

# The Therapeutic Landscape: Challenges and Opportunities

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# Overview



Standard therapeutic approaches

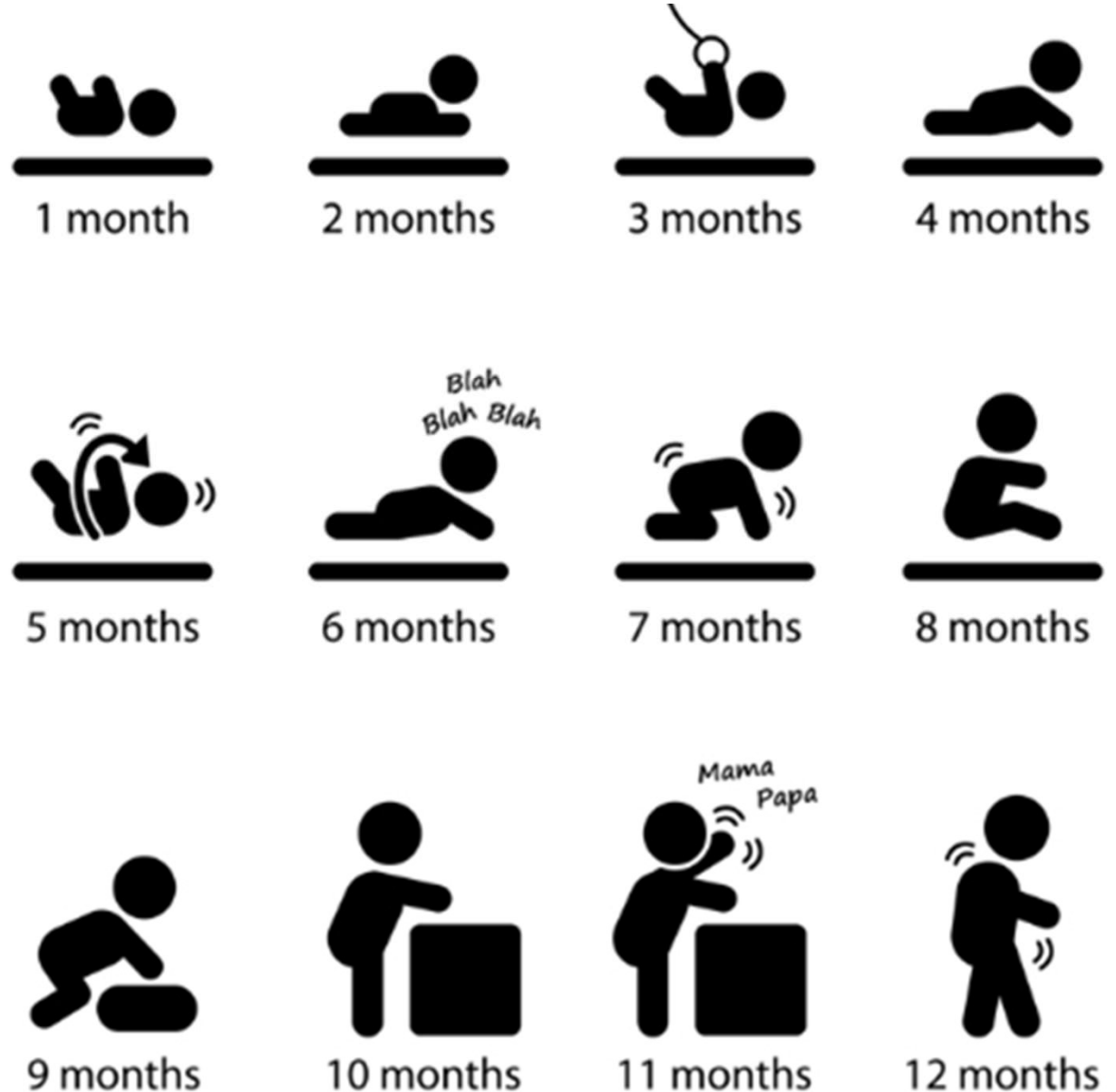


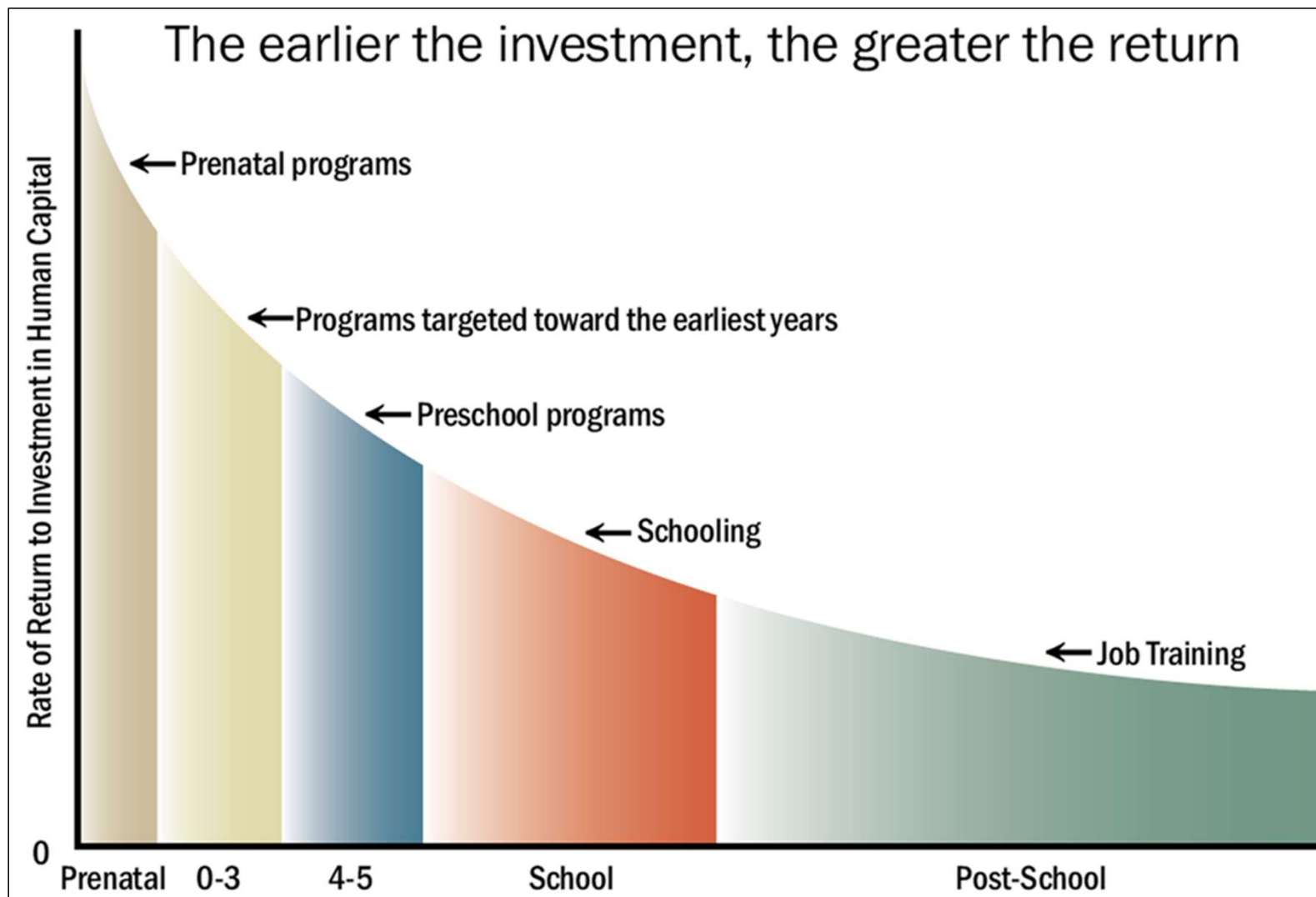
Precision medicine progress

# Standard therapeutic approaches

## Skills

- Gross motor
- Fine motor
- Language
- Social skills





## Early intervention is key

*“Skills beget skills in a complimentary and dynamic way. Efforts should focus on the first years (of life) for the greatest efficiency and effectiveness.”*

– James J. Heckman  
PhD

<https://hhs.texas.gov/services/disability/early-childhood-intervention-services>

# Early Childhood Intervention

## **Seven Key Principles:**

- (1) Infants/toddlers learn best through everyday experiences & interactions with familiar people in familiar contexts.
- (2) All families, with the necessary supports and resources, can enhance their children's learning and development.
- (3) The primary role of a service provider in early intervention is to work with and support family members and caregivers in children's lives.
- (4) The ECI process must be dynamic and individualized to reflect the child's and family members' preferences, learning styles, and cultural beliefs.

<https://hhs.texas.gov/services/disability/early-childhood-intervention-services>

# Early Childhood Intervention

## **Seven Key Principles:**

- (5) Individualized Family Service Plan (IFSP) outcomes must be functional and based on children's and families' needs and family-identified priorities.
- (6) The family's priorities, needs and interests are addressed most appropriately by a primary provider who represents and receives team and community support.
- (7) Interventions with young children and family members must be based on explicit principles, validated practices, best available research, and relevant laws and regulations.

