

Genetic Counseling and Testing in Dementia

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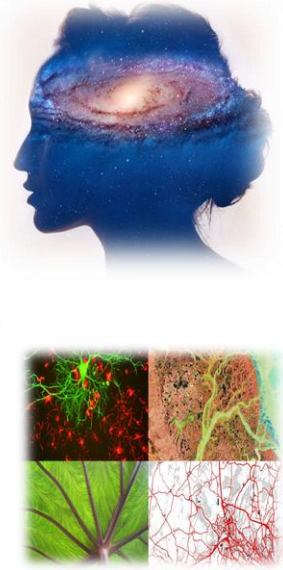
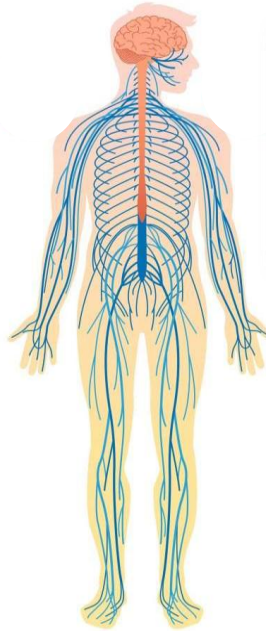
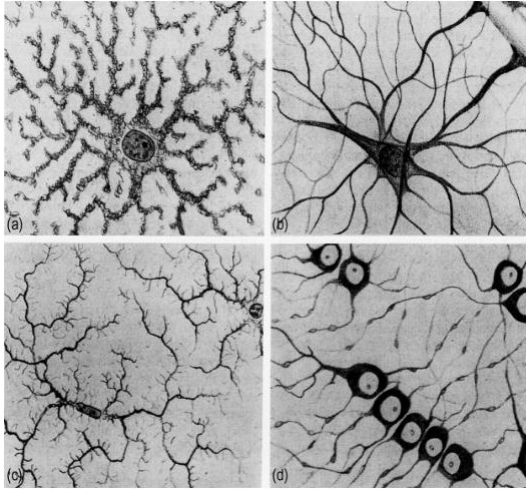
1

Learning Objectives

- Summarize the genetic architecture of Alzheimer's dementia and the current genetic testing landscape.
- Examine common themes in genetic counseling for dementia.
- Evaluate current access to genetic counseling for patients and families affected by dementia.

