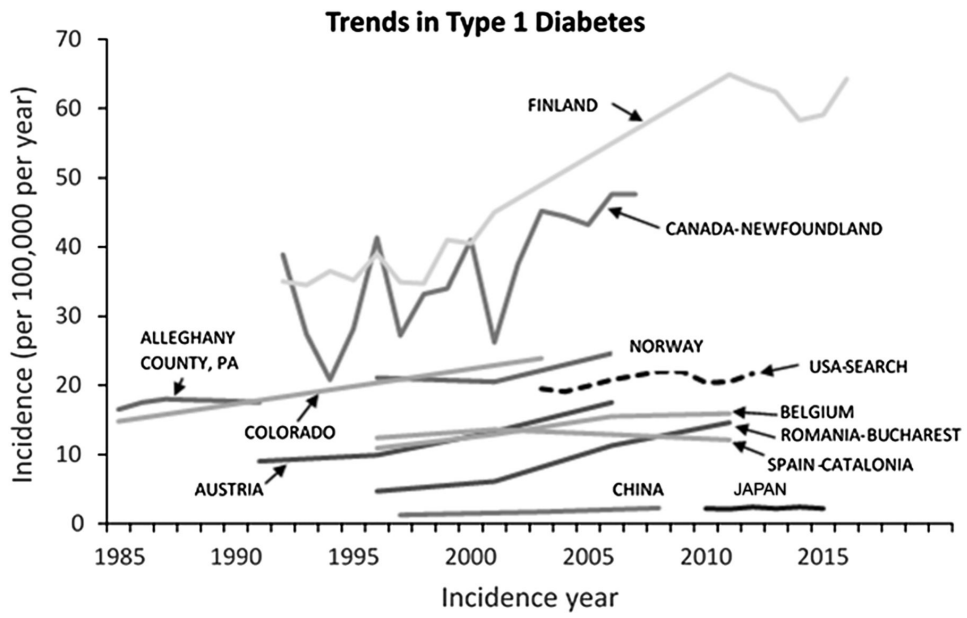
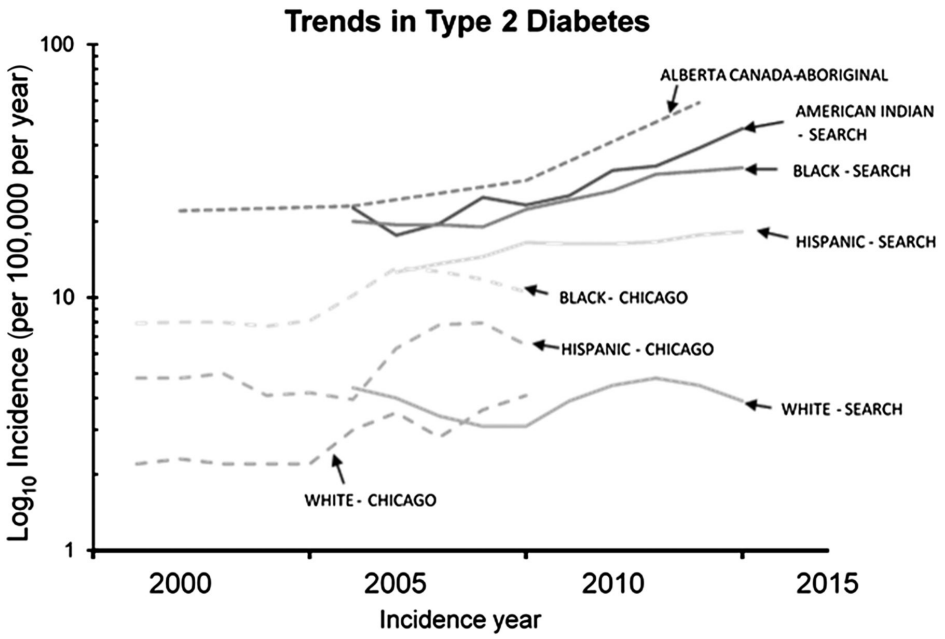
We are not fine

Top: Sun et al., PLoS One (2014);
Bottom (L&R): Dabelea, Diabetes Care (2018)