# Typical treatments

**PHYSICAL & SPEECH  
THERAPIES**

**SUPPORTIVE BREATHING  
ASSISTANCE AT NIGHT**

**INDIVIDUALIZED  
EDUCATION  
PROGRAM**

**POSITIONING &  
ORTHOPEDIC  
DEVICES**

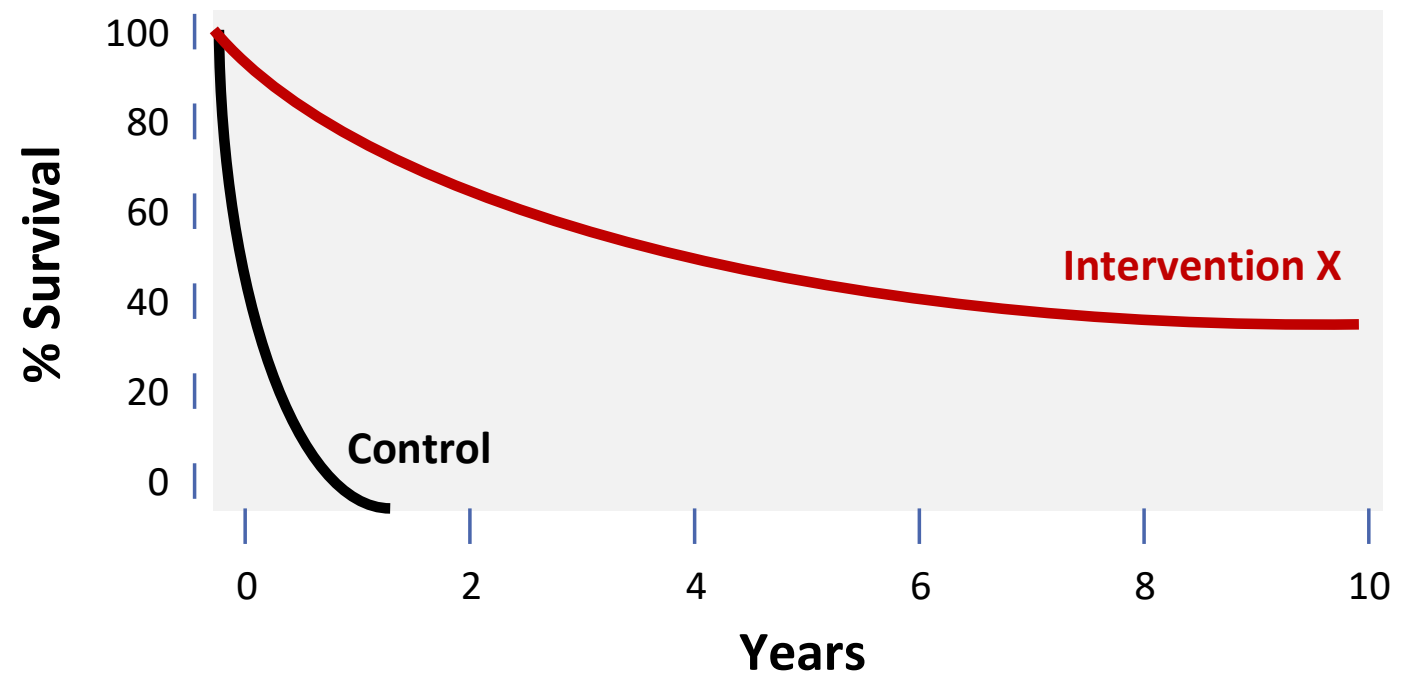
**VISION  
TREATMENT**

**HEARING  
AIDS**

**ANTI-SEIZURE  
MEDICATIONS**

# Assessing the evidence

A randomized controlled trial of 1000 individuals demonstrated that 10-year survival following a medical event improved substantially with **intervention X**.