2

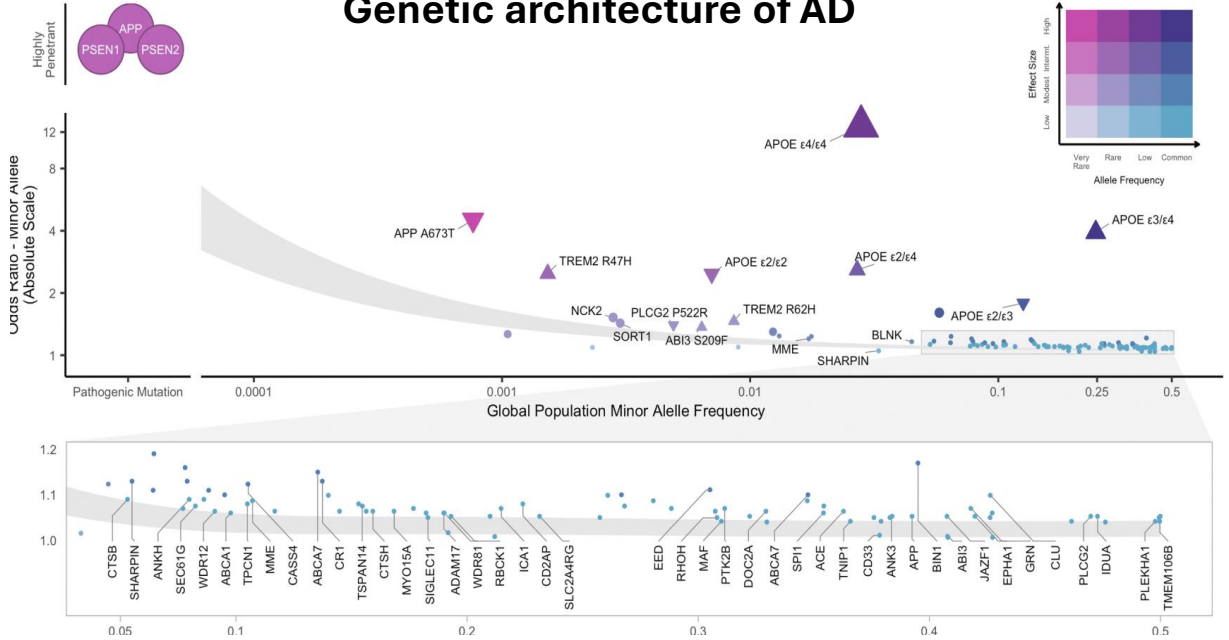
Nervous system



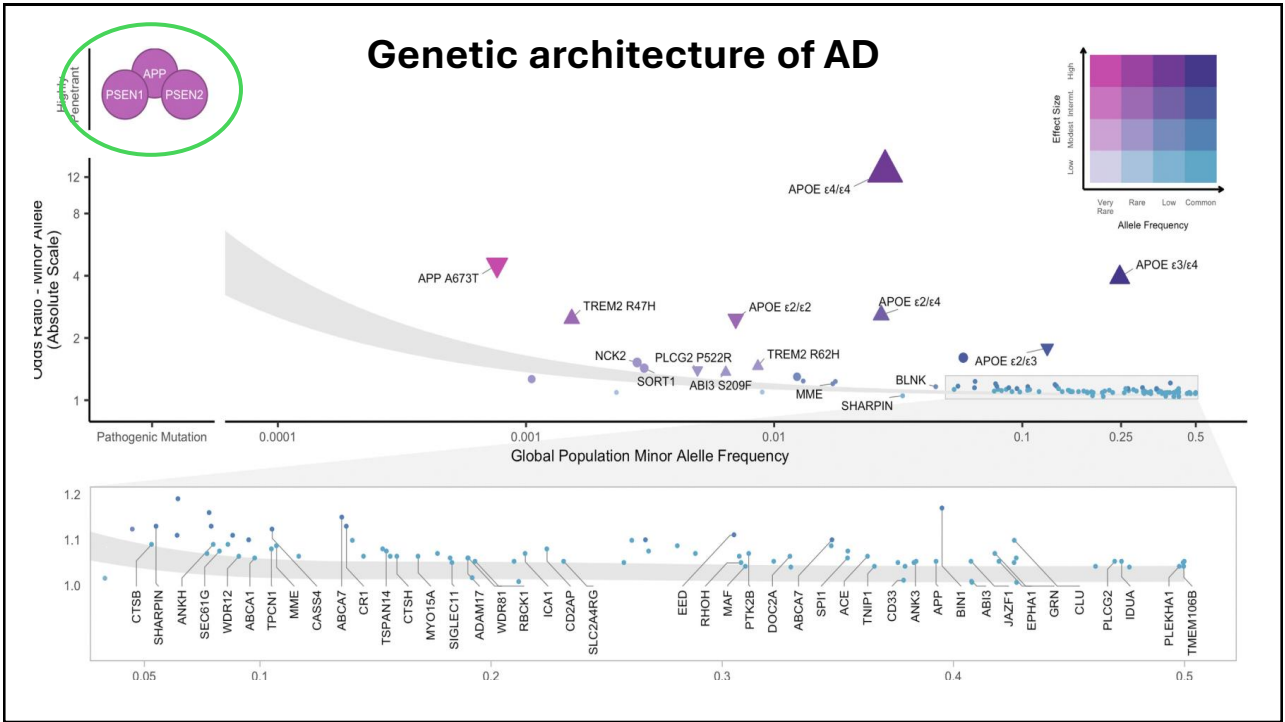
Images: An Atlas of Comparative Vertebrate Histology, *Diagnostic and Translational Research Guide*, *Scientific American*