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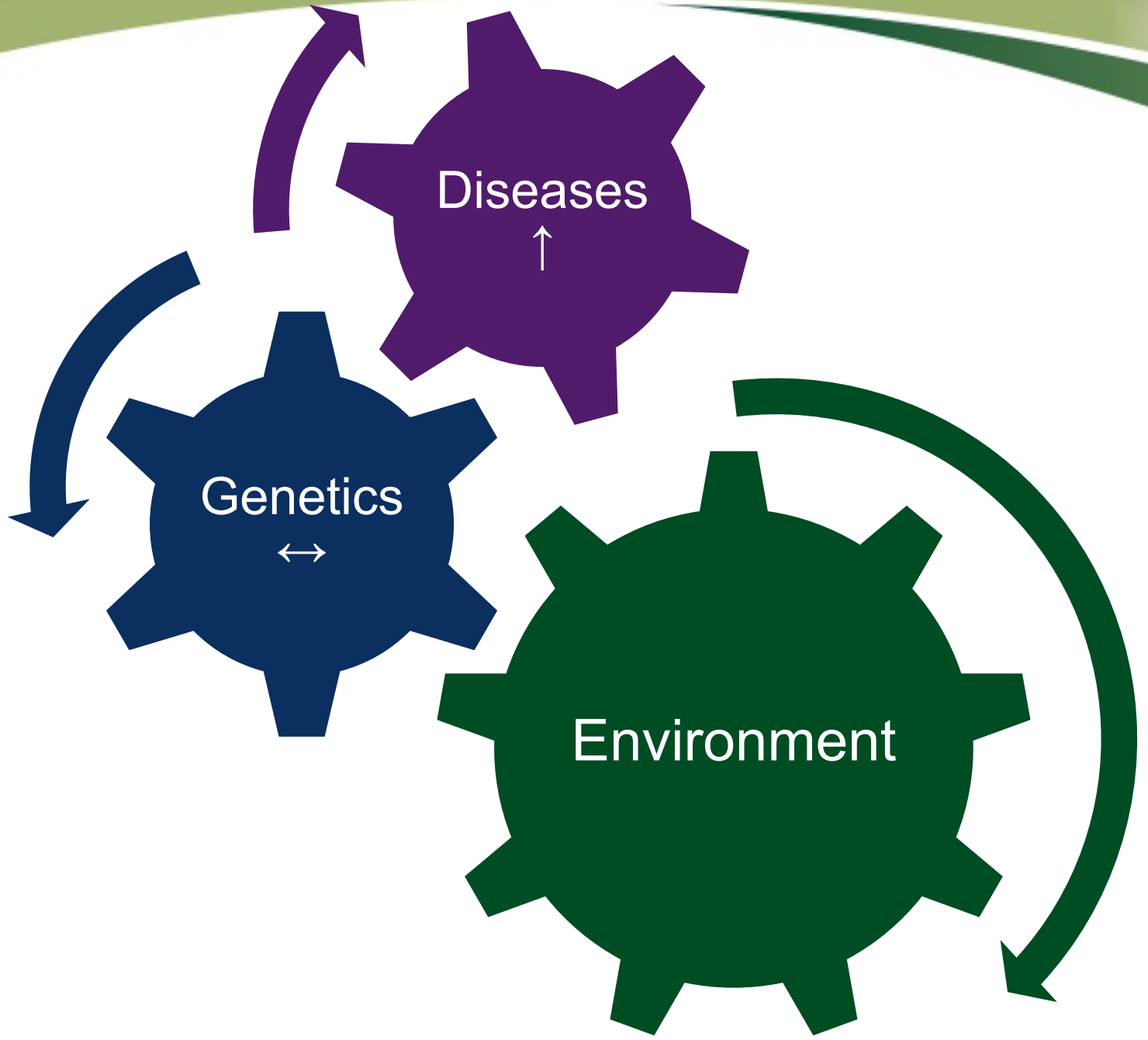

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Applying the principles of endocrinology to the study & understanding of EDCs

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1. The endocrine system coordinates the tissues & organs of the body

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2. The endocrine system is important at all stages of life, from conception until death

"From the day of conception until an individual is born or hatched, the development of each stage of life is fully under the control of hormones.

