The Ad Hoc Group for Medical Research
Luncheon Briefing for Senate and House Staff

The Growing Epidemic of Diabetes
and What the NIH Is Doing About It
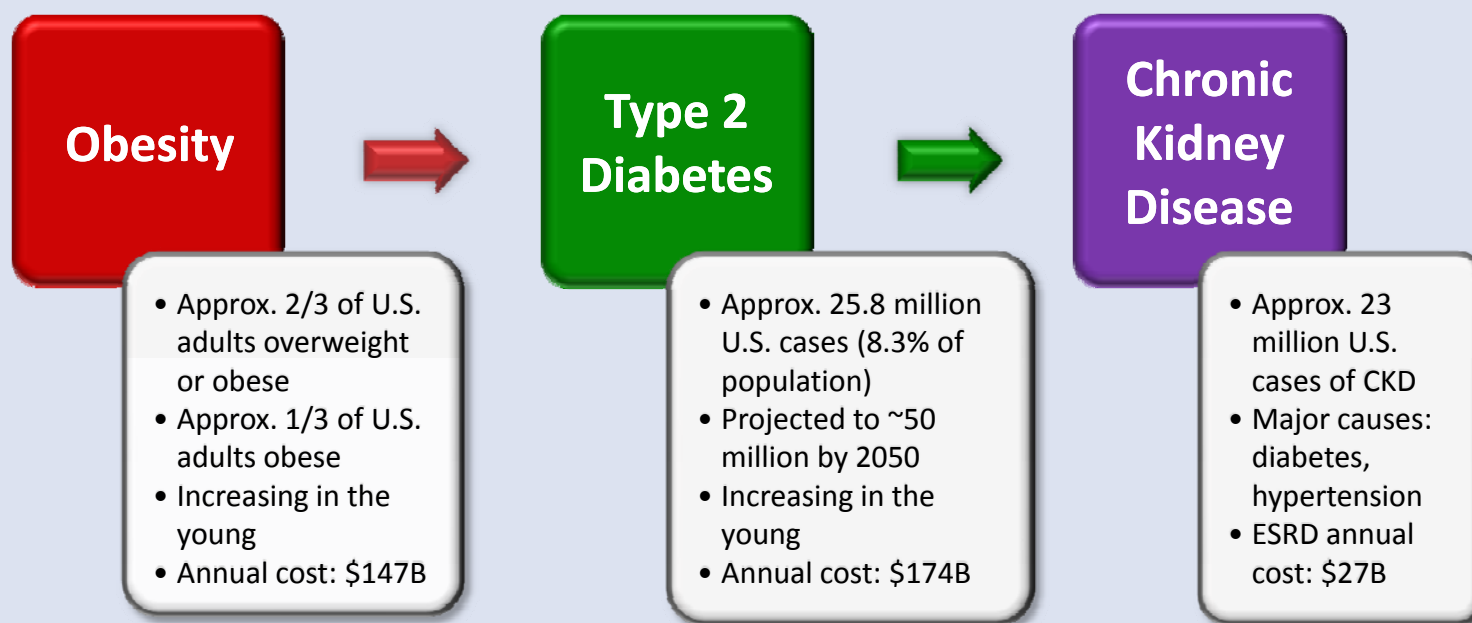
Griffin P. Rodgers, M.D., M.A.C.P.

