Strategic Planning for Transdisciplinary Science Within the Office of Behavioral and Social Science Research

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About OBSSR: Mission and Responsibilities

- OBSSR sits in the Office of the Director of NIH
- OBSSR established by act of congress, 1995
- Stimulate and increase support for BSSR
- Advise the NIH director of developments in BSSR
- Serve as the focal point for BSSR, and lifestyle factors in the causation, treatment, and prevention of disease
- Integrate a ***biobehavioral*** perspective across the NIH
- Disseminate BSSR findings to the public.

Scope of the Science

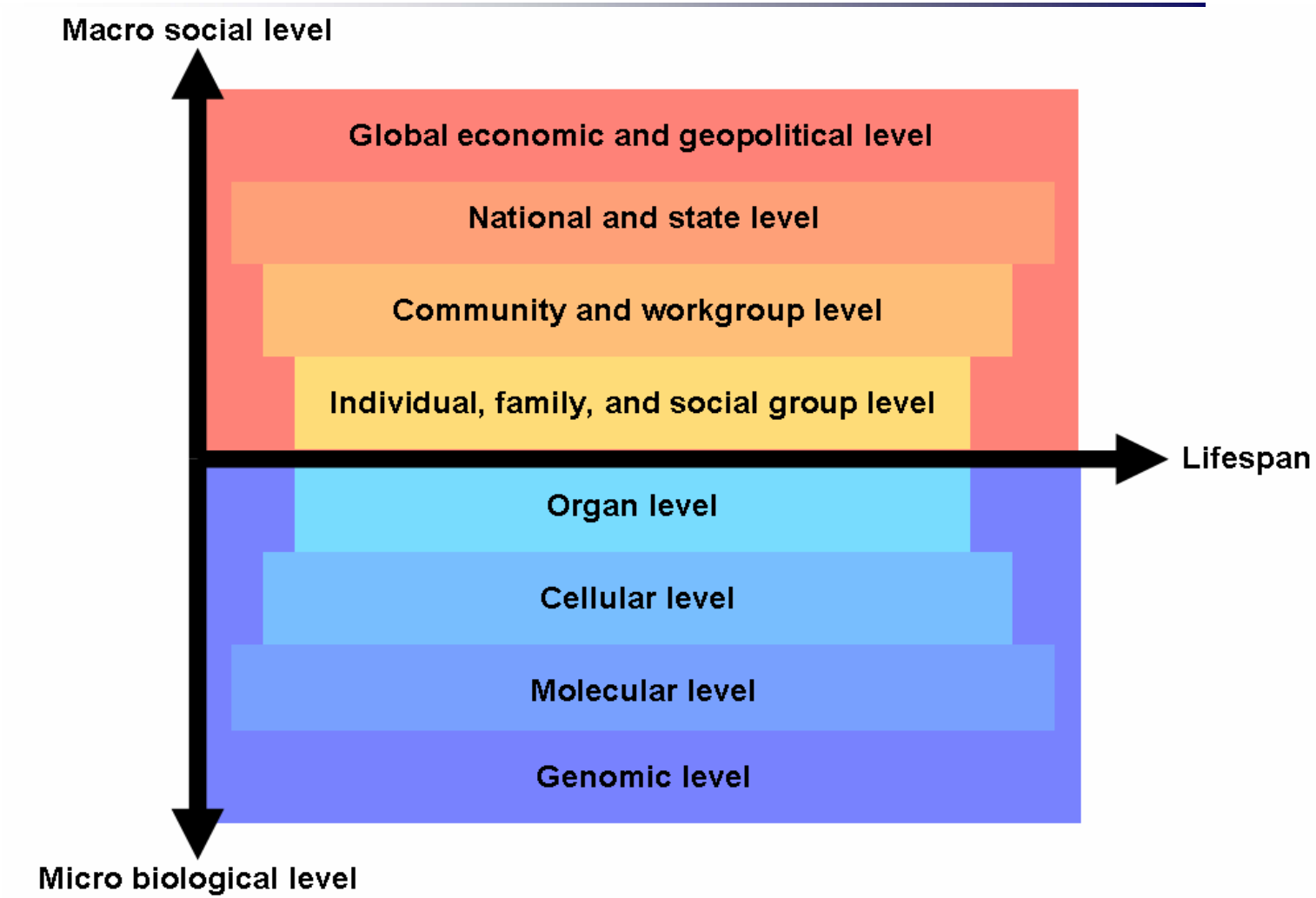


Figure 1. Health as a continuum between biological and social factors across the lifespan. (Adapted from Glass & McAtee, 2006).

OBSSR's Vision 2006 and Beyond

The vision of OBSSR is to mobilize the biomedical, behavioral, and social science research communities as partners to solve the most pressing health challenges faced by our society.

Programmatic Directions to Achieve the Vision:

- "Next generation" basic science
- **Interdisciplinary research**
- Systems-thinking approaches to health
- Population Impact Research

Next Generation Basic Science

- Gene x Environment Interactions:
  - Meany, Szyf – maternal behavior and stress responses in offspring
  - Szyf M, Weaver IC, Champagne FA, Diorio J, & Meaney MJ. (2005) *Maternal programming of steroid receptor expression and phenotype through DNA methylation in the rat*. Frontiers in Neuroendocrinology; Oct-Dec;26 (3-4):139-62. Review.

Basic behavioral mechanisms underlying genetically-mediated alterations in the development of stress responsivity

Meaney, Szyf et al.

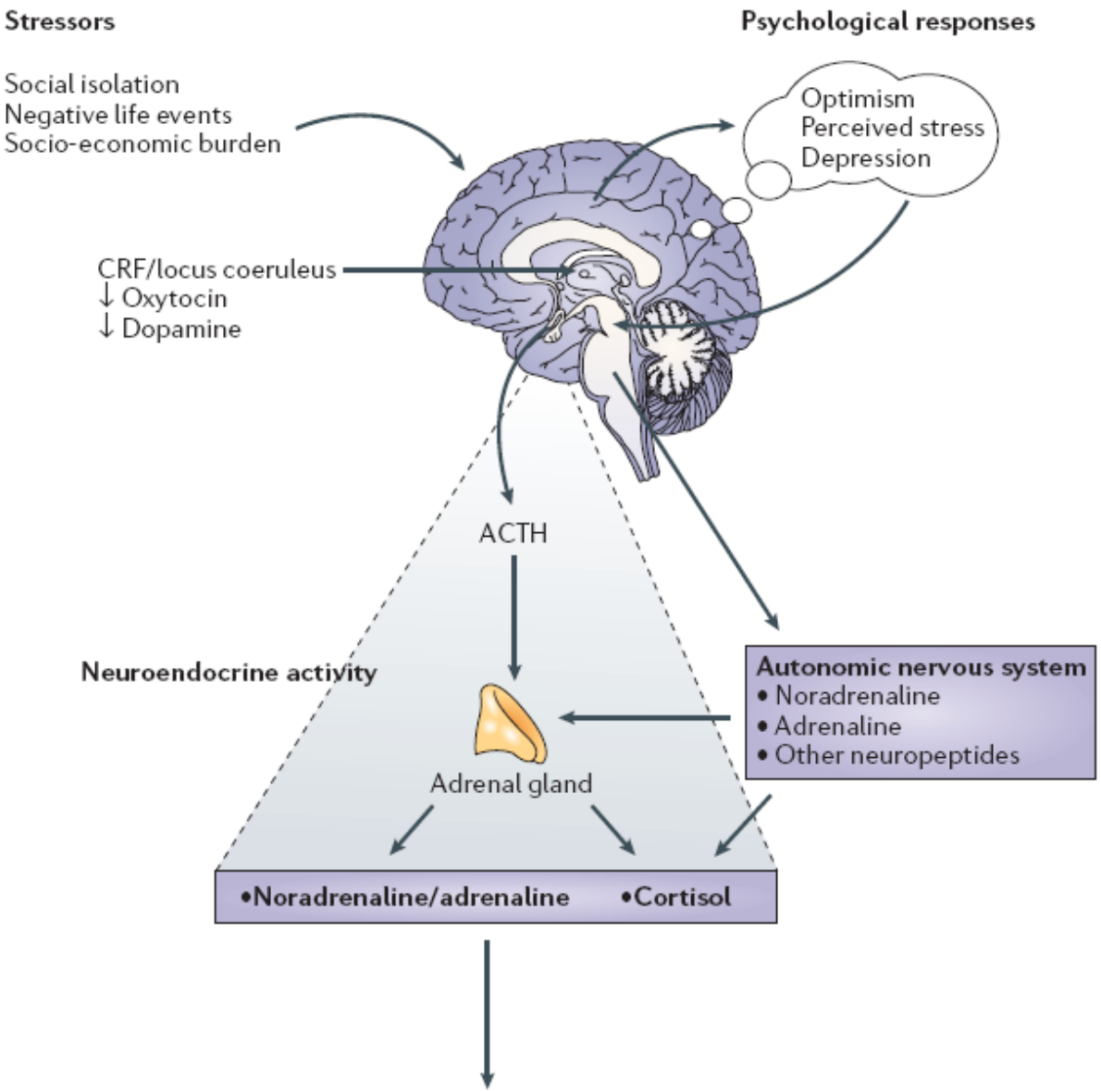
- Low maternal rat pup licking & arched back nursing during 1st wk
- Leads to permanently reduced glucocorticoid receptor gene expression in the hippocampus of pups.
- Increased & prolonged reactivity of the HPA axis.

