

# Research in AATD

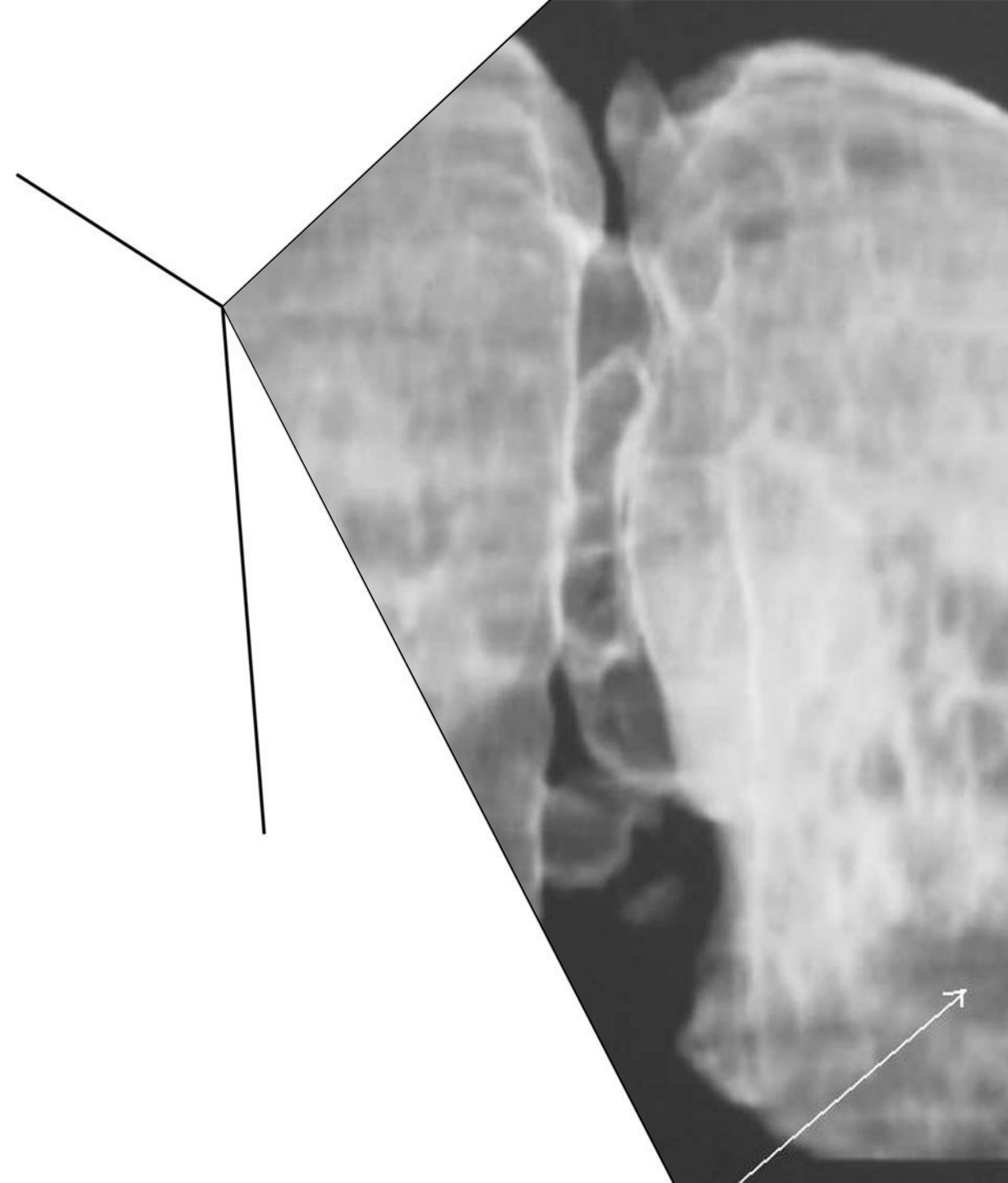
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X @AlphaCOPDdoc