Director
National Institute of Diabetes and Digestive
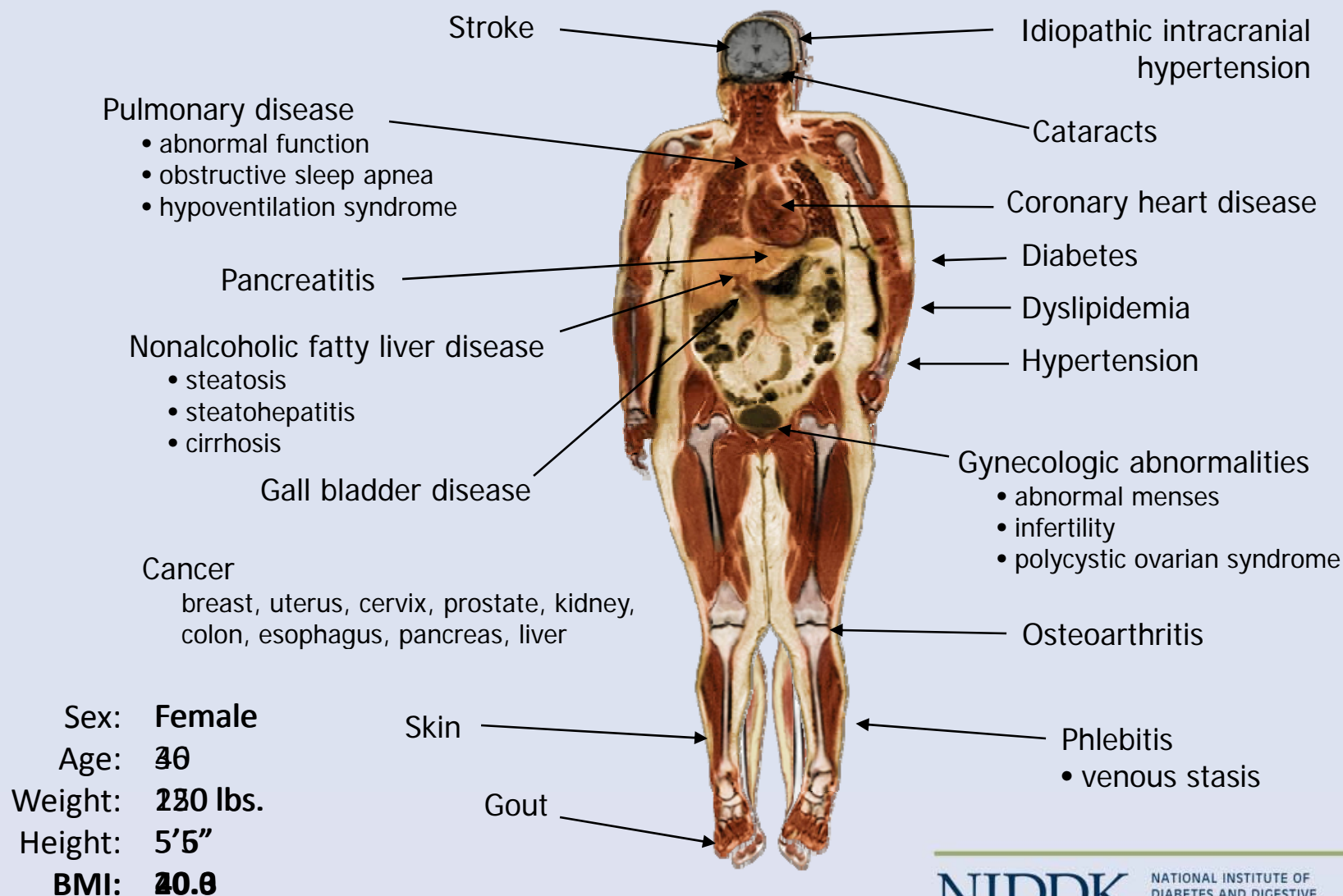and Kidney Diseases

September 15, 2011

NIDDK's Integrated Research Programs

Obesity

→

Type 2 Diabetes

→

Chronic Kidney Disease

- Approx. 2/3 of U.S. adults overweight or obese
- Approx. 1/3 of U.S. adults obese
- Increasing in the young
- Annual cost: $147B

- Approx. 25.8 million U.S. cases (8.3% of population)
- Projected to ~50 million by 2050
- Increasing in the young
- Annual cost: $174B

- Approx. 23 million U.S. cases of CKD
- Major causes: diabetes, hypertension
- ESRD annual cost: $27B

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Obesity Fuels Multiple Medical Problems

Stroke

Idiopathic intracranial hypertension

Cataracts

Pulmonary disease
- abnormal function
- obstructive sleep apnea
- hypoventilation syndrome

Coronary heart disease

Diabetes

Pancreatitis

Dyslipidemia

Nonalcoholic fatty liver disease
- steatosis
- steatohepatitis
- cirrhosis

Hypertension

Gall bladder disease

Gynecologic abnormalities
- abnormal menses
- infertility
- polycystic ovarian syndrome