- Mediated by ↑DNA methylation, preventing NGFI-A binding to the promoter for the glucocorticoid receptor gene – inhibiting transcription and ↓ Gc expression

What are the implications for human relationships in early childhood?

Interdisciplinary Research

- Mechanisms underlying relationship between stress and cancer
- Stress, chronic depression and lack of social support might serve as risk factors for cancer…how?
- Antoni MH, Lutgendorf SK, Cole SW, Dhabhar FS, Sephton SE, McDonald PG, Stefanek M, Sood AK. (2006). *The influence of bio-behavioural factors on tumour biology: pathways and mechanisms.* Nature Reviews in Cancer; 6(3):240-8. Review.


Stressors
Psychological responses
Social isolation
Negative life events
Socio-economic burden
Optimism
Perceived stress
Depression
CRF/locus coeruleus
↓ Oxytocin
↓ Dopamine
ACTH
Neuroendocrine activity
Autonomic nervous system
• Noradrenaline
• Adrenaline
• Other neuropeptides
Adrenal gland
•Noradrenaline/adrenaline
•Cortisol

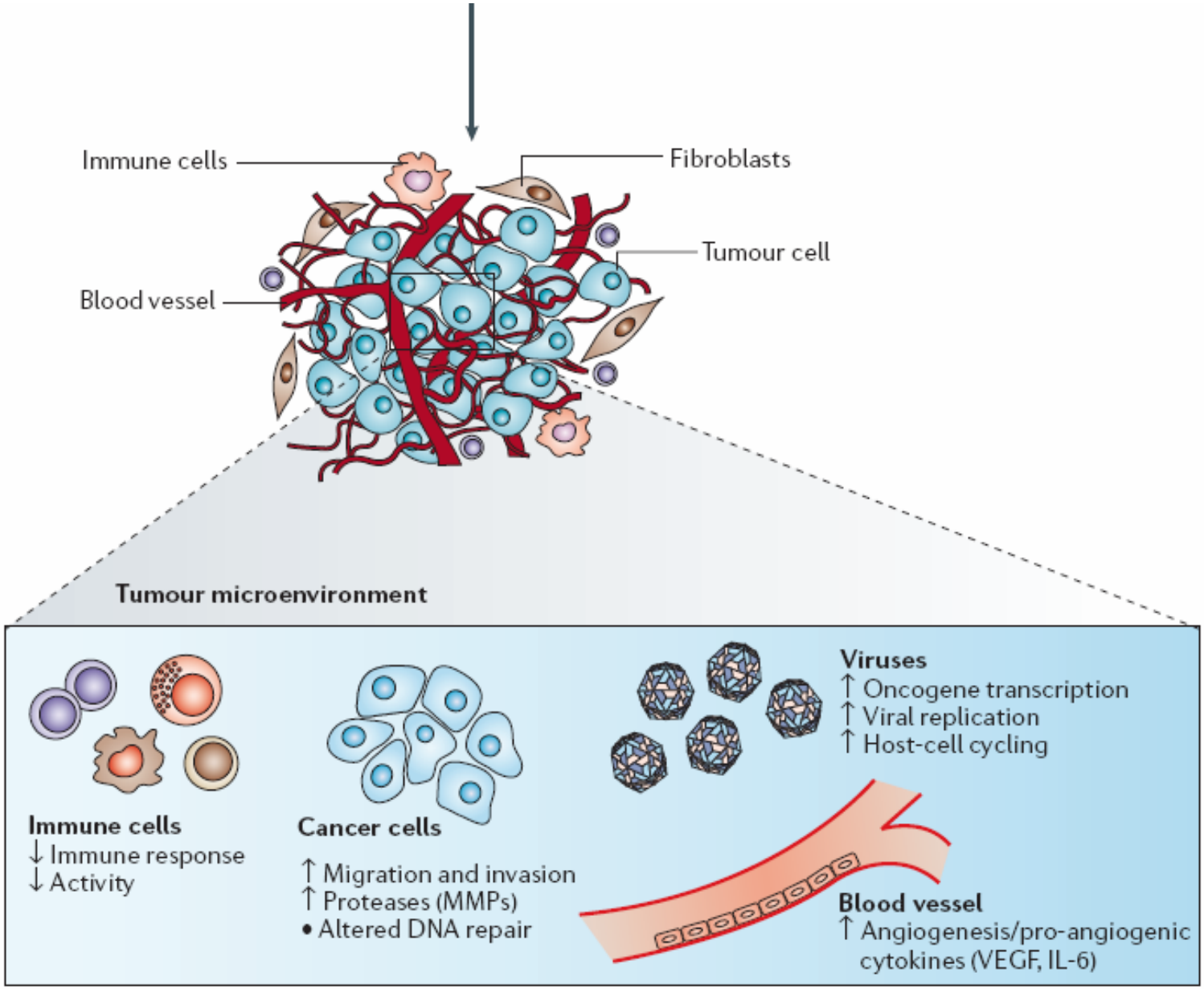
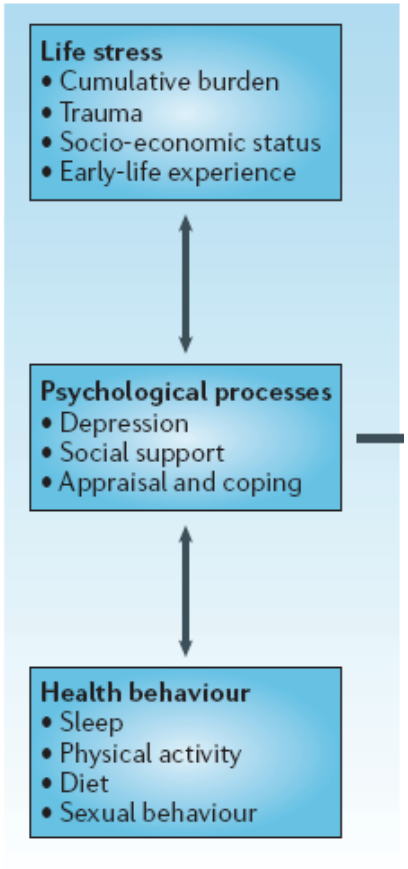
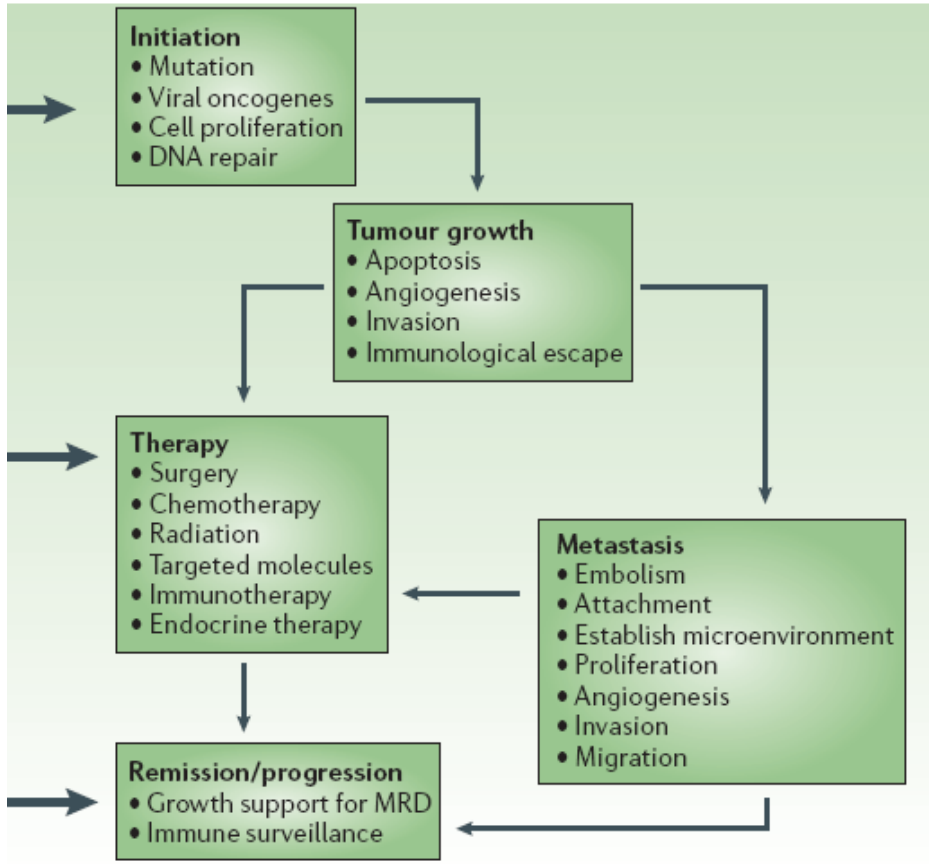