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# What we will cover today

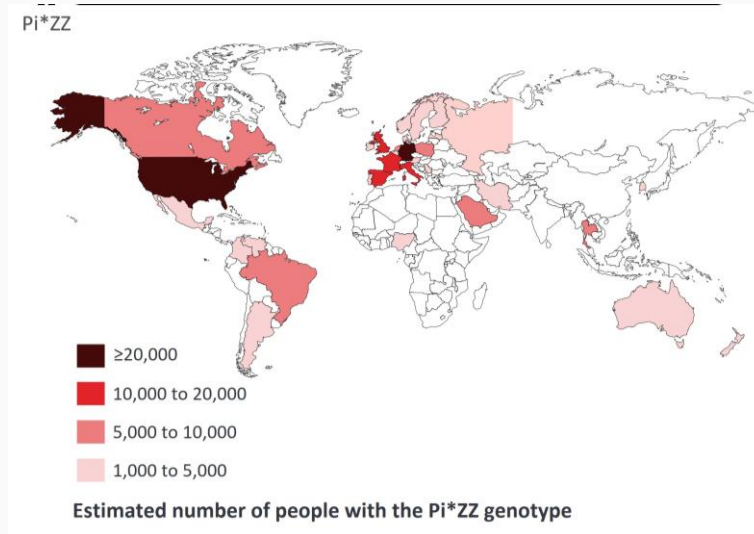
- Types of research
- Examples of research in AATD
- How each kind of research can benefit patients
- Ways to get involved



