Vision of the Future

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Promise

- Individualized health care based on testing for inherited risk
- Improved clinical management based on molecular characterization of disease
- New therapeutics

Compelling examples

Individualized health care

BRCA, Lynch syndrome, HLA/abacovir

Improved clinical management

Gene expression profiling of tumors

New therapeutics

Fomiversen, Imatinib, Trastuzumab

Uncertainties

- Strategy that will yield greatest benefit for a given condition
- Scope of harms
- Proportion of good ideas that will fail in development process
- Effect on health care costs

Strains to the system

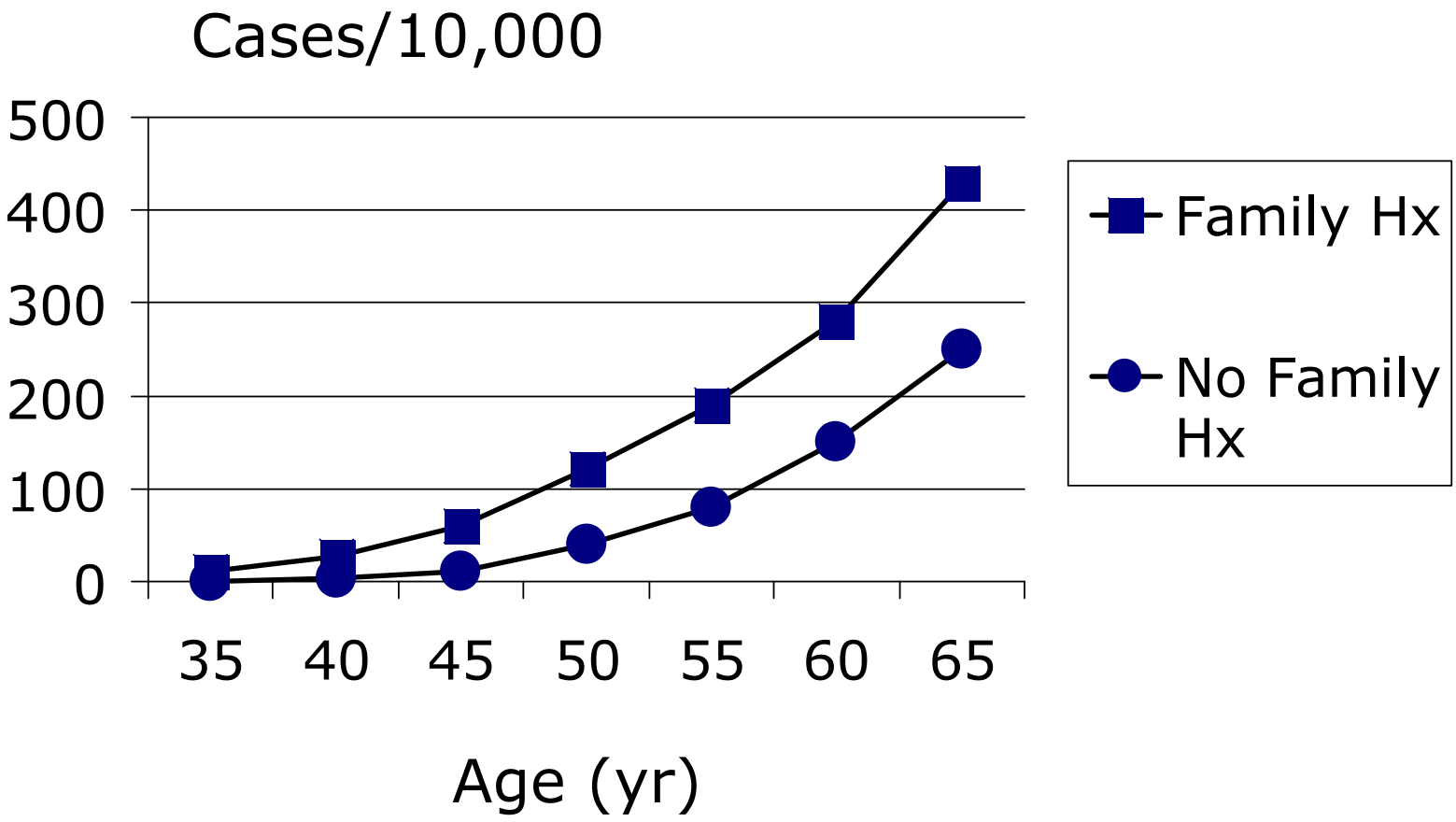
Rapid assessment of emerging technology

- Adequate study populations
- Funding
- Appropriate settings for assessment of comparative effectiveness