Changes that happen during development are far less reversible [than those occurring in an adult]; you can't go back and rewire the brain".
-Theo Colborn, zoologist, writer

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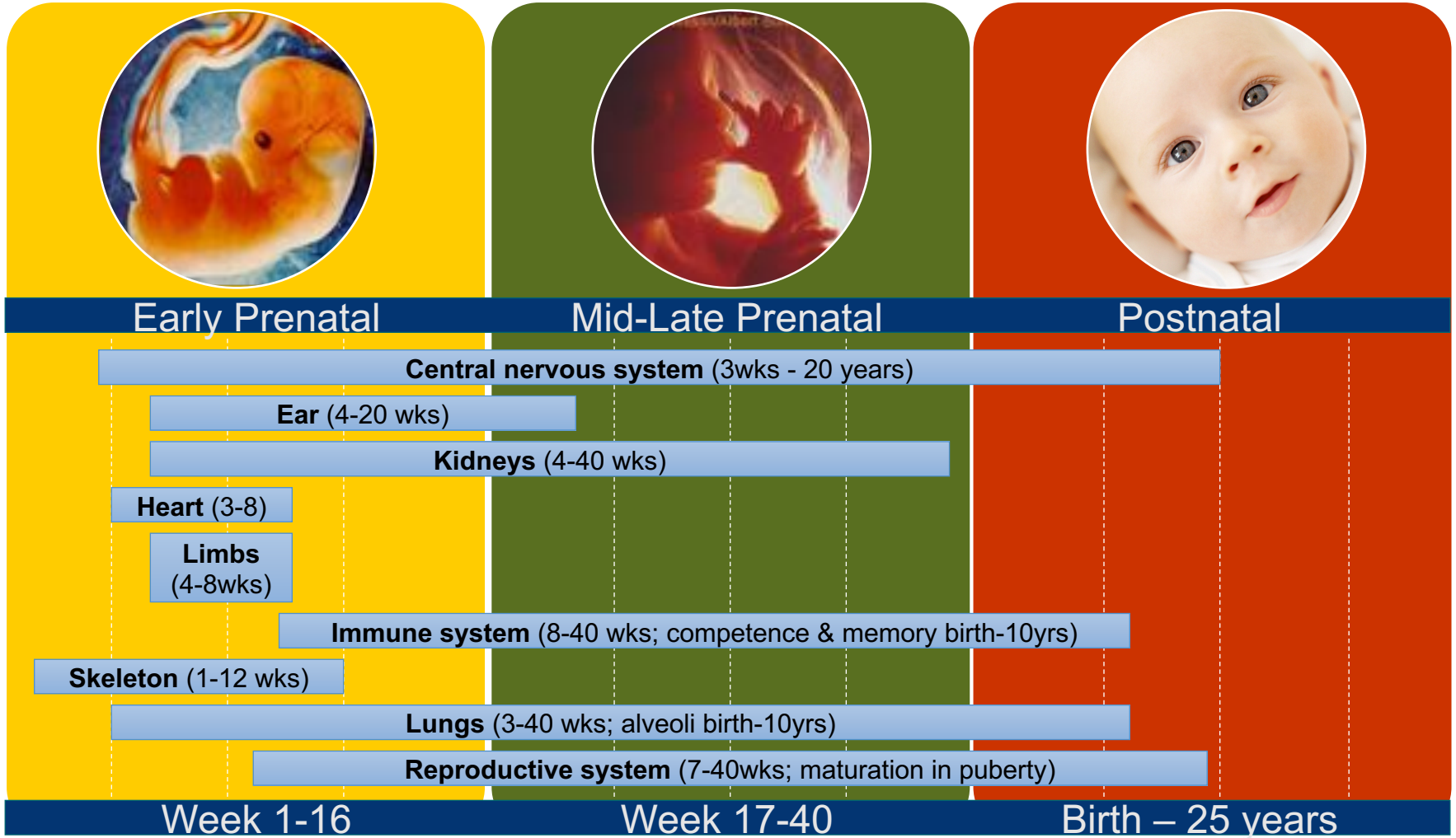