# Types of research



**Basic**



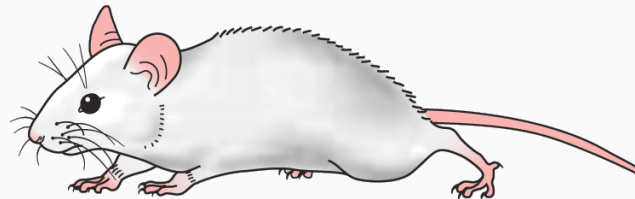
**Epidemiology & databases**



**Qualitative**



**Clinical trials**



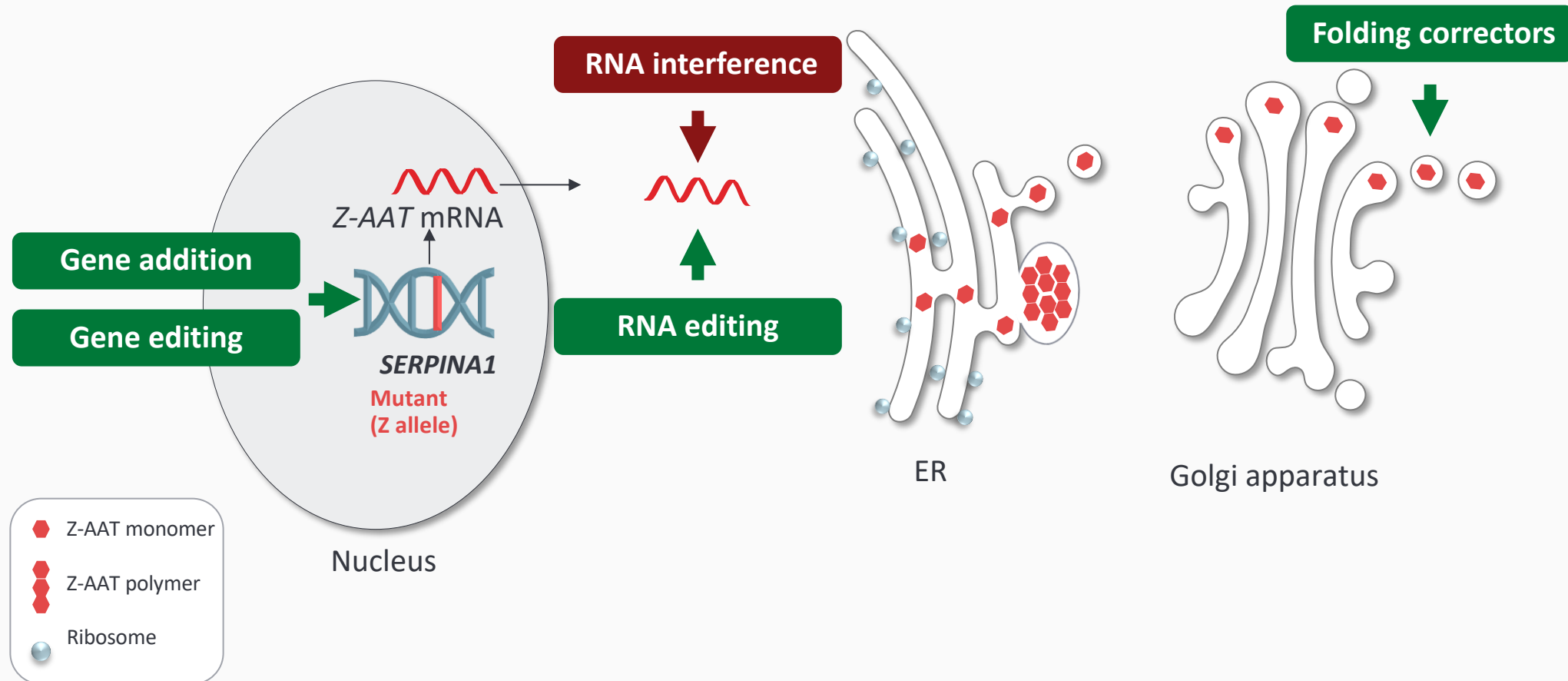
**Animal**



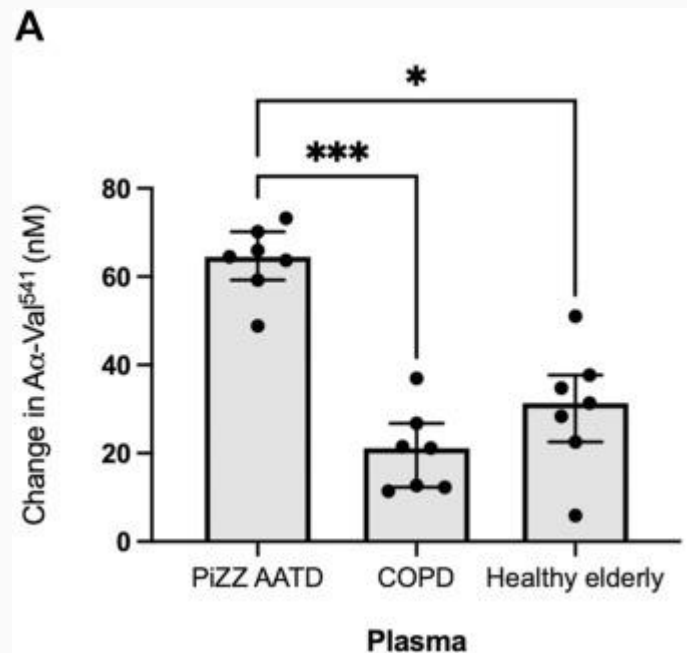
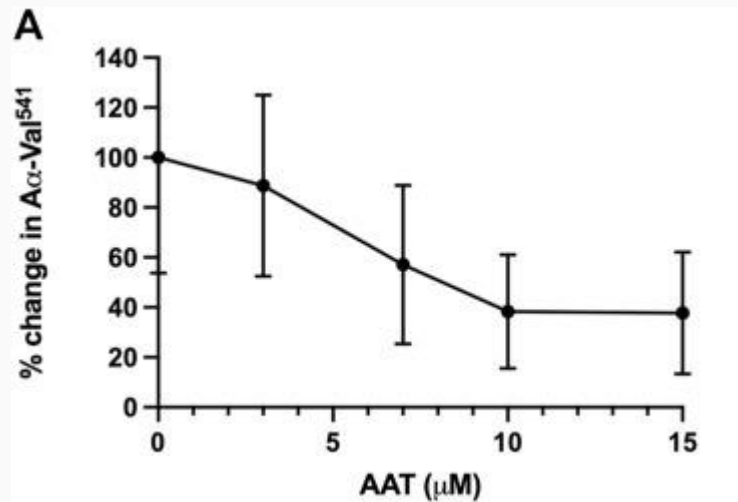
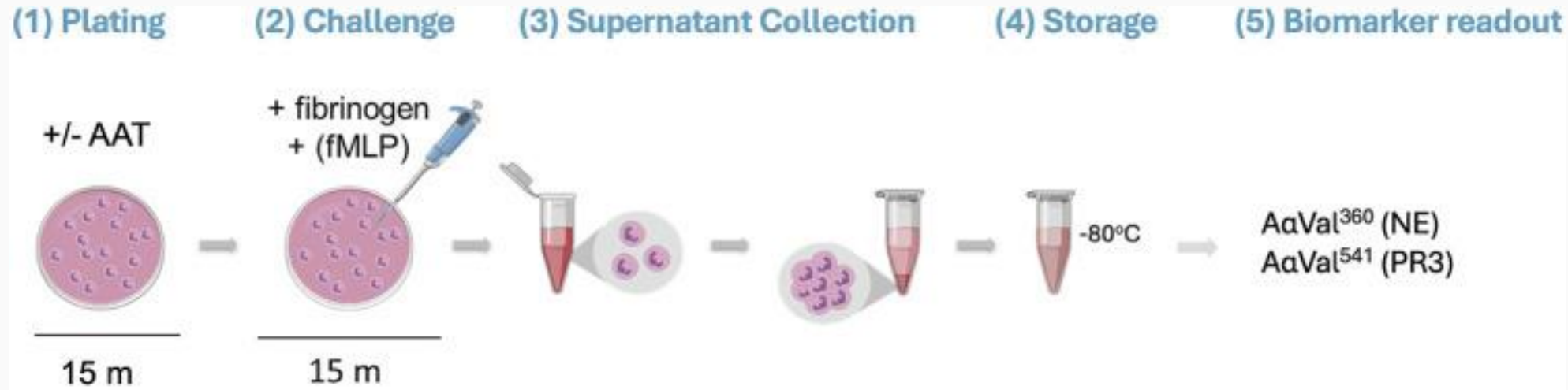
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# Basic research

