Pre-clinical studies

• Poor correspondence of animal models to human disease.

Phase I studies

• Focus on safety; efficacy signal is relatively unattended.

• Wrong dose or route of drug.

• Wrong stage of disease targeted.

Phase II studies

Phase III studies

• Increased heterogeneity of sample compared to Phase II.

• More raters with less experience.

• MMSE used for inclusion/exclusion.

• Flawed outcome measures.

• Short study durations.

• High placebo response rates.