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3. Hormones act at low doses

Hormone	Free concentration (females)	Total concentration (females)	Free concentration (males)	Total concentration (males)
Estradiol	0.5 – 9 pg/ml (adult female)	< 20 pg/ml (prepubertal) 20 - 800 pg/ml (premenopausal) < 30 pg/ml (postmenopausal)		10 - 60 pg/ml (adult)
Progesterone		0.2 – 0.55 ng/ml (prepubertal) 0.02 – 0.80 ng/ml (follicular phase) 0.90 – 4 ng/ml (luteal phase) < 0.5 ng/ml (postmenopausal)		0.1 – 0.4 ng/ml (prepubertal) 0.2 – 2 ng/ml (adult)
Insulin		0 – 250 pmol/L		0 – 250 pmol/L
Prolactin		0 – 15 ng/ml		0 – 10 ng/ml
Testosterone	9 – 150 pg/ml (adult)		0.3 – 250 ng/ml	
Thyroid hormone	8 – 30 pg/ml (10-35 pM)		8 – 30 pg/ml (10-35 pM)	
TSH	0.5 – 5 µU/ml		0.5 – 5 µU/ml	

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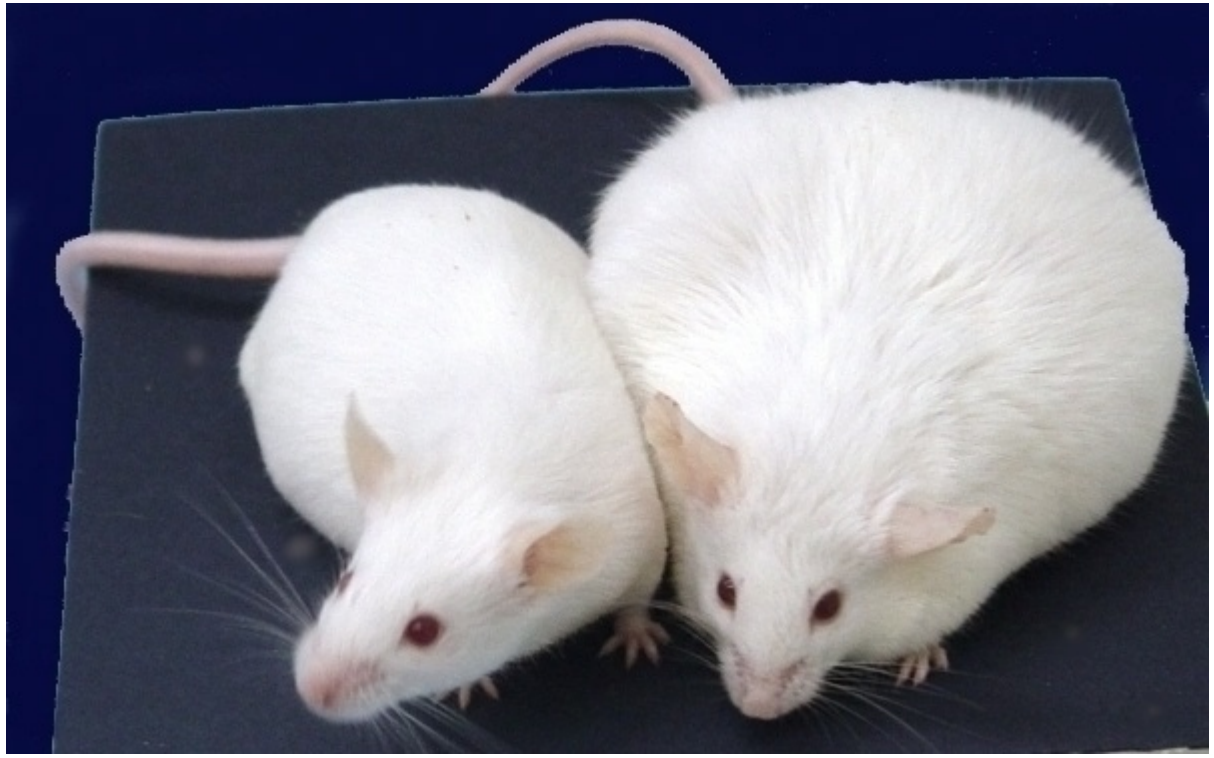
DES and Obesity