Cancer
breast, uterus, cervix, prostate, kidney, colon, esophagus, pancreas, liver

Osteoarthritis

Sex: **Female**
Age: **40**
Weight: **230 lbs.**
Height: **5'6"**
BMI: **40.0**

Skin

Gout

Phlebitis
- venous stasis

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Images courtesy of Dr. Steven B. Heymsfield

Age-adjusted Percentage of Obese and Diabetic U.S. Adults

Obesity   1994   2000   2009
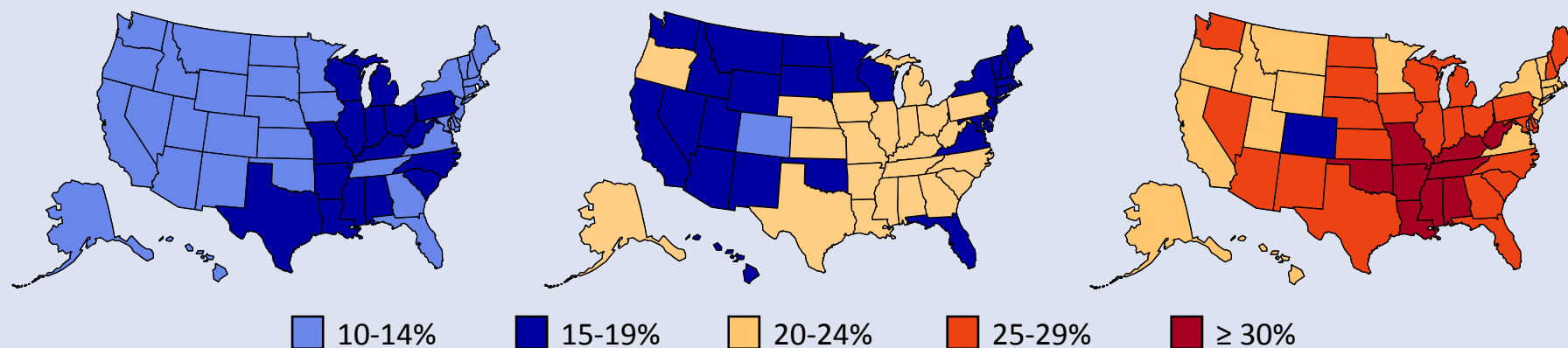
10-14%   15-19%   20-24%   25-29%   ≥ 30%

Diabetes (diagnosed)
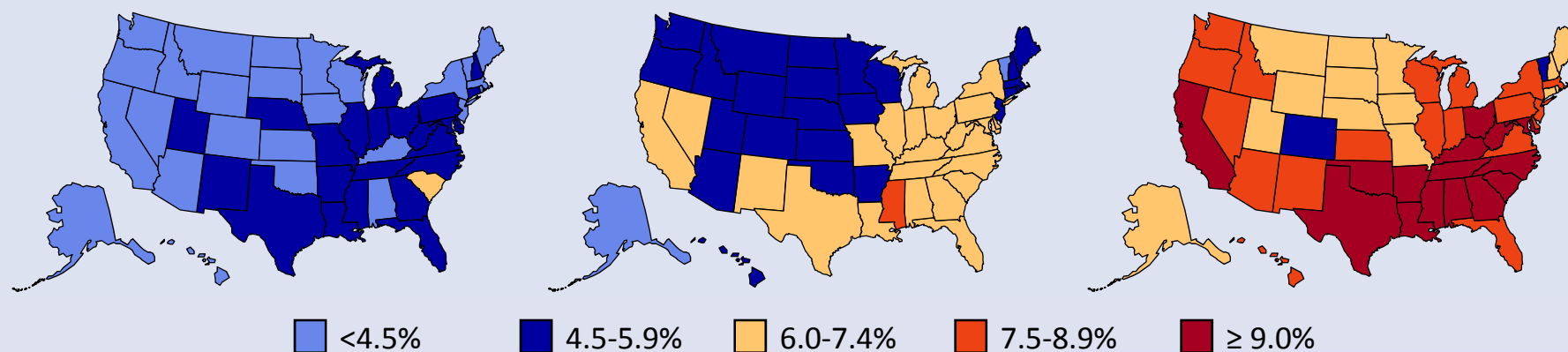
<4.5%   4.5-5.9%   6.0-7.4%   7.5-8.9%   ≥ 9.0%