- Trustworthy processes for creation of guidelines / education
- Access

Colorectal CA risk

Family history as a risk factor

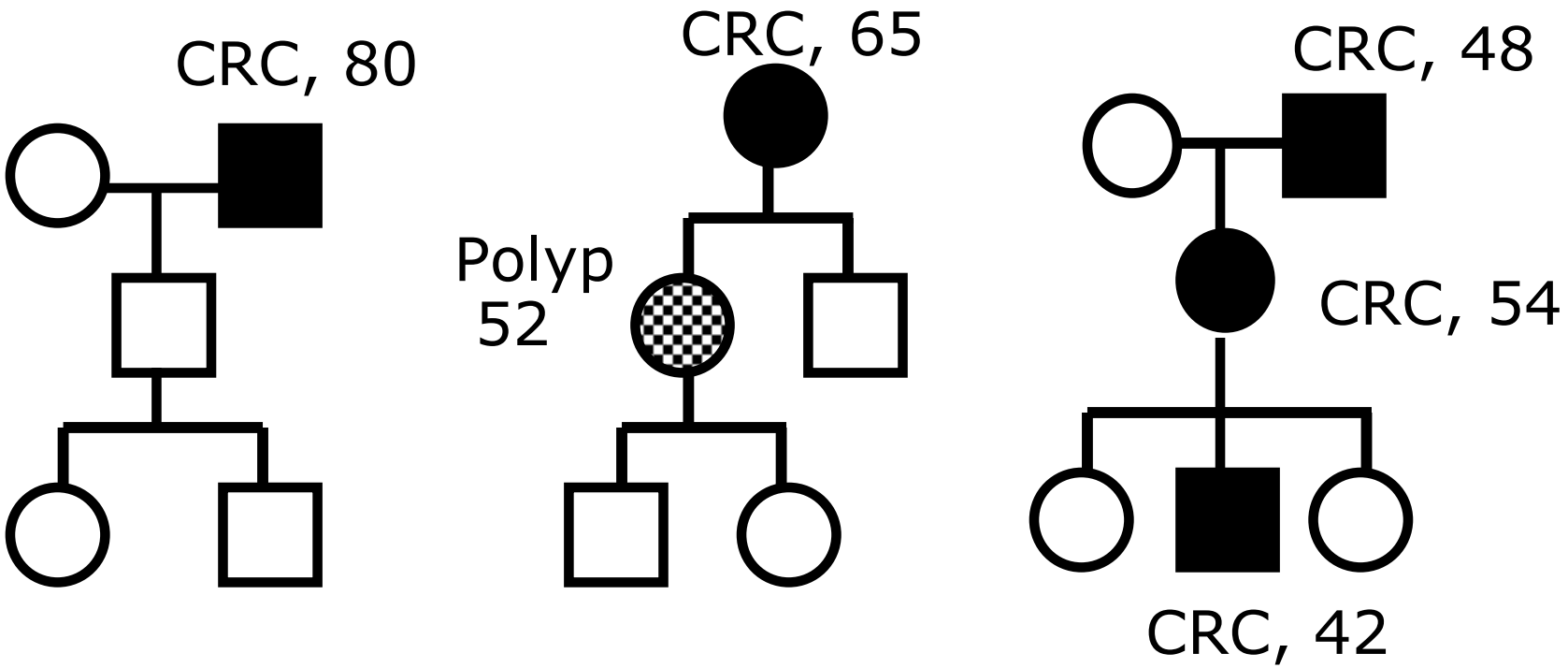


NEJM 1994; 331:1669

Argument for CRC screening at age 40 in people with + family history

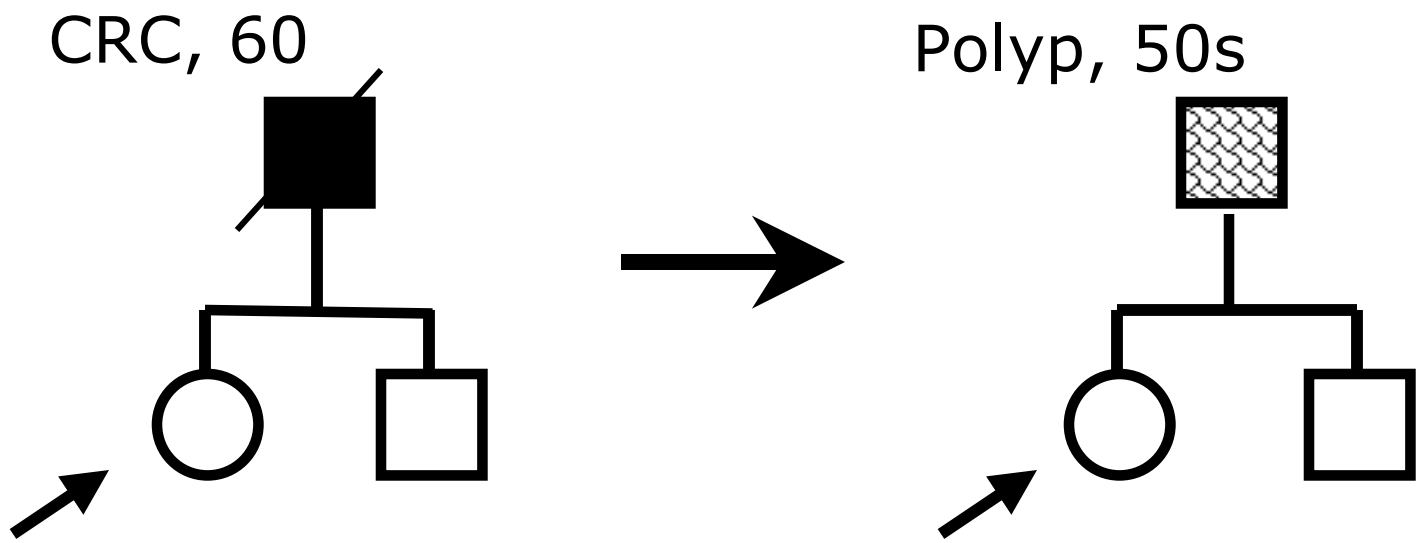
- Risk of CRC is ~ 2x higher
- CRC occurs earlier in people with an affected first degree relative
- Screening test performance expected to be the same at earlier ages

Continuum of family history of CRC



CRC = colorectal cancer

“Vanishing” family history with effective prevention



CRC = Colorectal CA

Polyp = Adenomatous polyp

Strains to the system

- Time to take and assess family history
  - Self-administered? Linked to medical records?
  - Processed by information technology?
- Availability of genetic services
- Balancing care to individual and family
  - Provider obligations
  - Confidentiality
  - Funding

Genomic profiling for CRC risk
Hypothetical benefits

- Not dependent on recall of family history or age of family members
- Might result in reduced mis-classification compared to family history - & might be less costly
- If variants are associated with polyp dwell time or age of onset of CRC, profile could inform timing and frequency of screening

Predictive value of APC mutation test
Familial adenomatosis polyposis (FAP)

	Family mutation	General population
Chance of FAP	1/2	1/32,000
Sensitivity	.999*	.999*
Specificity	.999*	.999*
PPV	.999	.03
NPV	.999	.999

*Assumed

Potential for disruptive technology

e.g.,

- Virtual colonoscopy
- Therapy to inhibit polyp formation

If safe and effective, might change thresholds for risk assessment

Rapid pace of development

Disease characterization

- Measurement of acquired genetic change, gene expression, proteomics, metabolomics

New therapeutics

- Genome wide association studies
- Identification of disease pathways (many unanticipated)
- New insights / drug targets

Strains to the system