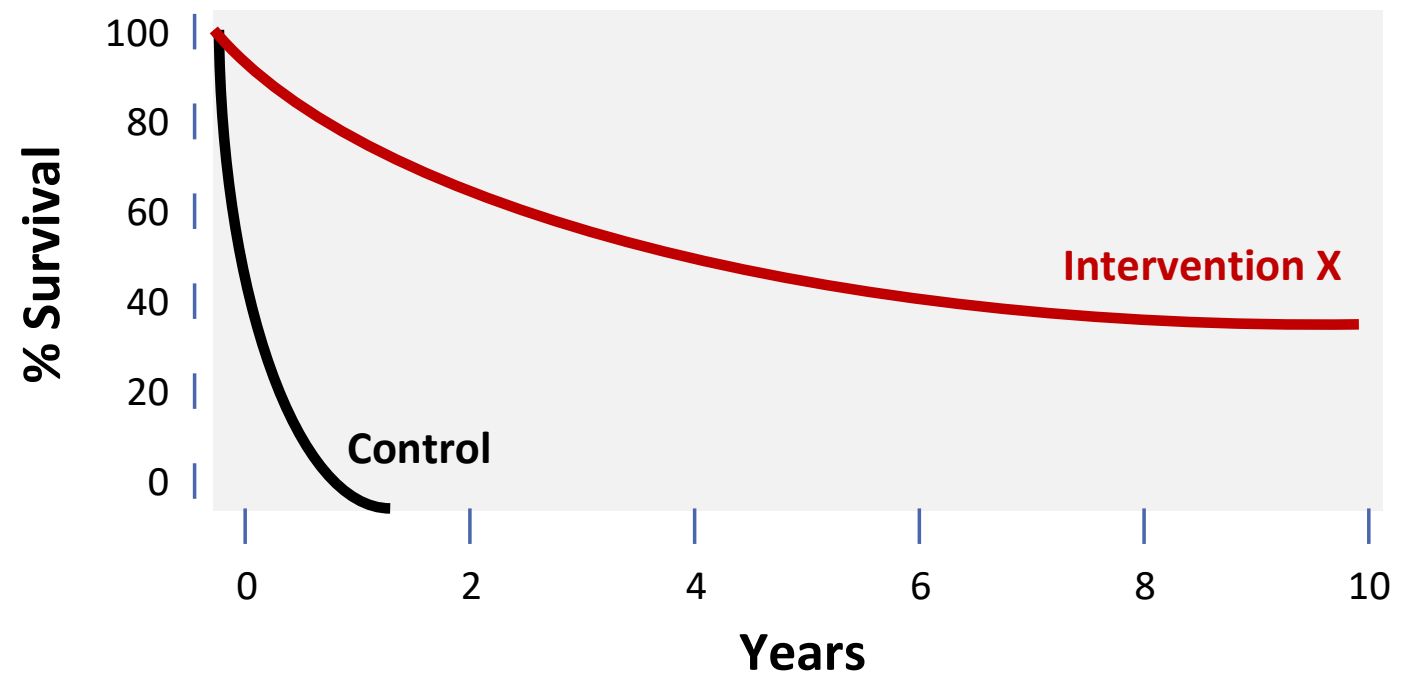




What can you  
conclude from  
this study?

# Assessing the evidence

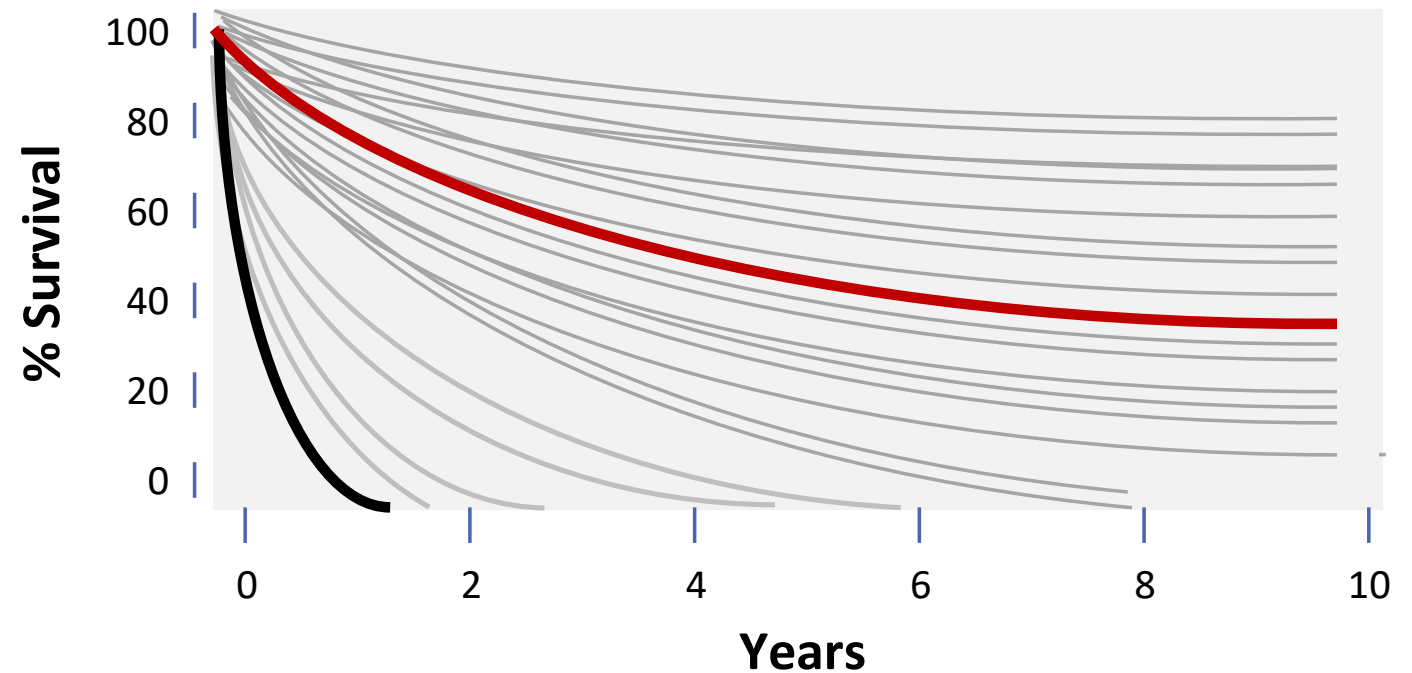
A randomized controlled trial of 1000 individuals demonstrated that 10-year survival following a medical event improved substantially with **intervention X**.