Figure 2 | **Effects of stress-associated factors on the tumour microenvironment.**

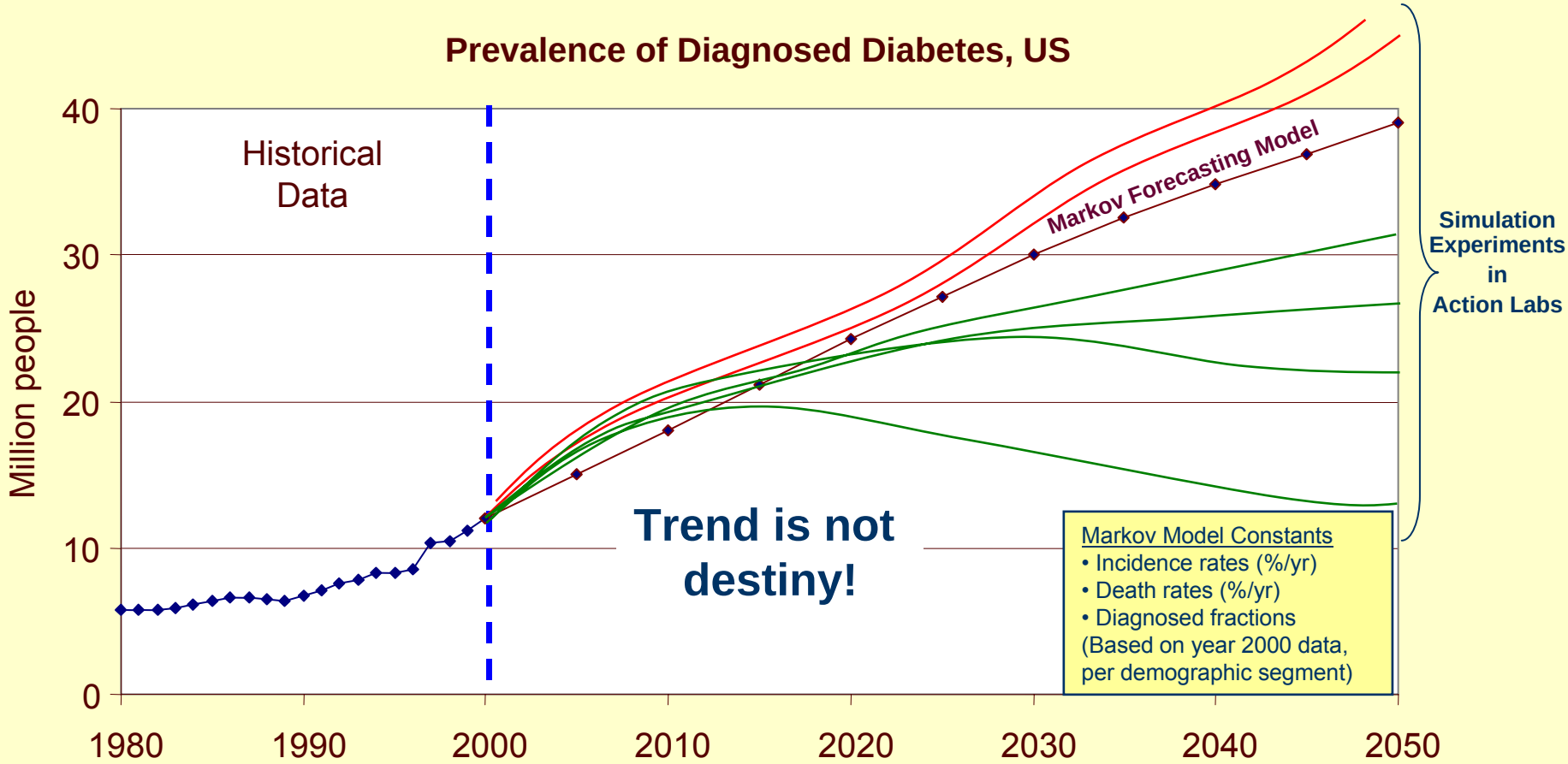

Life stress
• Cumulative burden
• Trauma
• Socio-economic status
• Early-life experience
Psychological processes
• Depression
• Social support
• Appraisal and coping
Health behaviour
• Sleep
• Physical activity
• Diet
• Sexual behaviour


Initiation
• Mutation
• Viral oncogenes
• Cell proliferation
• DNA repair
Tumour growth
• Apoptosis
• Angiogenesis
• Invasion
• Immunological escape
Therapy
• Surgery
• Chemotherapy
• Radiation
• Targeted molecules
• Immunotherapy
• Endocrine therapy
Metastasis
• Embolism
• Attachment
• Establish microenvironment
• Proliferation
• Angiogenesis
• Invasion
• Migration
Remission/progression
• Growth support for MRD
• Immune surveillance

Systems Thinking

- Promote a variety of systems methodologies to address public health problems, including
  - System Dynamics Simulation Modeling
  - Agent-based modeling
  - Network mapping and analysis
- Example: CDC System Dynamics Simulation Modeling
- Jones AP, Homer JB, Murphy DL, Essien JD, Milstein B, Seville DA. (2006). *Understanding diabetes population dynamics through simulation modeling and experimentation.* American Journal of Public Health;96(3):488-94.