- Aims to understand the pathways that lead to disease
- Could be theoretical or may use cells from people



# Making a cellular model of AAT lung



Results showed that using cells from healthy people along with different concentrations of AAT produced similar patterns of protease imbalance to experiments with AATD patient blood

# Epidemiology & databases

- Help us to understand patterns and develop services
- May use data given by patients to research databases but can also use routine care records
- Level of detail and accuracy vary according to the type of data being examined

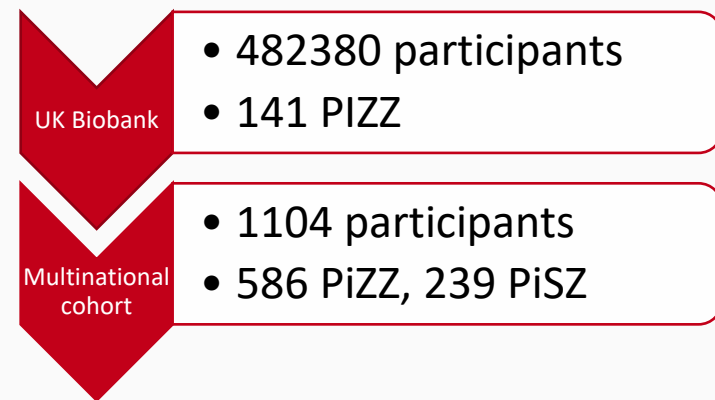


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# Epidemiology: fibrosis & cirrhosis in AATD

- F2+ fibrosis in ~ 30% PiZZ adults
- Up to 63% in PiZZ seen by hepatology
- Assoc with
  - Male sex
  - Age >50
  - Obesity
  - Diabetes
- Biopsy & VCTE agreement
  - AUROC 0.7

Genotype	Phenotype	OR
ZZ	Fibrosis	21.7 (8.8-53.7)
	HCC	44.5 (10.8-183.6)
SZ	Fibrosis	3.1 (1.1-8.2)
	HCC	6.6 (1.6-26.9)
MZ	Fibrosis	1.7 (1.2-2.2)
SS	Fibrosis	Not increased