3

Genetic architecture of AD



4



5

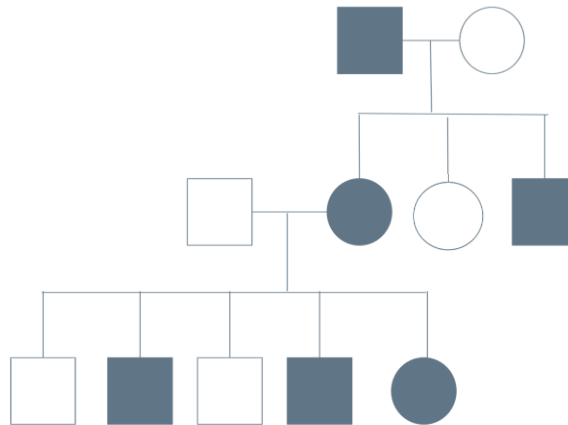
Monogenic AD

Gene	Proportion of early onset familial AD	Average age of onset
<i>APP</i>	10%-15%	Usually 40s & 50s, occasionally 60s
<i>PSEN1</i>	20%-70%	Usually 40s or early 50s
<i>PSEN2</i>	~5%	40-75

- All three genes are involved in the production of beta amyloid.
- Harmful variants in these genes are **rare** but are inherited in the **dominant** pattern.