Newbold et al. 2009

- 1000 ppb exposures cause weight loss (not shown here)
- 1 ppb exposures cause extreme obesity

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Atrazine: disruptions to sexual development

Hayes et al. 2010

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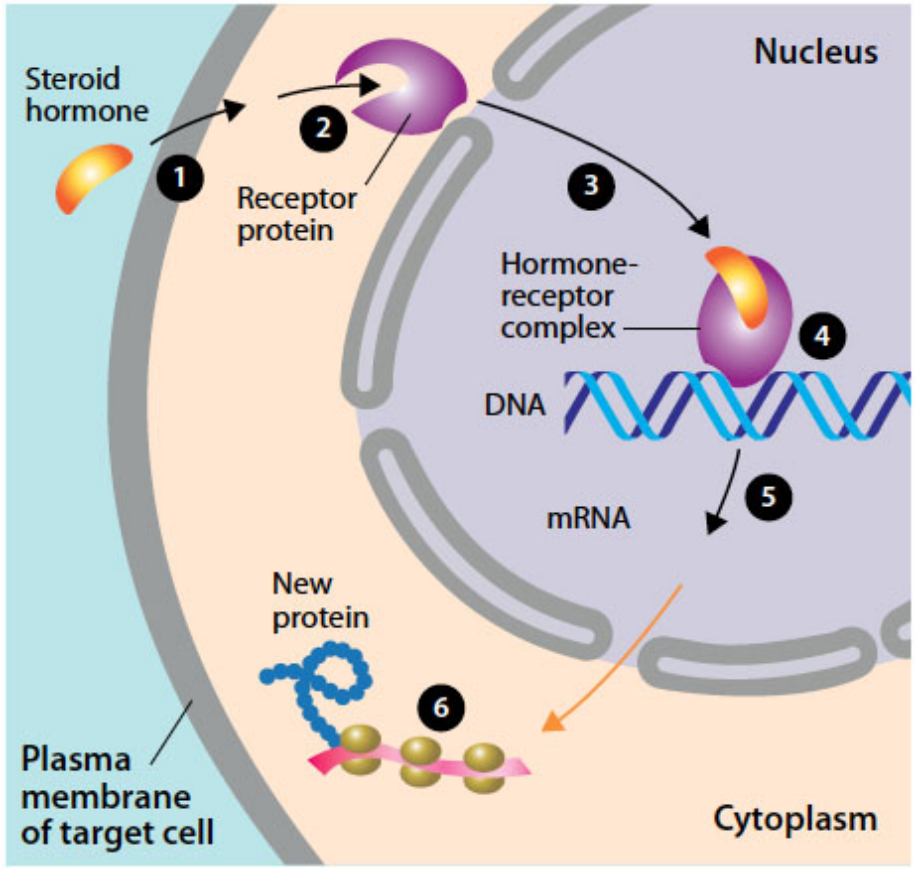
4. Hormones have very specific interactions with receptors

- Hormone receptors are the “business end” of hormones.
- EDCs interfere in some way with the ability of hormone to activate its receptor.