Do you think  
differently  
about these  
data seeing the  
varied response  
to Intervention  
X?

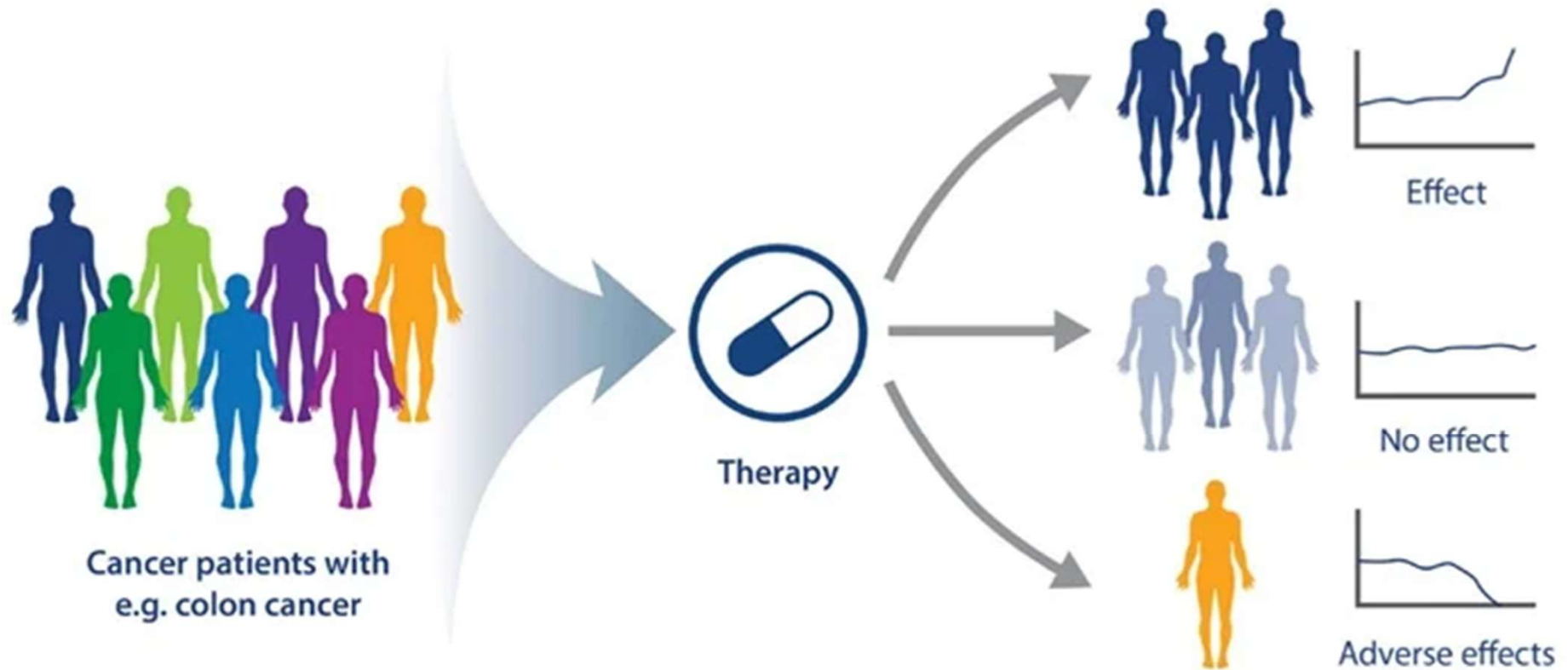
## Assessing the evidence

A randomized controlled trial of 1000 individuals demonstrated that 10-year survival following a medical event improved substantially with **intervention X**.