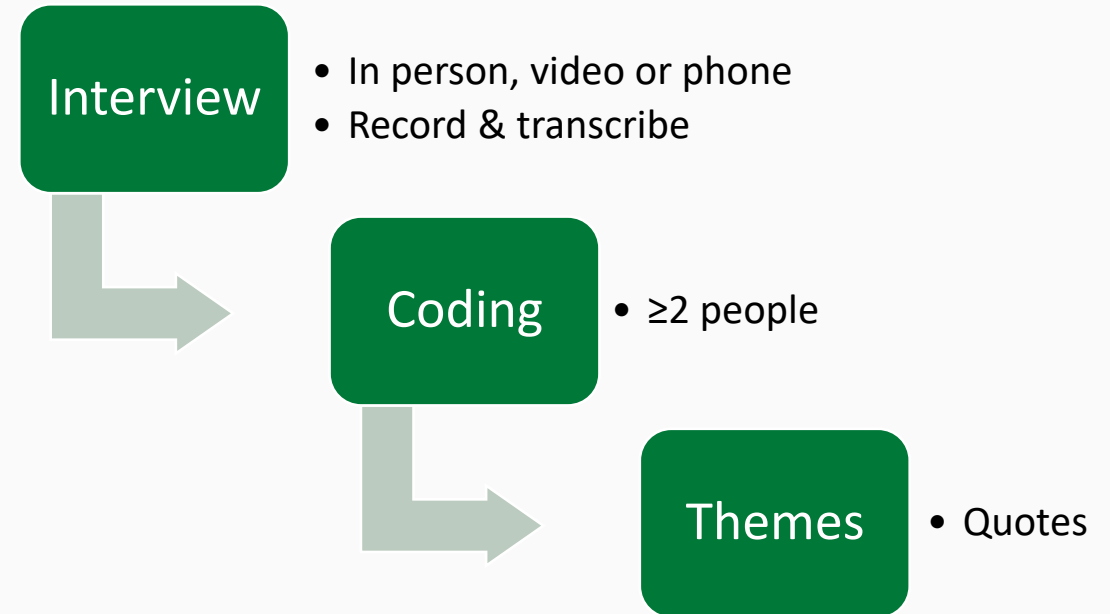
Assocs adjusted for age, sex, BMI, DM & alcohol



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# Qualitative research

- Analyses conversations where people tell of their experiences or opinions
- Allows deeper understanding than surveys but is only feasible with small numbers of people
- Surveys or bigger projects may follow afterwards
- Results are understood using themes and quotes



# Examples of qualitative research in AATD

## Understanding the impact on brothers and sisters

- Very different for illness in childhood compared to adults
- Recommendations for family testing & counselling

*I can remember her just riding her tricycle in a meadow. Then it would phase into her being in a hospital, and the hospital would get on fire, and flames would be all over the place. I remember trying to go get her, trying to go find her, and they wouldn't let me go*








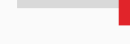


## Understanding the impact on new relationships/dating

- Adds pressure about having children or about illness symptoms
- Recommendations for topics in genetic counselling & for public health to reduce stigma

*I wait until I see whether it's somebody that I might be interested in on a longer term basis. I didn't bother telling anybody, until I met someone I wanted to date steadily and pursue the relationship. At that point, I would explain and say, "If this is a problem, then you should say so and move on." I never had anybody back out because of it. Most women—maybe the kind that I picked—would be understanding. (A4/Sx, +)*








# Trials that might help the lung

Class	Agent or trial name	Phase	Primary outcome
 DNA editing	BEAM-302	Ph1,2 	Safety
 Gene addition	Intellia	Ph1 	Safety
 RNA editing	WVE-006	Ph1 	Safety
 Inhaled AAT	InnovAATe	Ph3 	FEV1
 Synthetic augmentation	ElevAATe	Ph 2,3 	AAT level



# Trials that might help the liver

Class	Agent or trial name	Phase	Primary outcome
 RNA interference	Fazirsiran, REDWOOD	Ph3	Liver biopsy
 DNA editing	BEAM-302	Ph1,2	Safety
 Gene addition	Intellia	Ph1	Safety
 RNA editing	WVE-006, RestorAATion	Ph1	Safety
 Folding correctors	VX-634, VX-668 VX-814, VX-864	Ph1,2	Liver biopsy



# Getting involved

- Researchers must adhere to Good Clinical Practice, which protects patients participating in any research study
- Basic science often uses blood or sputum samples
- Database research may mean additional questions compared to normal medical care, and may mean repeated visits
- Qualitative research involves detailed interviews, but often only occurs once



# Questions?



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