Source: Centers for Disease Control and Prevention

Research Progress at All Stages of Type 1 Diabetes
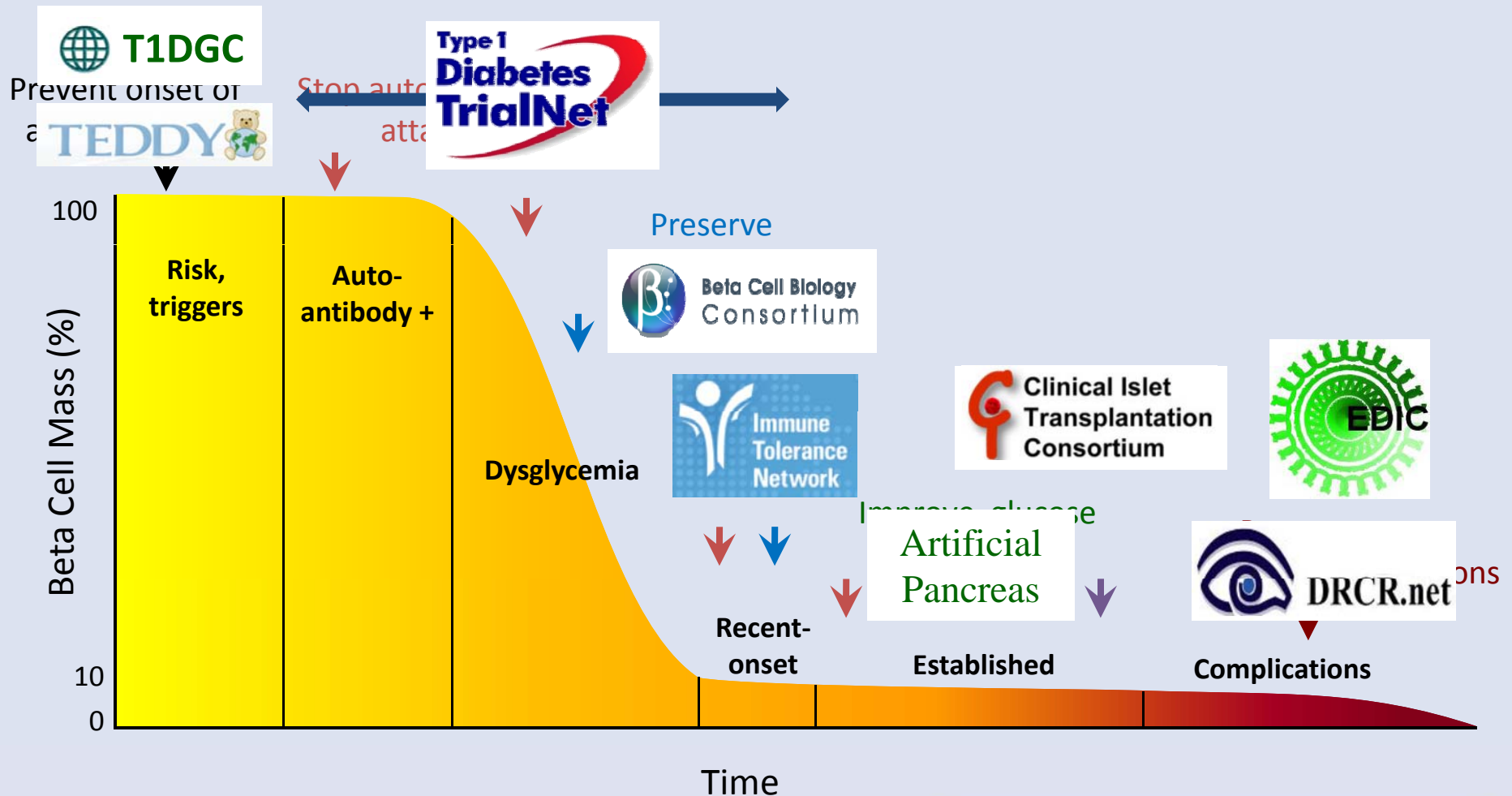
The Diabetes Prevention Program: Collaborative and Transformative