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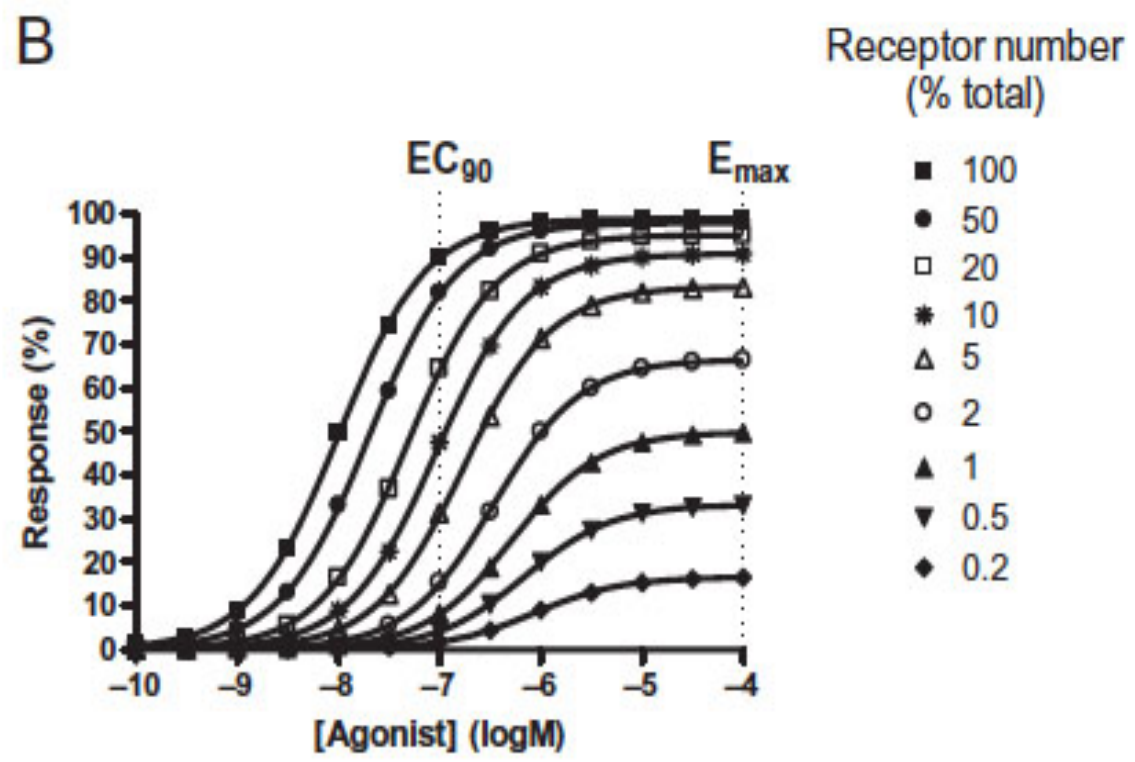
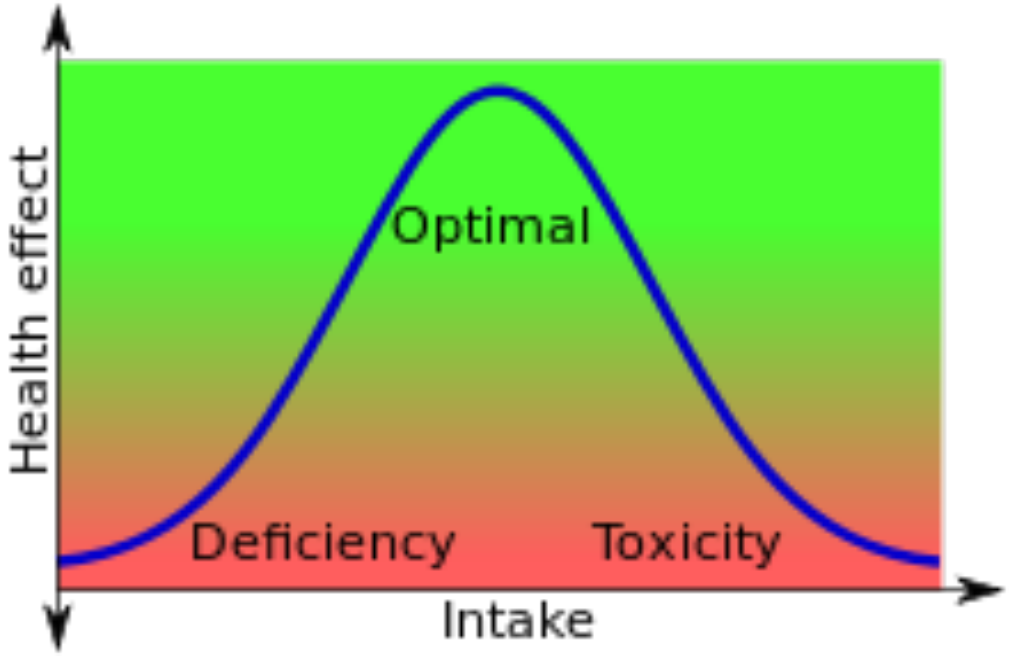
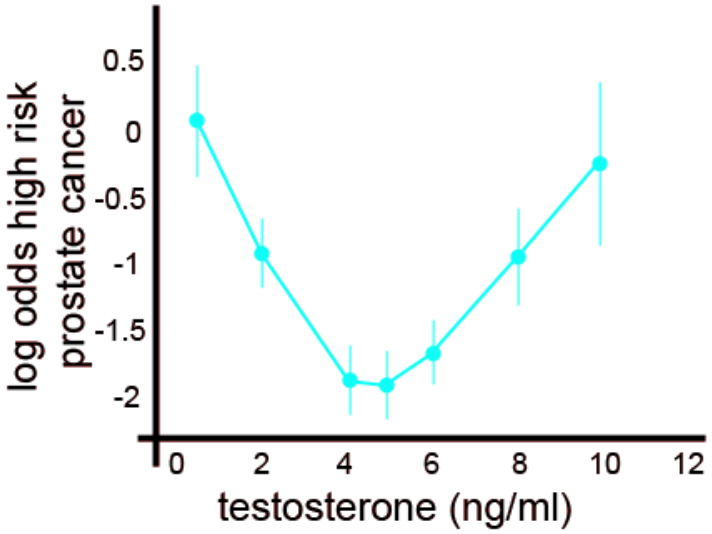
Response can be modulated by changing receptor number, hormone concentration, etc.