# Current Medicine

## One Treatment Fits All



<https://pressbooks.pub/anne1/chapter/personalized-medicine/>

# Future Medicine

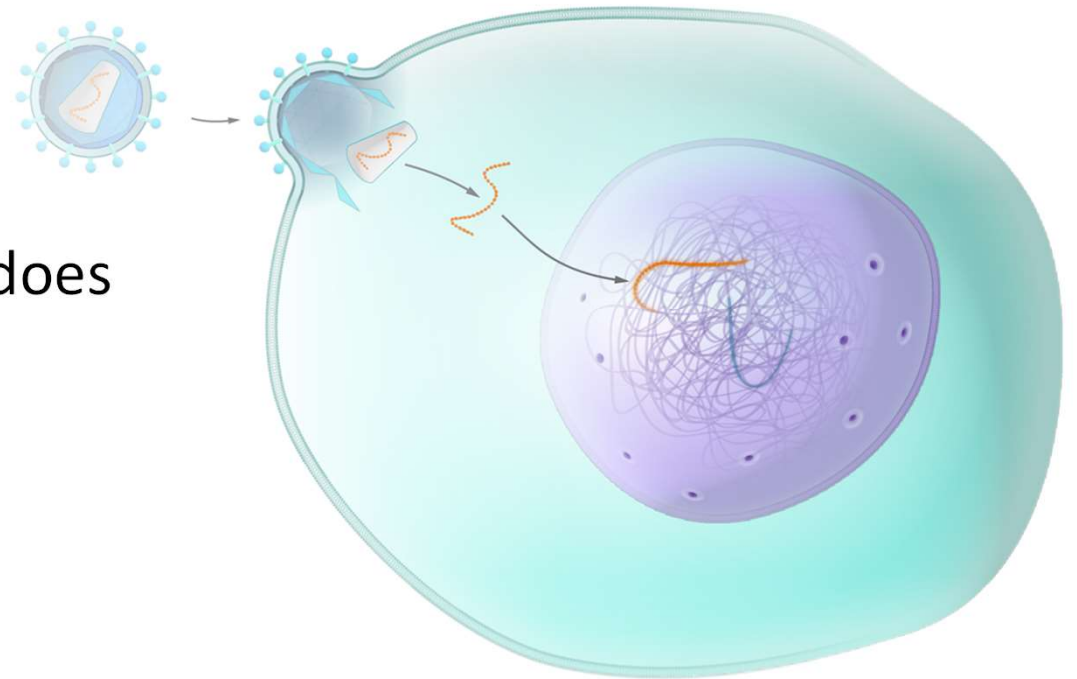
## More Personalized Diagnostics



<https://pressbooks.pub/anne1/chapter/personalized-medicine/>

# Gene Therapy

- Using a gene to treat, cure, or prevent disease
- Possible approaches
  - Add a new copy of a gene that does not function properly
  - Replace a missing gene
- Alternatives: gene editing