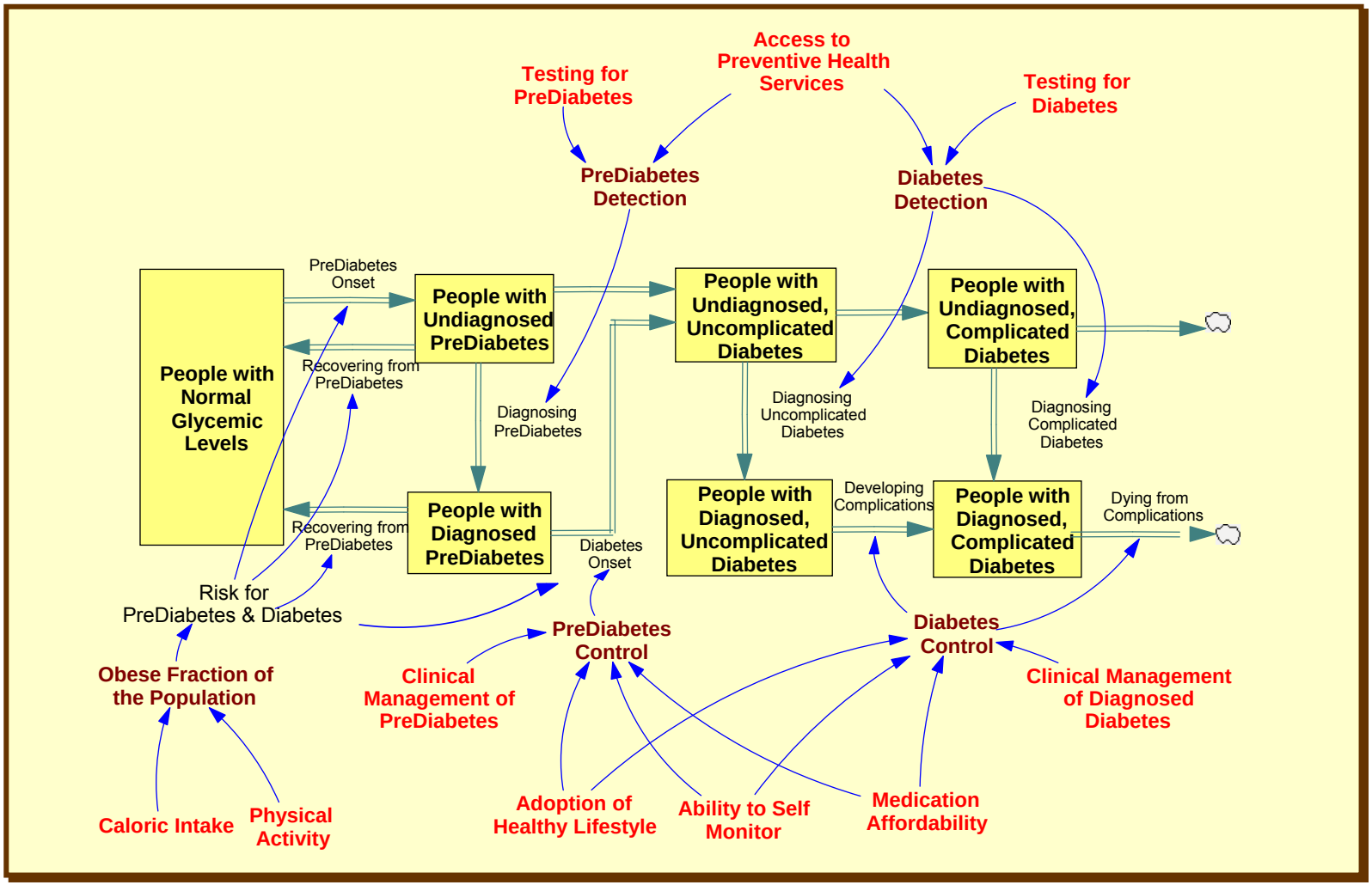
System Modeling Supports Navigational Policy Dialogues



Honeycutt A, Boyle J, Broglio K, Thompson T, Hoerger T, Geiss L, Narayan K. A dynamic markov model for forecasting diabetes prevalence in the United States through 2050. Health Care Management Science 2003;6:155-164.

Jones AP, Homer JB, Murphy DL, Essien JDK, Milstein B, Seville DA. Understanding diabetes population dynamics through simulation modeling and experimentation. American Journal of Public Health 2006;96(3):488-494.

Type 2 Diabetes: Where is the Leverage for Health Protection?



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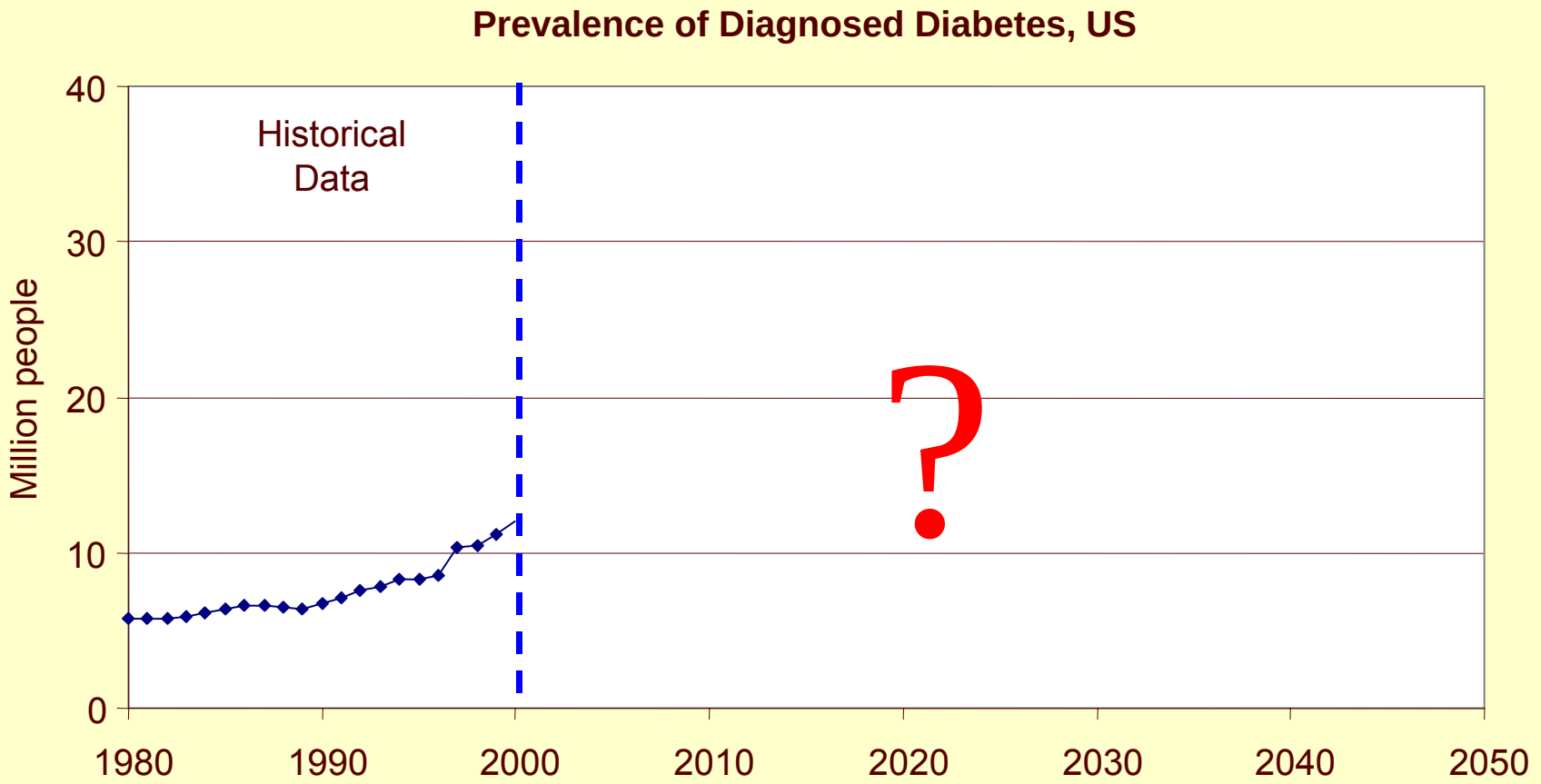
What does the model say about alternative futures for diabetes?