5. The relationship between hormones and effect is rarely linear, and often non-monotonic





Houshmand et al. 2009

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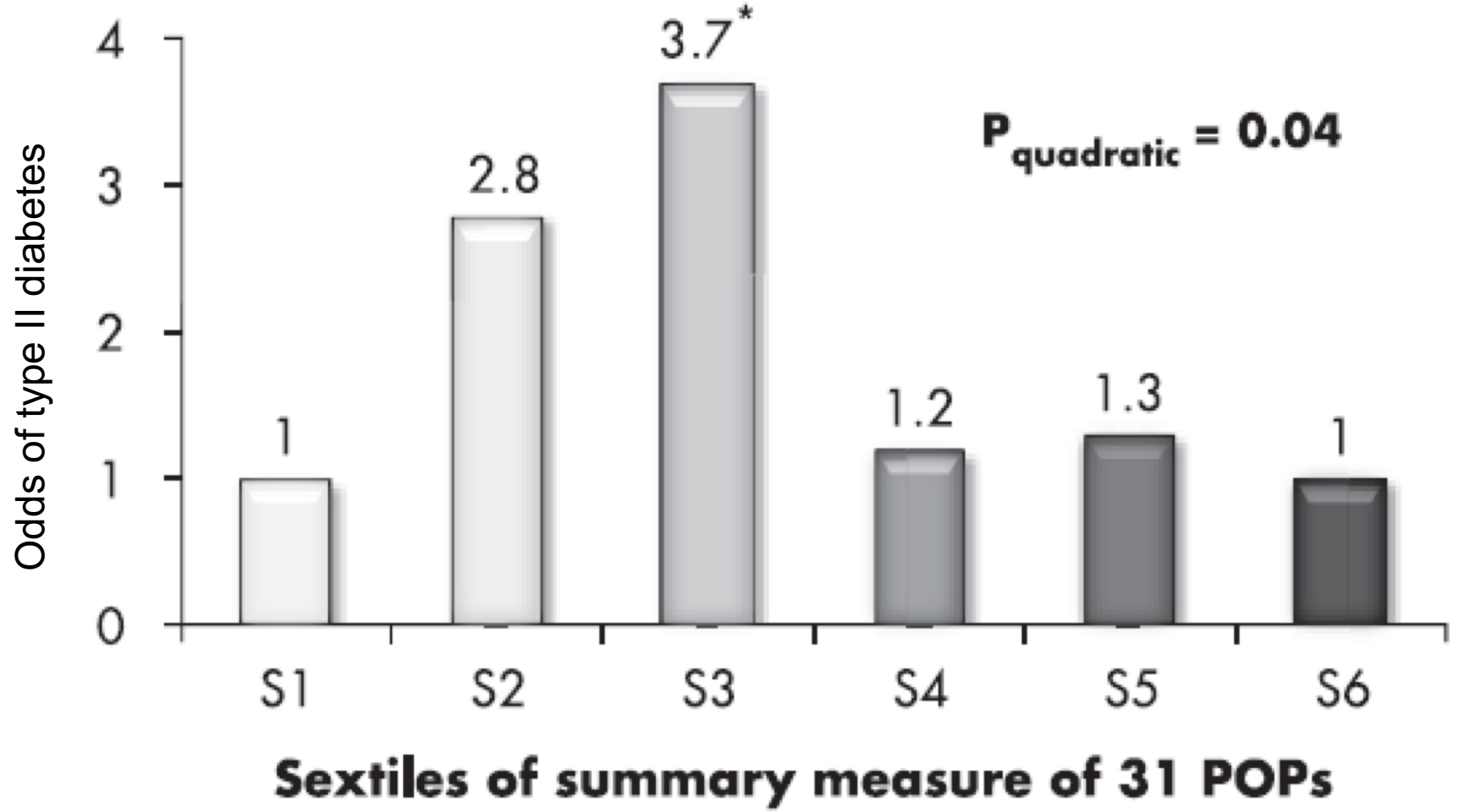