6

Dominant inheritance pattern



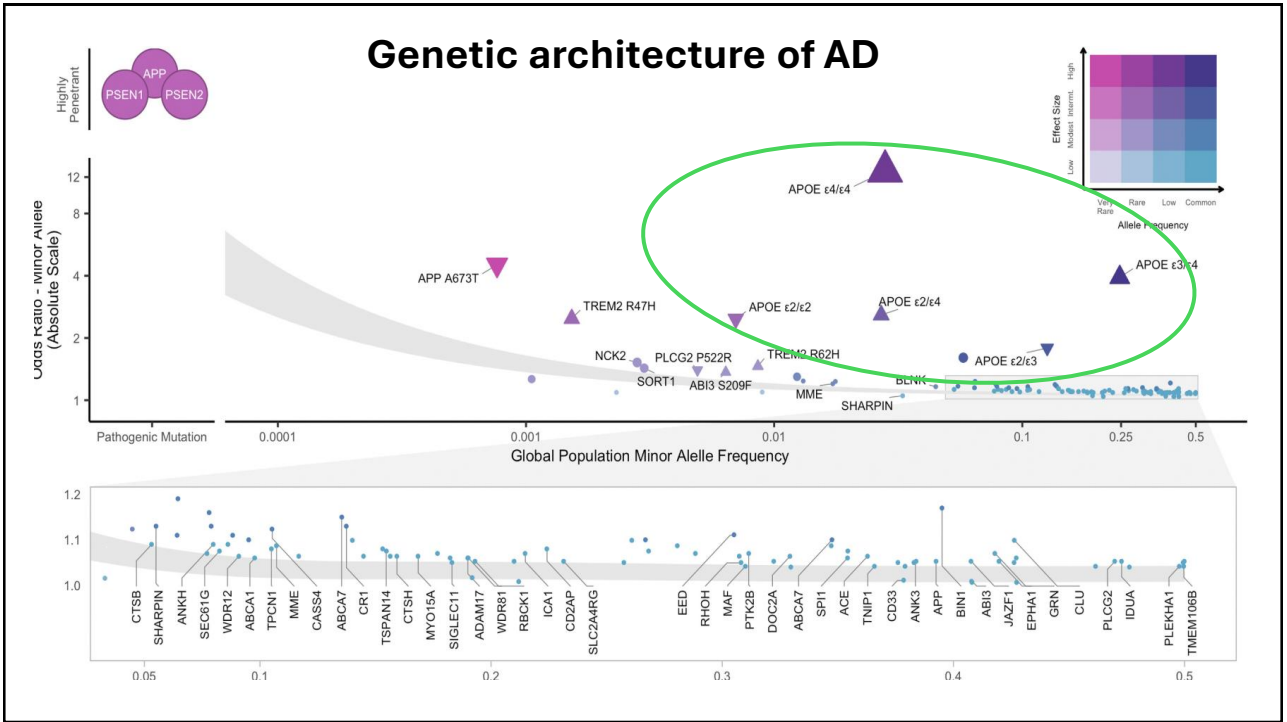
7

Genetic testing for monogenic AD

- Panels Including APP, PSEN1, and PSEN2 available from multiple clinical genetic testing labs
- Panel content ranges from 3 – 90+ genes
- Cost to patient = \$0 - \$1000 – but usually around \$300
- Turn around time - around 3 weeks



8



9

ApoE

APOE4:

receptor binding +

lipid binding (VLDL)

N-term C-term

APOE3:

receptor binding +

lipid binding (HDL)

N-term C-term

APOE2:

receptor binding X

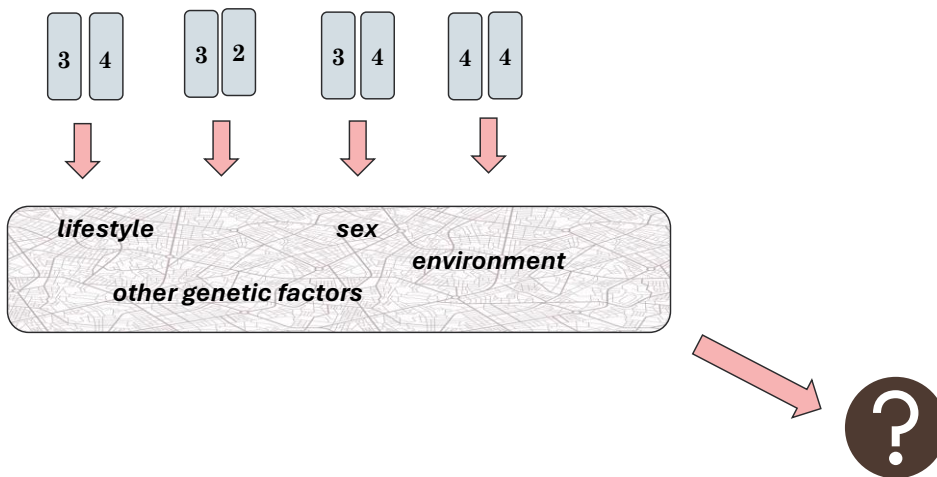
lipid binding (HDL)

N-term C-term

- Differ by only two bases of DNA
- Differ in affinity for lipids, receptors, and regulatory molecules

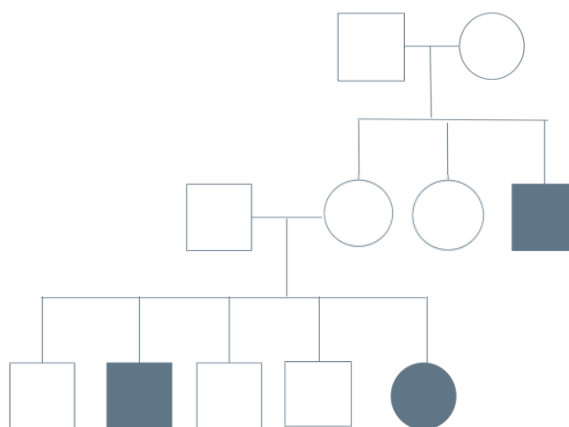
10

YOUR Patient....