Percent Reduction in Diabetes Incidence Compared to Placebo

Metformin

Intensive Lifestyle Intervention
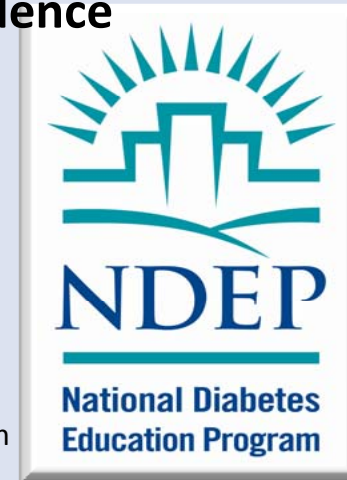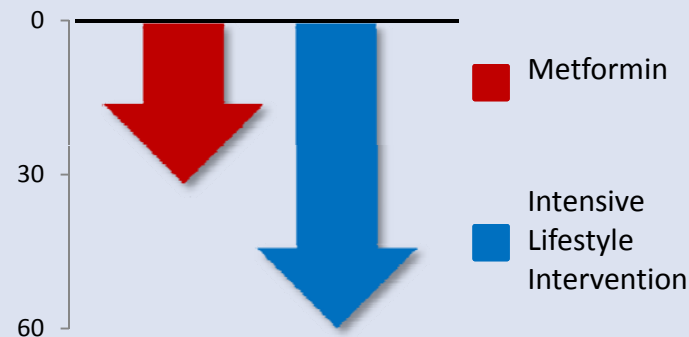
Diabetes Prevention Program (DPP)

3,234 individuals at risk for type 2 diabetes

- Lifestyle modification lowered risk by **58%** (modest weight loss, from exercise and reduced fat and caloric intake)

- Metformin medication lowered risk by **31%**

Strategic Planning for Research
Building on Advances, Seizing Opportunities

Common Genetics, but Environmental Differences

Pima Indian Family in Mexico

Pima Indian Family in the U.S.