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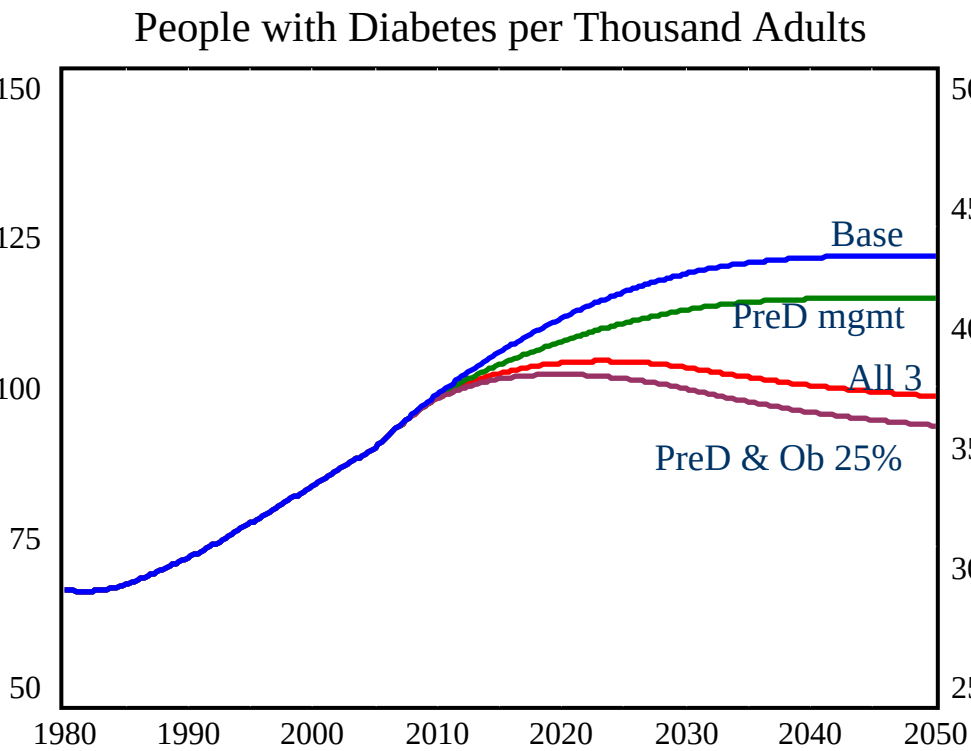
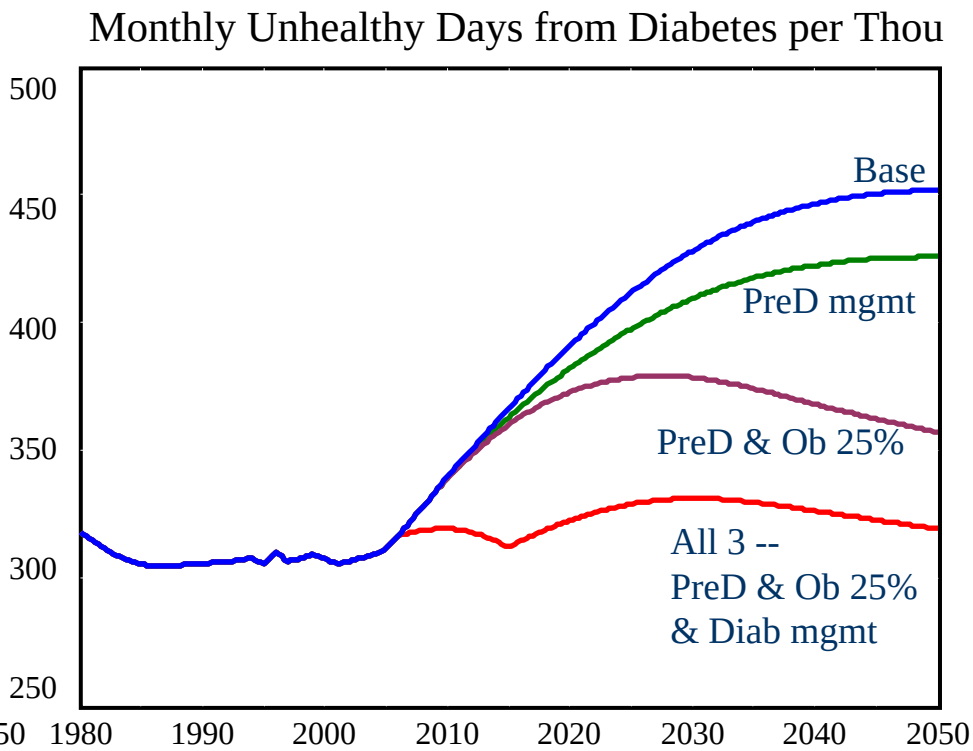
Diabetes Action Labs
Intervening Effectively Upstream and Downstream

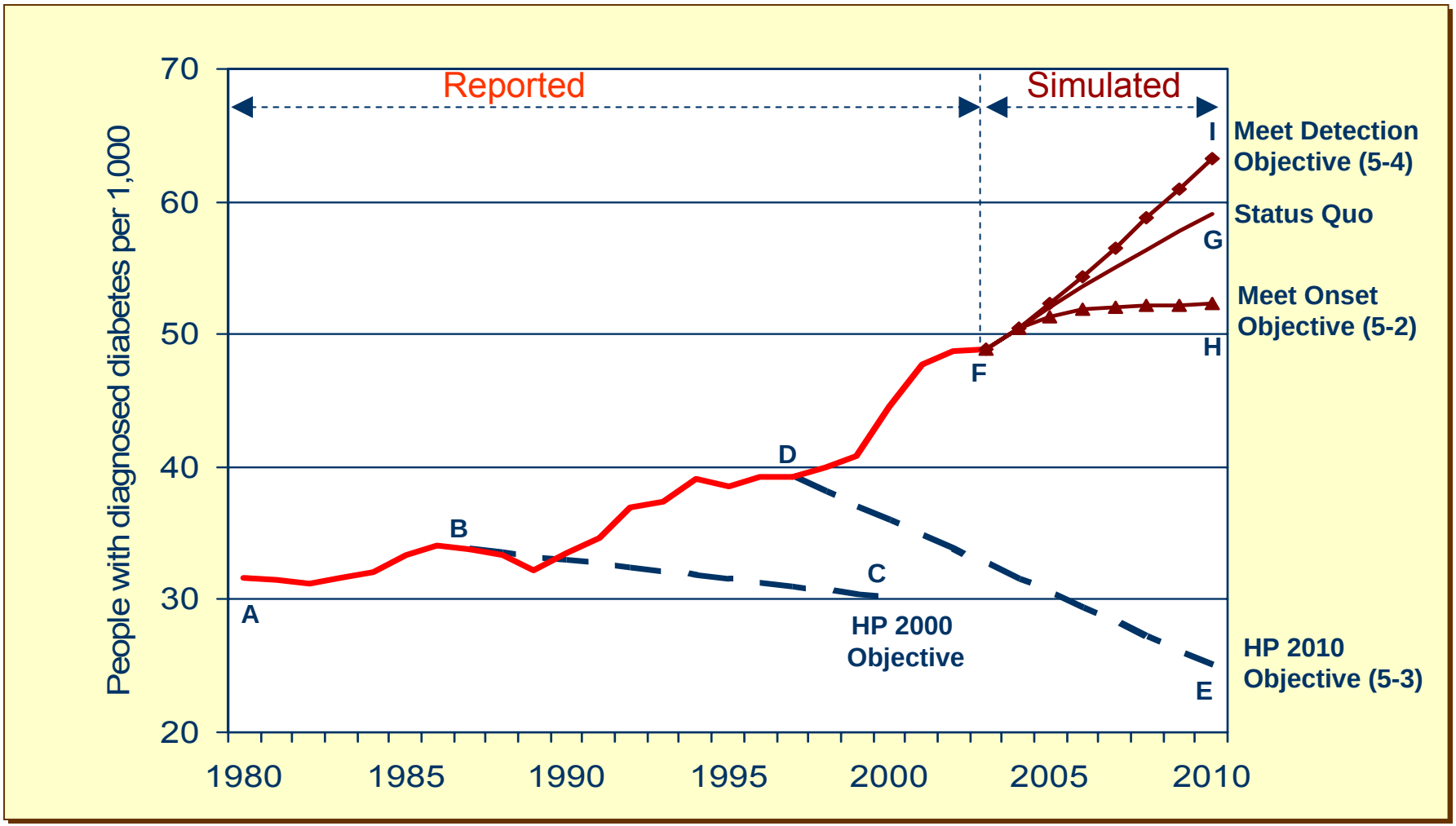




With a combination of effective upstream and downstream interventions we could hold the burden of diabetes nearly flat through 2050!