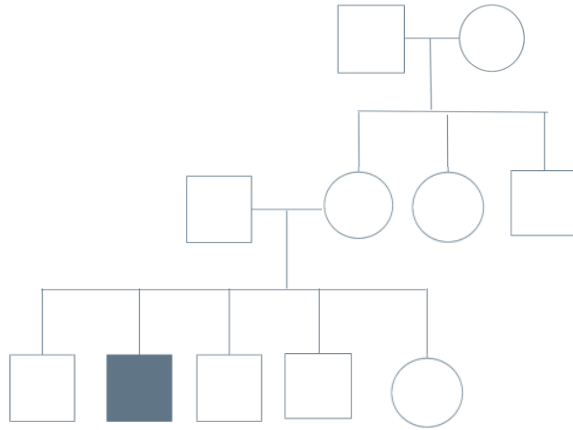
11

Familial



12

Sporadic



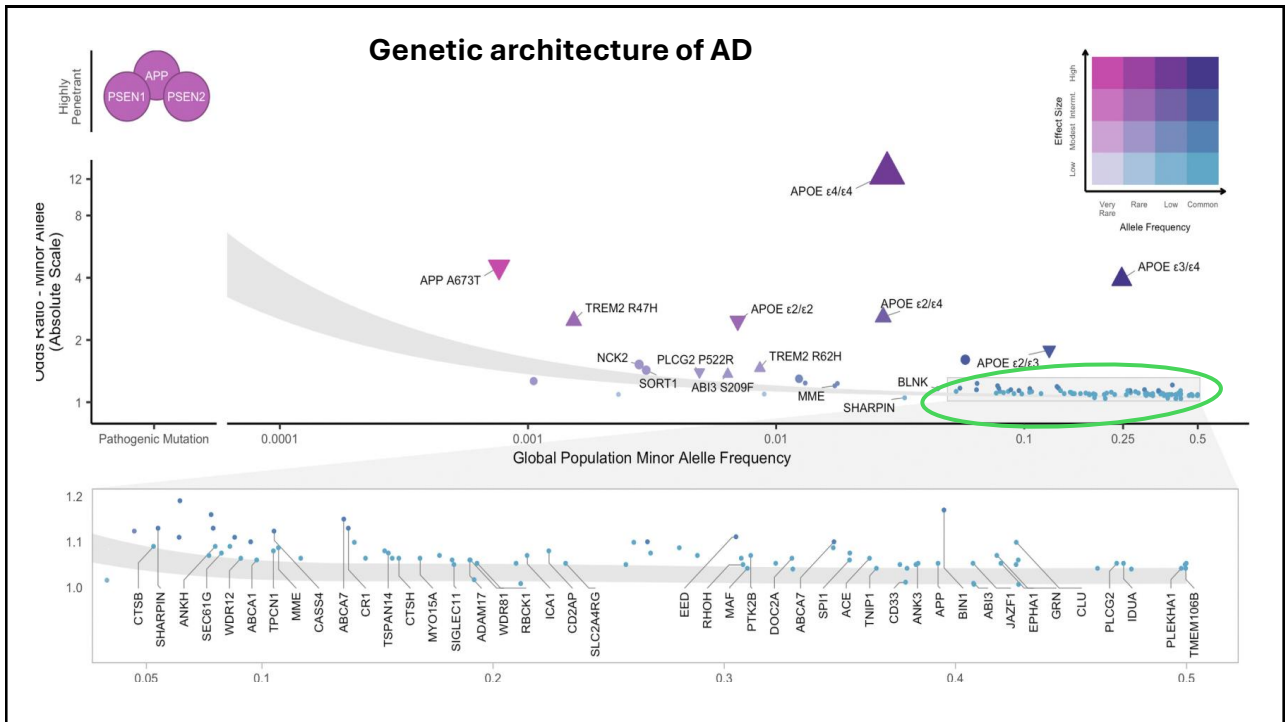
13

Genetic Testing Options ApoE *



LAB	COST TO PATIENT	NOTE
ARUP / LabCorp	\$0-300	<ul style="list-style-type: none"> • Part of medical record better outcome tracking • Access to genetic counseling
DIRECT to CONSUMER	\$50-\$500	Variability in <ul style="list-style-type: none"> • Lab quality • Risk estimates and patient education • Privacy policies