Lee et al. 2014

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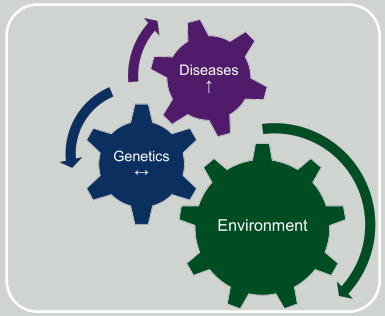
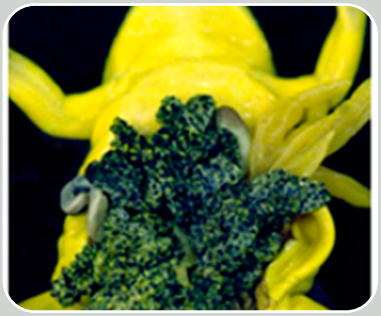
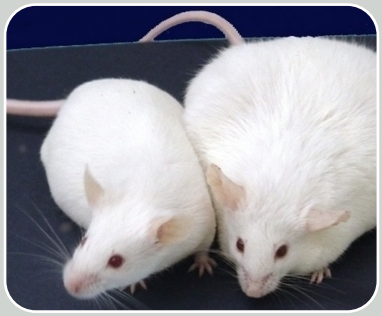
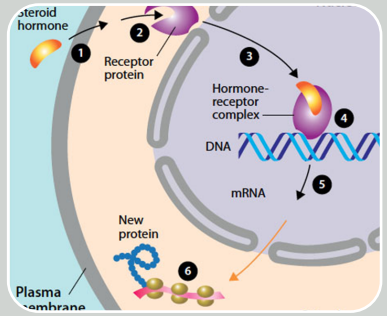
There is a strong case that EDCs affect human health









Even low exposures to EDCs can induce adverse health effects

Human and animal studies support causal relationships between EDCs & disease

Many endocrine diseases are increasing in prevalence

Animal studies have helped to identify the mechanisms by which EDCs cause harm

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More educational materials available from the Endocrine Society

- www.endocrine.org/edc
- Scientific statements:
  - Diamanti-Kandarakis et al., *Endo Reviews* 2009
  - Gore et al., *Endo Reviews 2015*
- Position statements:
  - Zoeller et al., *Endocrinology 2012*
- Policy perspectives:
  - Vandenberg, *Endocrinology* 2016
- More:
  - Vandenberg et al., *Endo Reviews* 2012

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