Sustainability Institute

History and Futures for Diabetes Prevalence
Reported Trends, HP Objectives, and Simulation Results



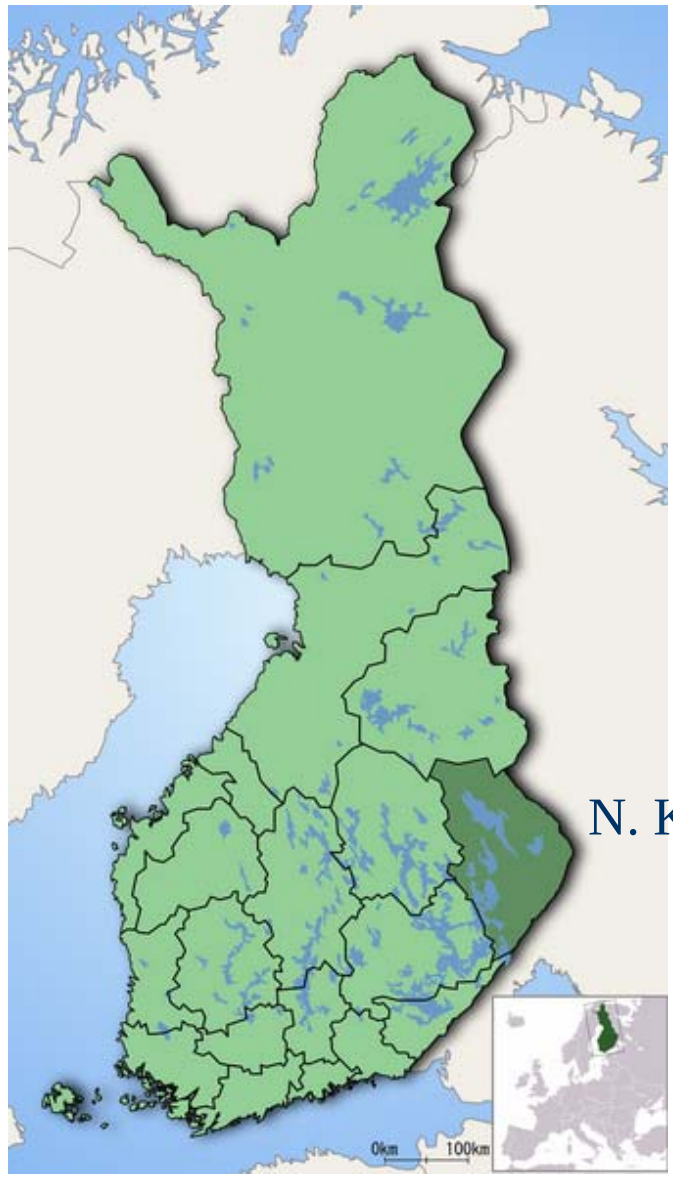
Milstein B, Jones A, Homer J, Murphy D, Essien J, Seville D. Charting plausible futures for diabetes prevalence: a role for system dynamics simulation modeling. Preventing Chronic Disease (under review).

The Modeling Process is Having an Impact

- HP2010 prevalence goal has been modified
  - from a large reduction to no change (but still not an increase)
- Budget for primary prevention was doubled
  - from meager to modest

Population Impact

- North Karelia Project
- Pekka Puska



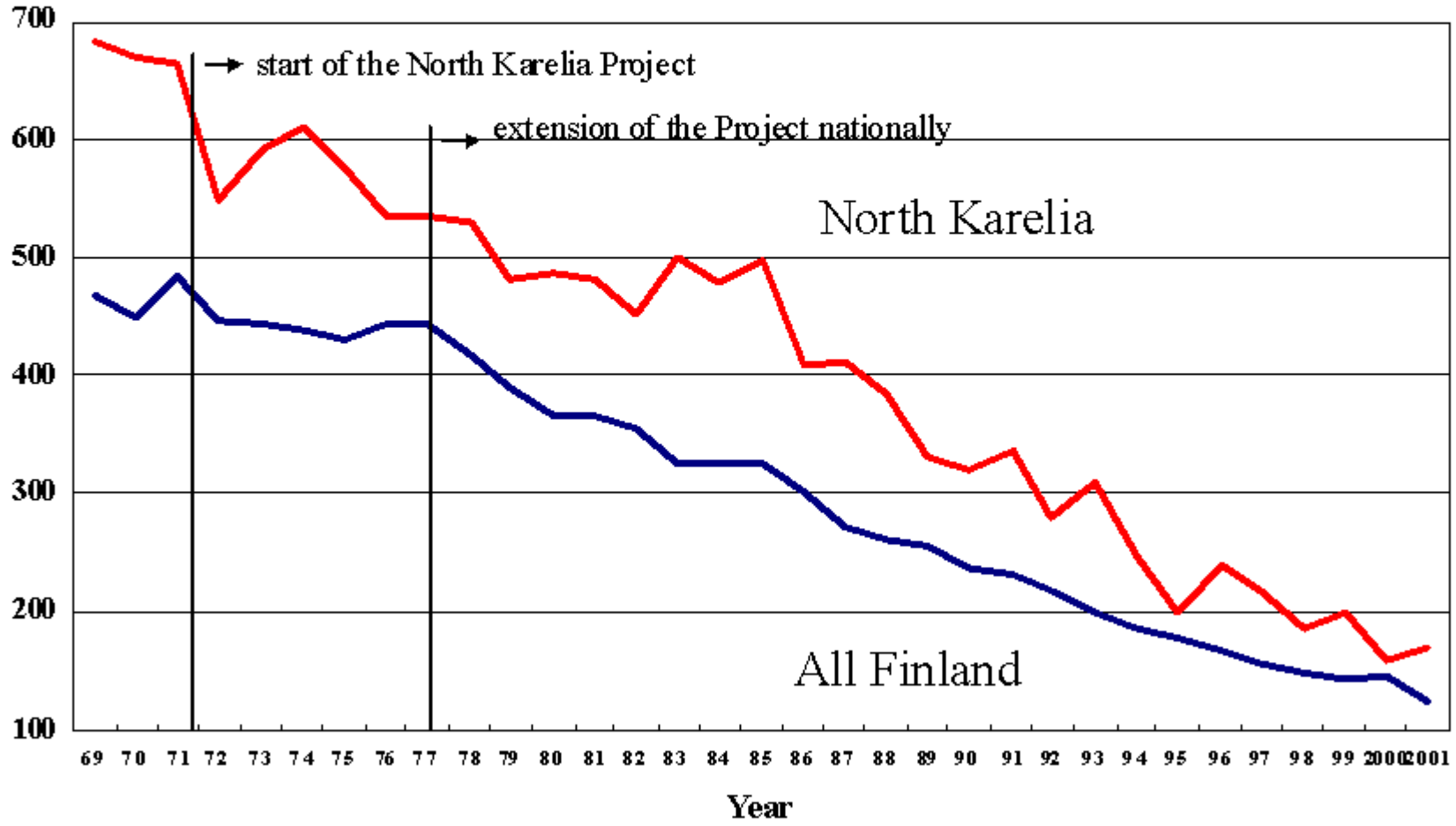
N. Karelia

- 1970's – Highest rate of CVD, 2x that of Finland
- Diet – butter, cheese, cream, whole milk, no veggies
- Comprehensive behavior modification program
- Diet, smoking reduction, and increasing exercise