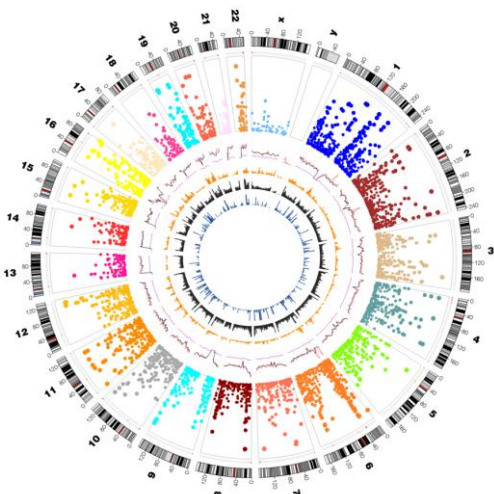
14



15

polygenic risk

- At least 100 polymorphisms each contribute a very small amount to risk for AD.
- These variants are common in the population.
- Polygenic risk is **not captured by current clinical genetic testing strategies.**



16

Results... now what?

All genetic results have familial implications.

Genetic status may be shared by parents, siblings, children, and other family members.

Results may impact treatment plan, career decisions, family planning, insurance eligibility.

Receiving predictive genetic testing results can be a psychologically impactful event.



17

Genetic counselors..

Are medical providers with training in genetics and counseling.

We help families understand and adapt to the psychological, familial, & medical aspects of genetic disease.



Image <https://www.nsgc.org/>

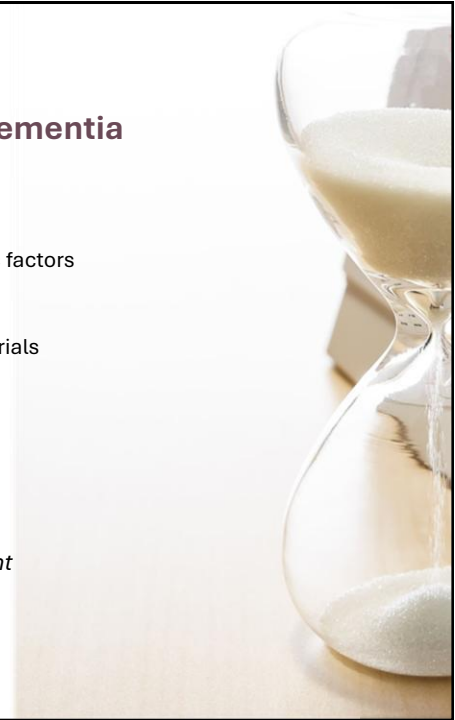
18

Evaluating utility of genetic testing for dementia

- ❑ **Purpose** – Predictive? diagnostic or for treatment decisions?
- ❑ **Age of onset** – early onset <65 = more likely to be driven by genetic factors
- ❑ **Inheritance pattern** – dominant, familial, sporadic
- ❑ **Specific diagnosis** – prognostic information, eligibility for clinical trials
- ❑ **Follow up plans** – support and medical management

ACMG/ NSGC Joint practice guidelines from 2011:

Genetic testing is most useful when there is an autosomal dominant family history of dementia with one or more cases of early onset.



19



Considerations for genetic testing

What benefit do you expect from testing?

How would the result impact your...?

- Treatment
- Life plans
- Family members
- Employment

Who can support you during this process?

Who have you told? Who will you tell?

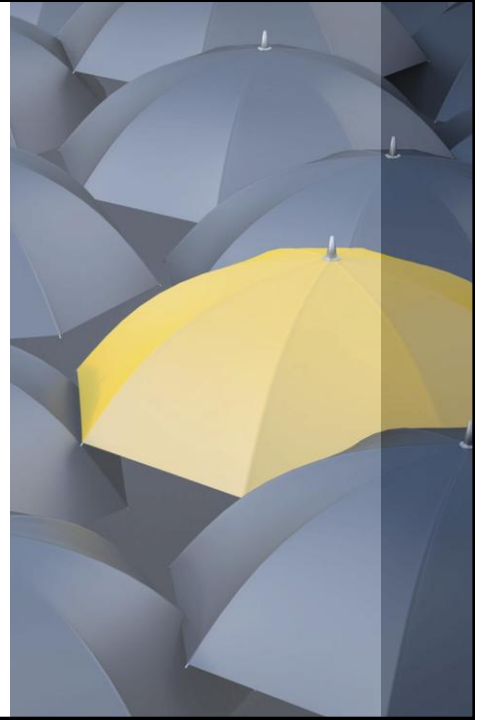
20

Concerns about insurance discrimination

Discrimination risk does not apply to symptomatic individuals.