<https://www.genome.gov/genetics-glossary/Gene-Therapy>

# Gene Therapy in Immunodeficiency

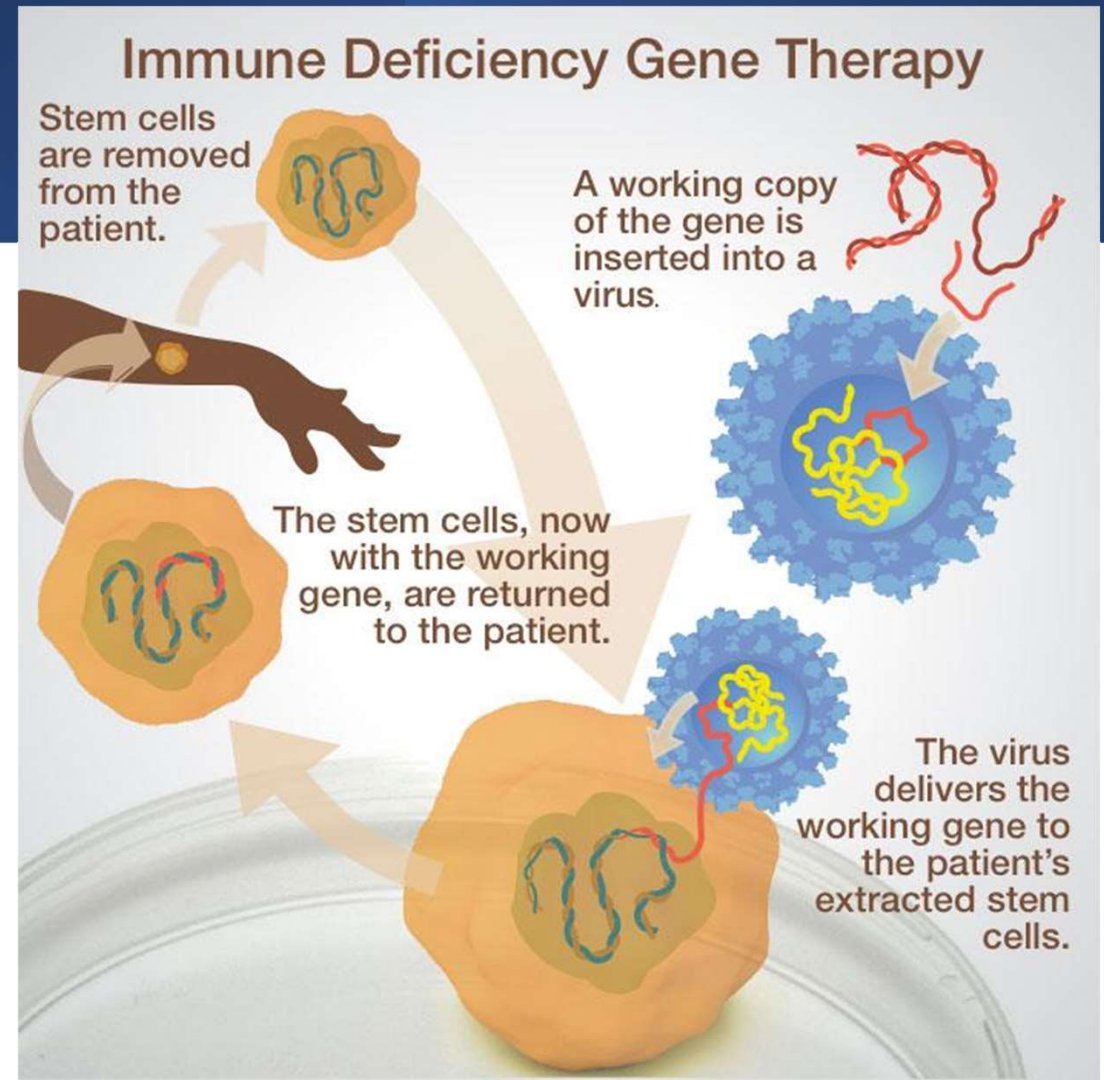
## Severe Combined Immune Deficiency (SCID) Therapy

Target: **stem cells**

Approach: **viral**

***Ex vivo*** (outside body)

Challenge: **viral vector resulted in leukemia**



<http://learn.genetics.utah.edu/content/genethrapy/success/>



# Gene Therapy in Hereditary Blindness

## Leber's Congenital Amaurosis (LCA)

Target: **retinal cells in the eye**

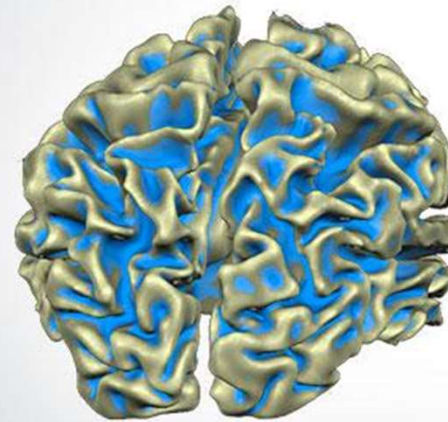
Approach: **viral**

***In vivo*** (but eye is a 'protected space')

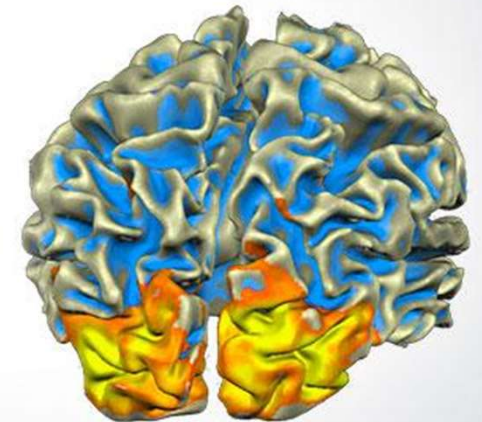
Challenge: initial improvement, then further degeneration; focused on one gene: *RPE65*