Lifestyle Changes in N.Karelia

- Smoking among middle-aged men dropped from ½ to less than 1/3 between 1972 and 1997
- Vegetable consumption went from rare to commonplace
- Buttering bread dropped from 90% to 10%
- Healthier practices spread across Finland by the late 1970's – early 1980's

CHD mortality in all Finland and in North Karelia
35-64 year old men



Population Impact:
N. Karelia 25 years later

- **Coronary Heart disease dropped 73%**
- **Lung Cancer dropped 71%**
- **All cardiovascular diseases dropped 68%**
- **All cancers down 44%**
- **Life expectancy increased about 8 years!**

Global Impact of N. Karelia Project

- NK project inspired the WHO to develop a *Non-communicable Disease Prevention and Health Promotion Program*
- Similar projects inspired by the NK project are now in the U.S., China, South America, and the Middle East
- CardioVision 2020 project in Olmstead Co., MN

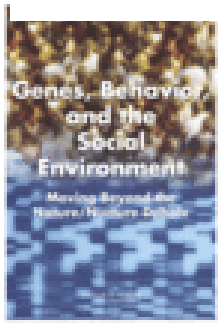
OBSSR Interdisciplinary Activities

How is OBSSR implementing the strategic prospectus?

What are the interdisciplinary activities of OBSSR?

OBSSR Participates in the NIH Roadmap Interdisciplinary Research Work Group

- NIH Roadmap Interdisciplinary Methodology and Technology Summit (August 21-22, 2006)
- Roadmap RFA: *Facilitating Interdisciplinary Research via Methodological and Technological Innovation in the Behavioral and Social Sciences (R21)* Applications due Feb 24



IOM Report: ***Genes, Behavior, and the Social Environment: Moving Beyond the Nature/Nurture Debate (2006)***

- Free download: http://www.nap.edu/catalog/11693.html
- *Committee on Assessing Interactions Among Social, Behavioral, and Genetic Factors in Health.* Lyla M. Hernandez and Dan G. Blazer, Editors
- Sponsored by OBSSR, NHGRI, and NIGMS. See: http://www.iom.edu/CMS/3740/24591.aspx for meeting dates and powerpoint presentations

Genes and Environment Initiative

- Four-year, $68 M, NIH-wide program (although not Roadmap)
- Two parts:
  - Genetics Program $26M yr 1 (NHGRI lead)
  - Exposure Biology Program $14M yr 1(NIEHS lead)
- OBSSR participates in the Exposure Biology Program (U01)
  - Environmental Sensors for Personal Exposure Assessment
  - Improved measures of Diet and Physical Activity for GEI
  - Field-deployable tools for Quantifying Exposures to Psychosocial Stress and to Addictive Substances for Studies of Health and Disesase
  - Biological Response Indicators to Environmental Stressors
  - Biological Response Indicators to Environmental Stressors Centers

OBSSR Training Institute in Genetics for BSS Scientists

- Purpose: to provide a foundation in basic concepts and principles of genetics, genetic research designs, and analysis of genetic data.
- Target audience: early-career BSS researchers with no to limited training in genetics.
- Goal: To equip the BSS researcher with the basic knowledge to *interpret* genetic/genomic studies or become members of transdisciplinary *research* team.

Symposia on Systems Methodology

- Purpose: to provide an overview of systems thinking and a foundation in basic concepts and principles of a few specific methodologies (i.e., networks, system dynamics simulation modeling, agent-based modeling).
- Target audience: All BSS researchers who wish to learn more about systems methodology
- Goal: To equip the BSS researcher with the basic knowledge to *interpret* studies using systems methodology and begin to explore use of these methods in their work.
- Spring 2007

Training and FOA's in Systems Methodology

- 2008 and beyond
- Conduct a week-long summer training institute in systems methodology
- Partner with IC's to develop initiatives to inspire BSS research utilizing systems methodology

END

System Dynamics Simulation Modeling

How is it done:

- Identify the problem
- Scope selection – define boundaries
- Hypothesize cause of the problem
- Causal diagramming – feedback loops (balancing and reinforcing)
- Quantify relationships
- Reliability testing
- Calibration
- Validation
- Test alternative policies aimed at alleviating the problem
- Sensitivity testing

Homer J, Milstein B, Dietz W, Buchner D, Majestic D. 2006

System Dynamics Simulation Modeling

Purpose – decision making support tool, e.g., policy

Advantages –

- Expert opinion and other sources can be used when you don't have data to drive the initial values and behavior of variables
- can run multiple scenarios under differing assumptions
- Sensitivity testing tells you how robust the model is in light of the calibration uncertainties
- Model can be validated with historic data