Lifestyle Interventions in Overweight and Obese Pregnant Women
A New NIH research initiative
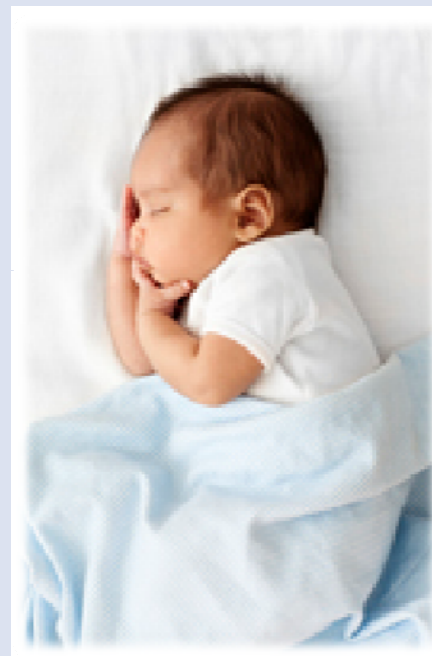
To test lifestyle interventions for overweight or obese pregnant women, in order to improve weight and metabolic outcomes in both the pregnant women and their offspring
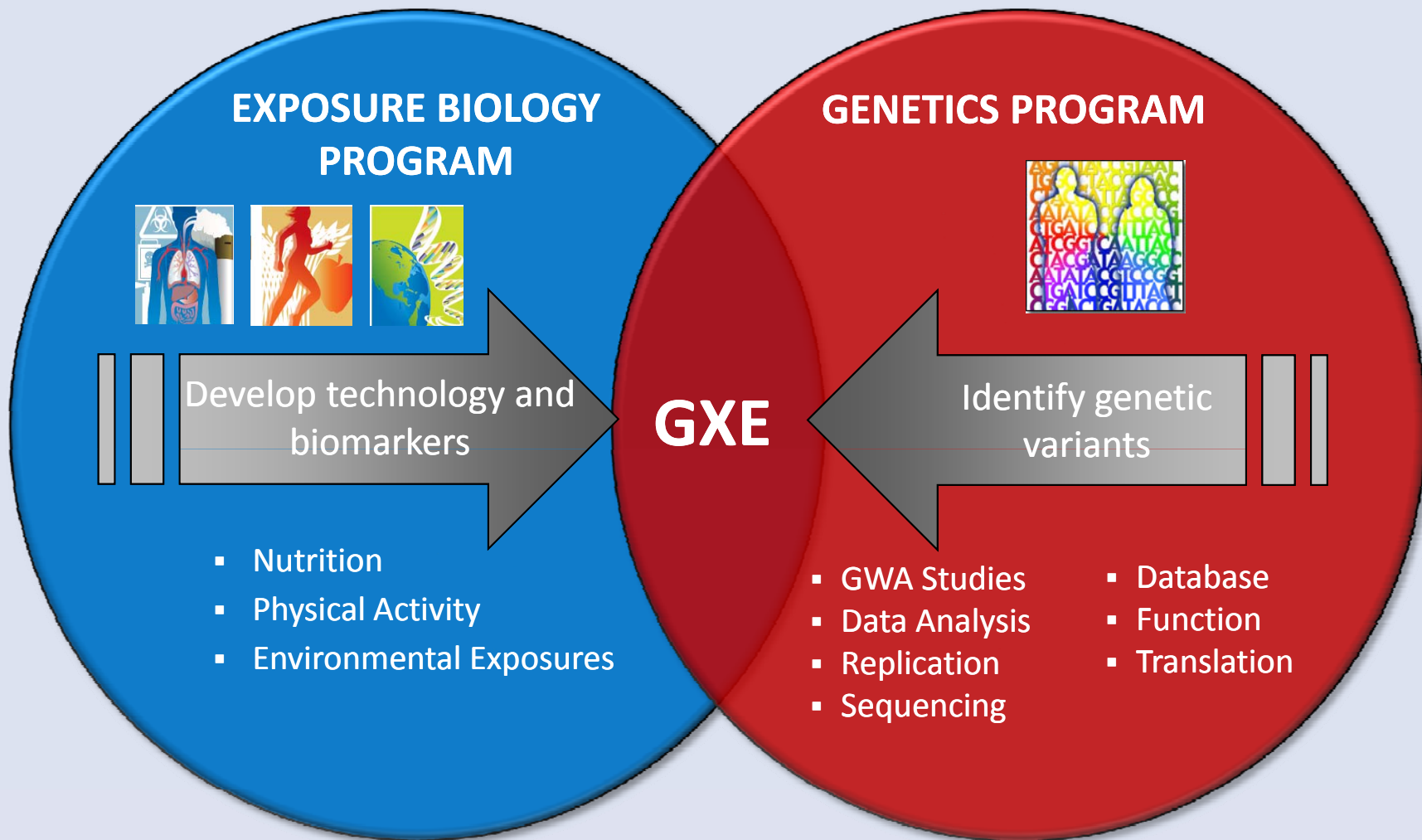
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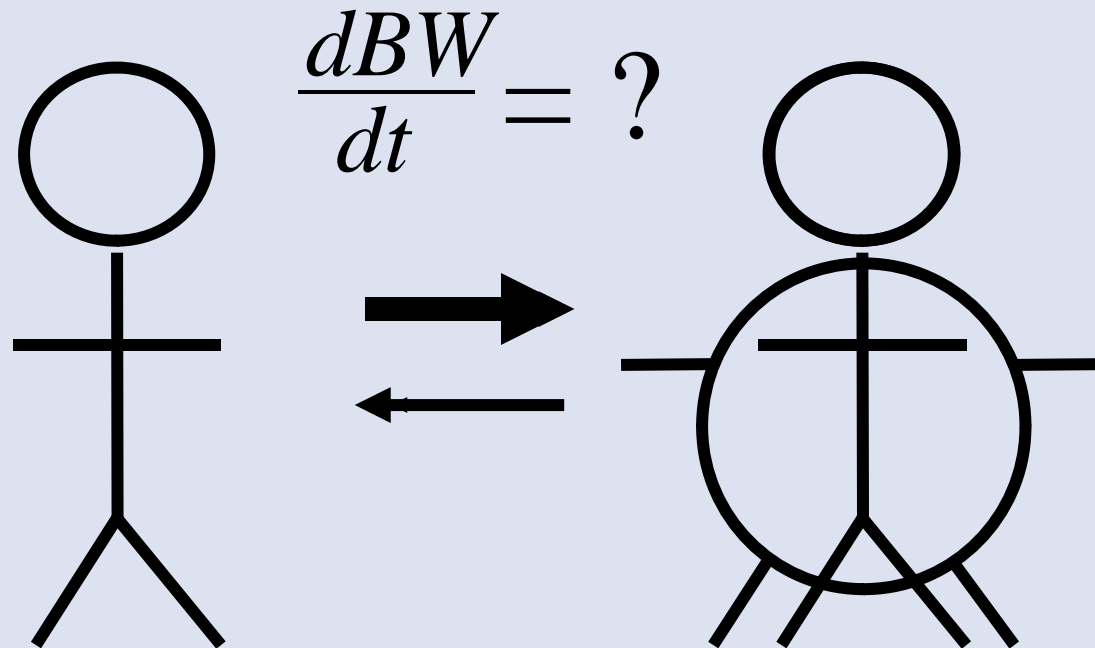
Genes and Environment Initiative