For pre-symptomatic individuals there is established **legal protection for employment and health insurance.**

There is limited legal protection for long-term care, disability and life insurance policies.

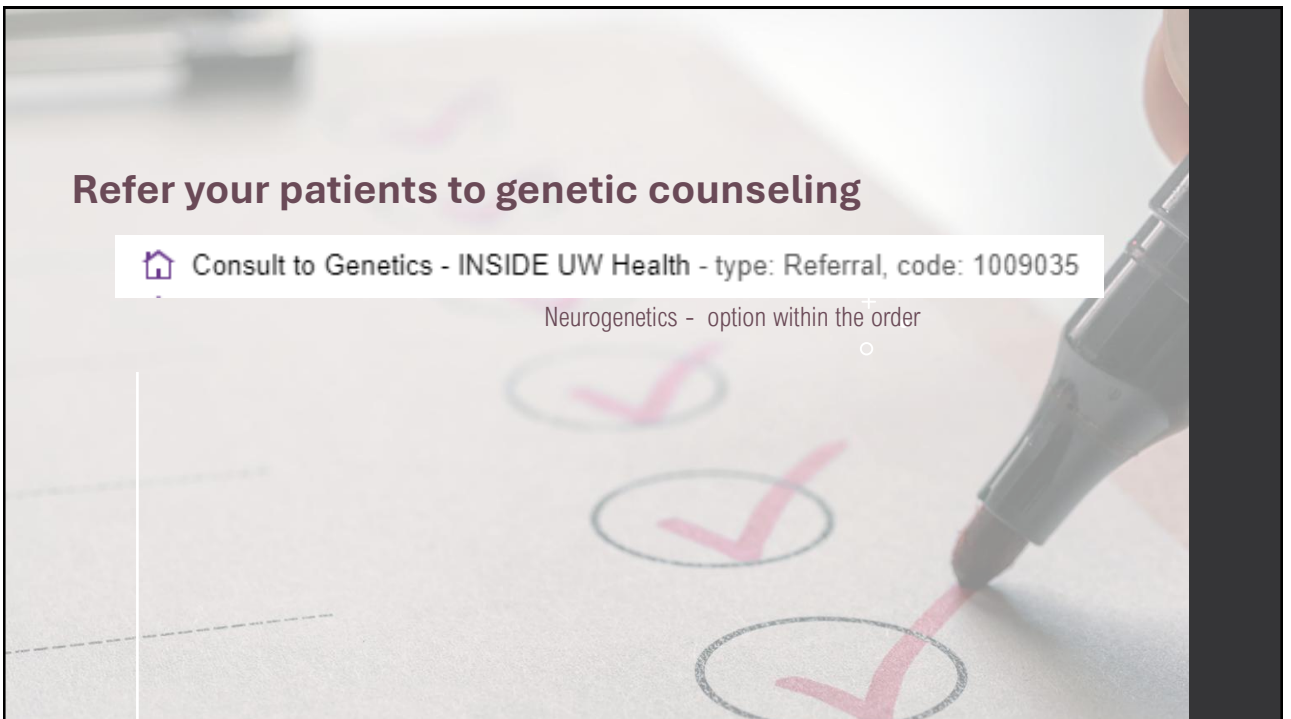


21

Refer your patients to genetic counseling

 Consult to Genetics - INSIDE UW Health - type: Referral, code: 1009035

Neurogenetics - option within the order



22

REFERENCES

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