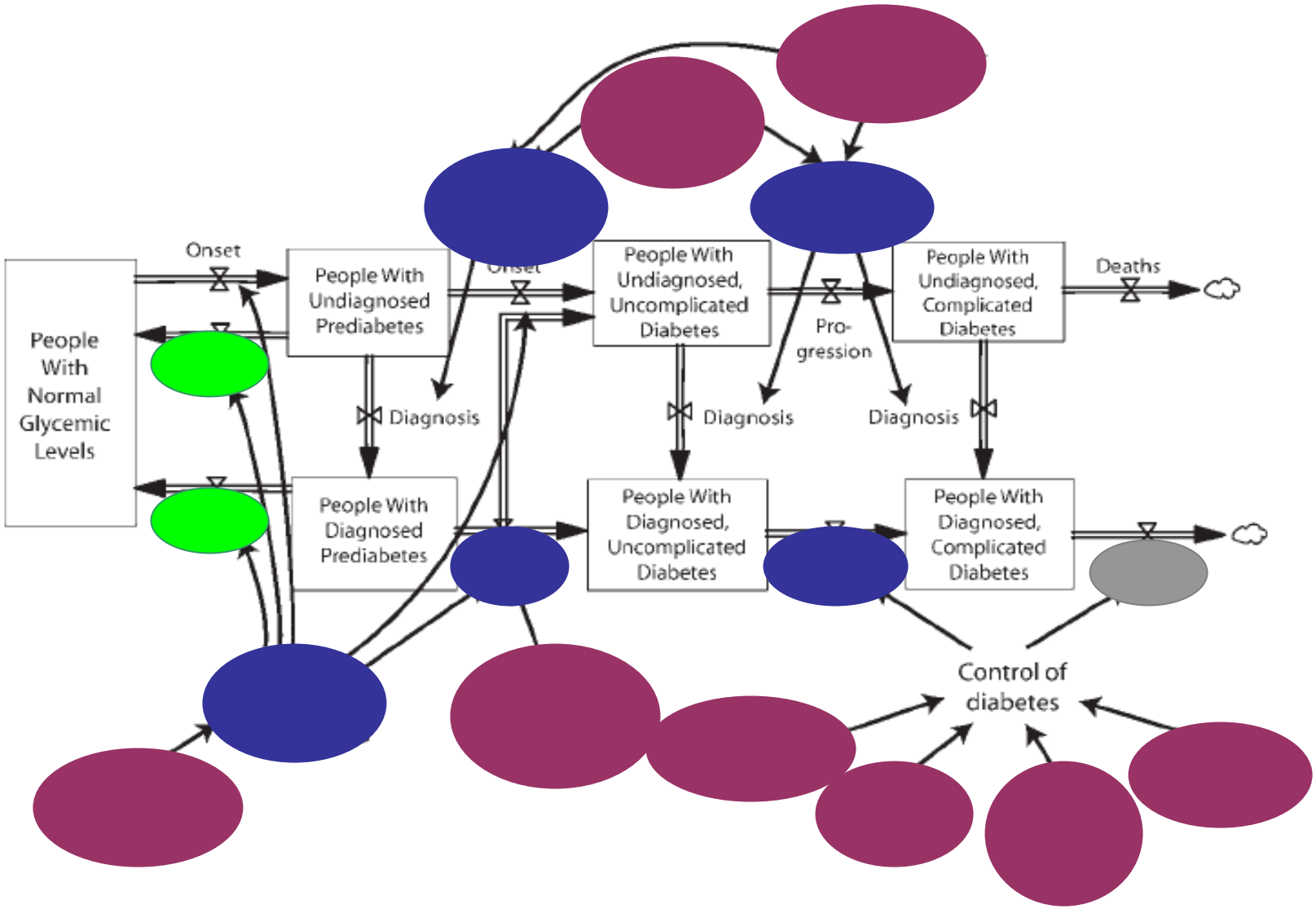
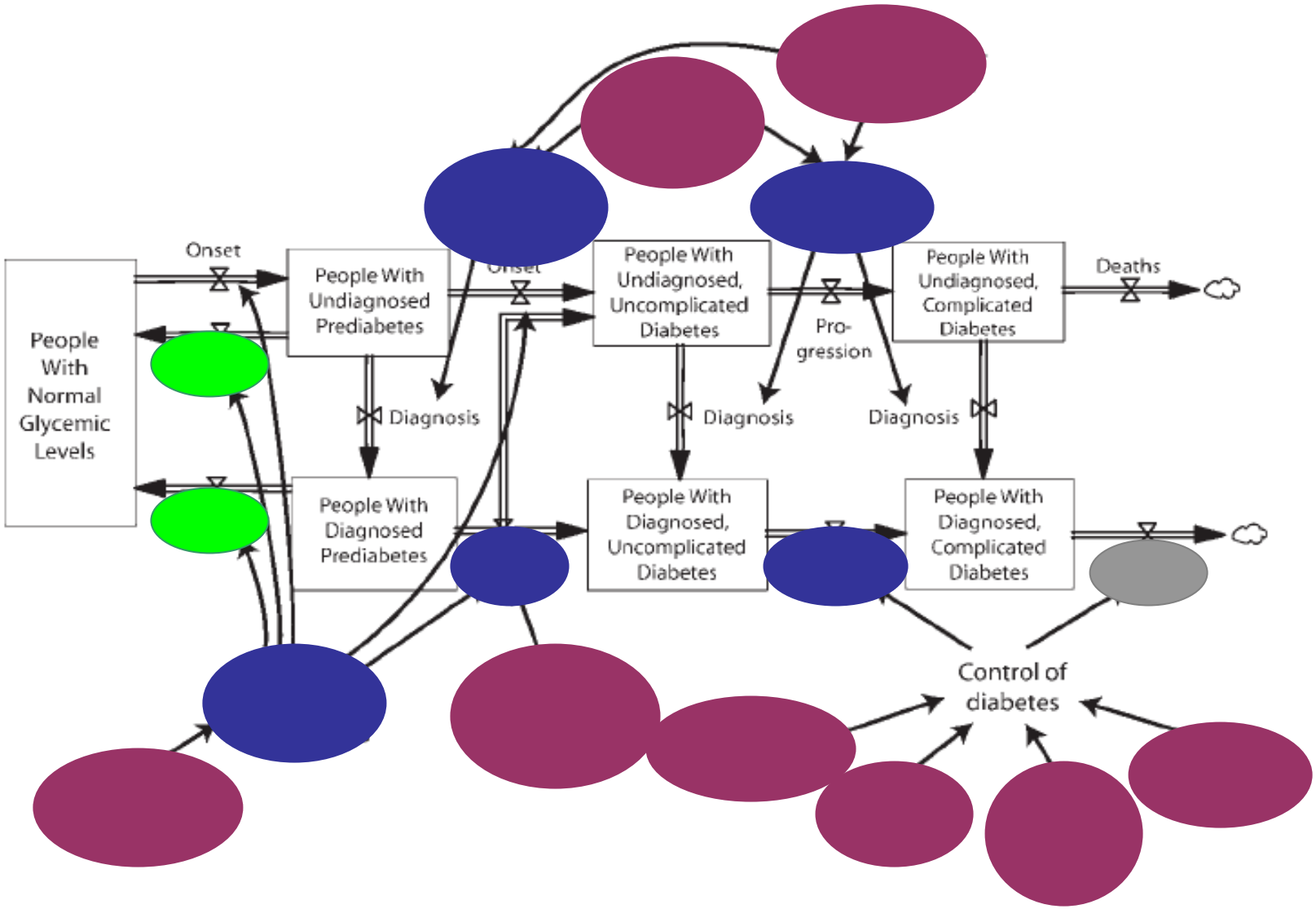


FIGURE 1—Overview of model structure, showing primary population stocks (boxes) and flows (arrows with valve symbols and cloud symbols for deaths), modifiable factors affecting flows (roman), and inputs amenable to policy intervention (italics).



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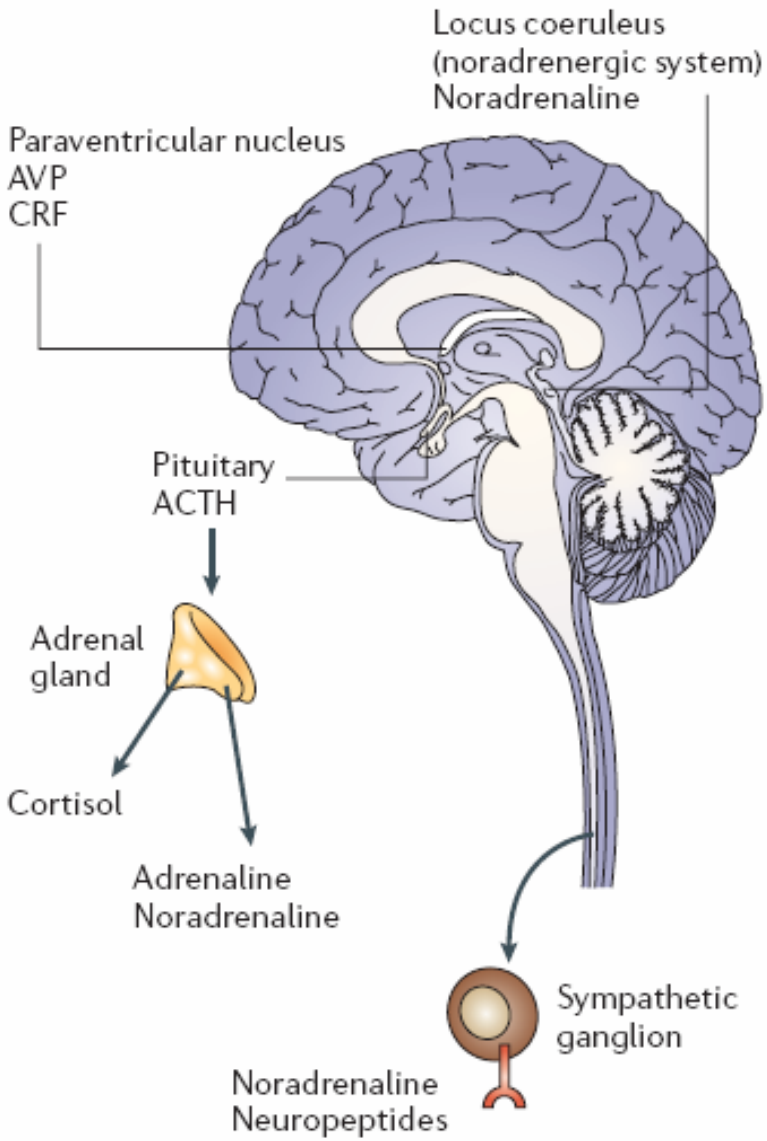

Figure 1 | **Important components of the central and peripheral stress systems.**

Counterintuitive Dynamics of the Diabetes System

- The better you do under the current strategy, the more you miss a primary goal
  - *Effective detection and disease management increase diagnosed prevalence*
- Over the next decade, enormous success in primary prevention won't actually reduce the overall burden of diabetes
  - *It will lead it to grow more slowly*
- What helps in short term doesn't help much in the long term. And vice versa.
  - *Disease management works in short; primary prevention works in long*