http://genesandenvironment.nih.gov/

EXPOSURE BIOLOGY PROGRAM

Develop technology and biomarkers

GXE

Identify genetic variants

GENETICS PROGRAM

- Nutrition
- Physical Activity
- Environmental Exposures

- GWA Studies
- Data Analysis
- Replication
- Sequencing

- Database
- Function
- Translation

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In a Nutshell...

$$\frac{dBW}{dt} = ?$$

Model Equations

$$\rho_C \frac{dG}{dt} = CI - DNL + GNG_P + GNG_F - G3P - CarbOx$$

$$\rho_F \frac{dF}{dt} = 3M_{FFA}FI/M_{TG} + \varepsilon_d DNL - KU_{excr} - (1-\varepsilon_k)KTG - FatOx$$

$$\rho_P \frac{dP}{dt} = PI - GNG_P - ProtOx$$

$$+\eta_N N_{excr} + (\eta_P + \varepsilon_P)D_P + \eta_P \frac{dP}{dt} + \eta_F D_F + \eta_F \frac{dF}{dt} + \eta_G D_G + \eta_G \frac{dG}{dt}$$

http://bwsimulator.niddk.nih.gov/

$$\hat{\gamma}_{FFM} = \sum_i \gamma_i \frac{dM_i}{dFFM}$$

$$\gamma_{FFM} = \hat{\gamma}_{FFM}\left[1 + (1-\sigma)T\right]$$

$$PAE = \delta(1+\sigma T)BW + \upsilon BW$$

$$TEF = \alpha_F FI + \alpha_P PI + \alpha_C CI$$

$$DNL = \frac{CI \times (G/G_{init})^d}{(G/G_{init})^d + K_{DNL}^d} \qquad D_G = \hat{D}_G\left(\frac{G}{G_{init}}\right)$$

$$CarbOx = GNG_f + GNG_p - G3P + f_C \times T\tilde{E}E$$

$$FatOx = KetOx + f_F \times T\tilde{E}E$$

$$ProtOx = f_P \times T\tilde{E}E$$

$$D_P = \hat{D}_P\left[\left(\frac{P}{P_{Keys}}\right) + \chi\left(\frac{\Delta PI}{PI_b}\right)\right]$$

$$D_F = \hat{D}_F\left(\frac{F}{F}\right)^{\frac{2}{3}}\left[L_{diet} + L_{PA}\right]$$

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Physical Activity has Become a "To Do" Item, Rather than a Lifestyle...