## LCA Patient Brain response to visual stimulus

BEFORE  
GENE THERAPY



3mo. AFTER  
GENE THERAPY

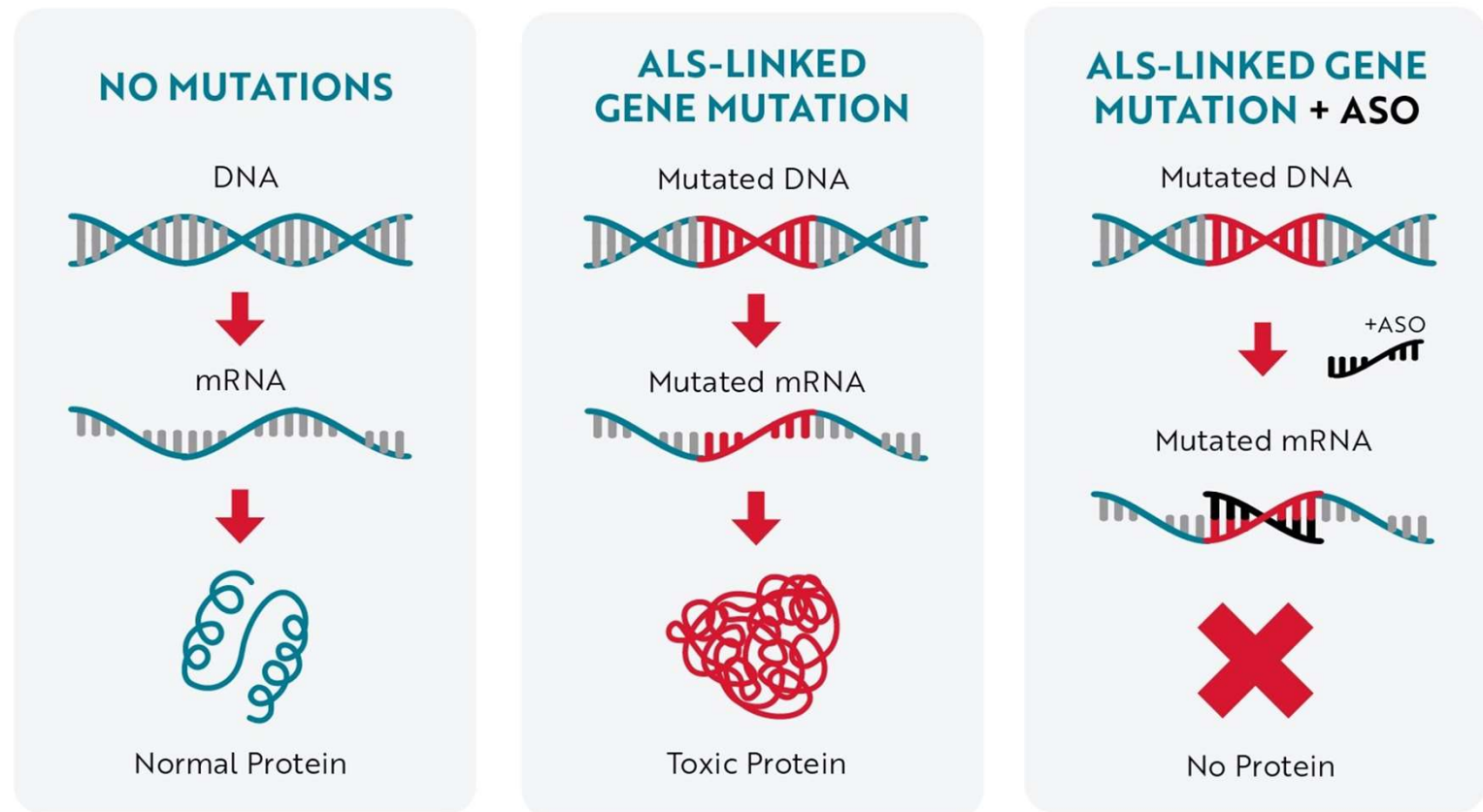


*Vision regions located in the back of brain.*

<http://learn.genetics.utah.edu/content/genethrapy/success/>

# Anti-sense Oligonucleotide Therapy

Short RNA-like molecules target the gene's message (mRNA) for degradation



<https://www.als.org/research/als-research-topics/genetics/antisense-therapy-for-als>



# Important Considerations with Precision Therapy

- **Risk of the treatment:** What are the potential adverse effects?
- **Delivery of treatment:** Can the therapy be successfully delivered to the correct organ/cells?
- **Duration of positive effects:** Is the treatment a 'cure'?
- **Timing of intervention:** Can the treatment be applied before irreversible damage or can it stimulate reversal of damage from disease?

# Conclusions

- Current treatment/therapies for XGS are largely symptomatic
- Precision therapies offer the potential for more targeted treatment of many rare disease conditions
- Precision therapies are not a one-size-fits-all approach, and generally must be tailored to the gene/variant and molecular mechanism of disease
- Understanding the molecular mechanism of disease (missing protein, toxic protein) is critical to successful design of precision therapeutics

Thank you!

QUESTIONS?