Multiplicity and Bayes

Multiplicity

What is the probability that my finding is real or chance (i.e. spurious)?

Bayes

Quantifying the probability of a hypothesis

Bringing data to life.

Multiplicity and Bayes

Solanezumab – EXPEDITION STUDIES

The following is a Steve Ruberg analysis (post hoc).

It explicitly does not use information from Lilly.

It is meant solely to be illustrative and does not represent what analyses were done by Lilly, which were much more sophisticated than presented here, or how decisions were made by Lilly.

Bringing data to life.

Multiplicity and Bayes

Suppose our prior probability that Solanezumab works is 0.30 (i.e. the null hypothesis is false).

There are 5 hypotheses of interest:

- The overall population (primary)
- Mild population
- Moderate population
- *APOE* ε4 carriers
- *APOE* ε4 non-carriers

Multiplicity and Bayes

Split the prior (0.30) across the five hypotheses of interest.

1. Give most of the probability (0.14) to the Overall population.
2. Divvy the remaining probability to the other subpopulations
   a) Equally – i.e. 0.16/4 = 0.04
   b) Weighted – i.e. give larger prior (0.06) to Mild and *APOE* ε4 carriers

Multiplicity and Bayes

Hypothesis	Prior (version A)	Prior (version B)
Overall	0.14	0.14
Mild	0.04	0.06
Moderate	0.04	0.02
APOE ε4 (+)	0.04	0.06
APOE ε4 (-)	0.04	0.02
Total	**0.30**	**0.30**

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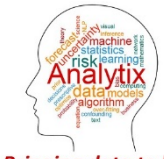
Multiplicity and Bayes

Hypothesis	Prior (version A)	Prior (version B)
Overall	0.14	0.14
Mild	0.04	0.06
Moderate	0.04	0.02
APOE ε4 (+)	0.04	0.06
APOE ε4 (-)	0.04	0.02
Total	**0.30**	**0.30**



Multiplicity and Bayes

EXPEDITION 1
(Mild and Moderate AD Patients)

ADAS-Cog11
- Overall: p=0.24
- Mild: p=0.008

ADAS-Cog14
- Mild: p=0.003

Is the finding in Mild patients real or spurious?

Doody, Rachelle S. et al. “Phase 3 Trials of Solanezumab for Mild-to-Moderate Alzheimer's Disease.” N Engl J Med 2014; 370:311-321. (with Supplementary Appendix)

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Multiplicity and Bayes

EXPEDITION 1
(Mild and Moderate AD Patients)

ADAS-Cog11
- Overall: p=0.24
- Mild: p=0.008

ADAS-Cog14
- Mild: p=0.003

MILD PATIENTS

ADAS-Cog11		
Initial Prior	P-value	Posterior *
0.04	0.008	0.28
0.06	0.008	0.38

* **Using Bayes Factor:** $O_0 \times [-e \times p \times \ln(p)] \leq O_1$

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Multiplicity and Bayes

EXPEDITION 1
(Mild and Moderate AD Patients)

ADAS-Cog11
- Overall: p=0.24
- Mild: p=0.008

ADAS-Cog14
- Mild: p=0.003

MILD PATIENTS

ADAS-Cog11					
Initial Prior	P-value	Posterior *	Revised Prior	P-value	Posterior *
0.04	0.008	0.28	0.02	0.008	0.16
0.06	0.008	0.38	0.03	0.008	0.23
ADAS-Cog14					
			0.02	0.003	0.30
			0.03	0.003	0.39

Bringing data to life.