How much improvement? At what cost?

Rapid assessment of emerging technology

- Adequate study populations
- Funding
- Appropriate settings for assessment of comparative effectiveness
- ***Cost & access***

Cascade effects of medical technology

Unnecessary test or false positive result

Further tests/treatment

Avoidable adverse effects or morbidity

Deyo, Annu Rev Public Health 2002; 23:23-44

Common triggers for the cascade effect

- Shotgun testing
- Underestimating the likelihood of false +
- Inappropriate screening
- Errors in data interpretation
- Overestimating benefit, underestimating risk
- Patient demand
- Low tolerance of ambiguity

Deyo, Annu Rev Public Health 2002; 23:23-44

Potential harms from expanding genetic risk assessment

- Unwanted information
  - False positive results
  - Variants of unknown clinical significance
  - Incidental findings
- Unnecessary / unproven care
- Limits to access based on genetics

  e.g., Gene variants associated with smoking & illegal substance abuse

Intensified discussion of scope & coordination of oversight

- Regulation
- Accreditation / Licensure
- Health technology assessment
- Guidelines
- Education

Opportunity to acknowledge complexity

"Technology is rarely inherently good or bad, always or never useful. The challenge is to evaluate when…it is effective, for whom it will enhance outcomes, and how it should be implemented or interpreted"

Eisenberg, JAMA 1999; 282:1865

Need for high quality health technology assessment

- Innovation and flexibility
- Not a one-time exercise
- Attention to measures of outcome
- Community practice as laboratory
- Link national HTA resources

Eisenberg, JAMA 1999; 282:1865

Importance of engaging both clinicians and the public

- Independent, trustworthy processes
- Transparent methods
- Simple language
- Readily available information

Emmanuel et al, JAMA 2007; 298:1323

Eisenberg, JAMA 1999; 282:1865

Deyo, Annu Rev Public Health 2002; 23:23-44