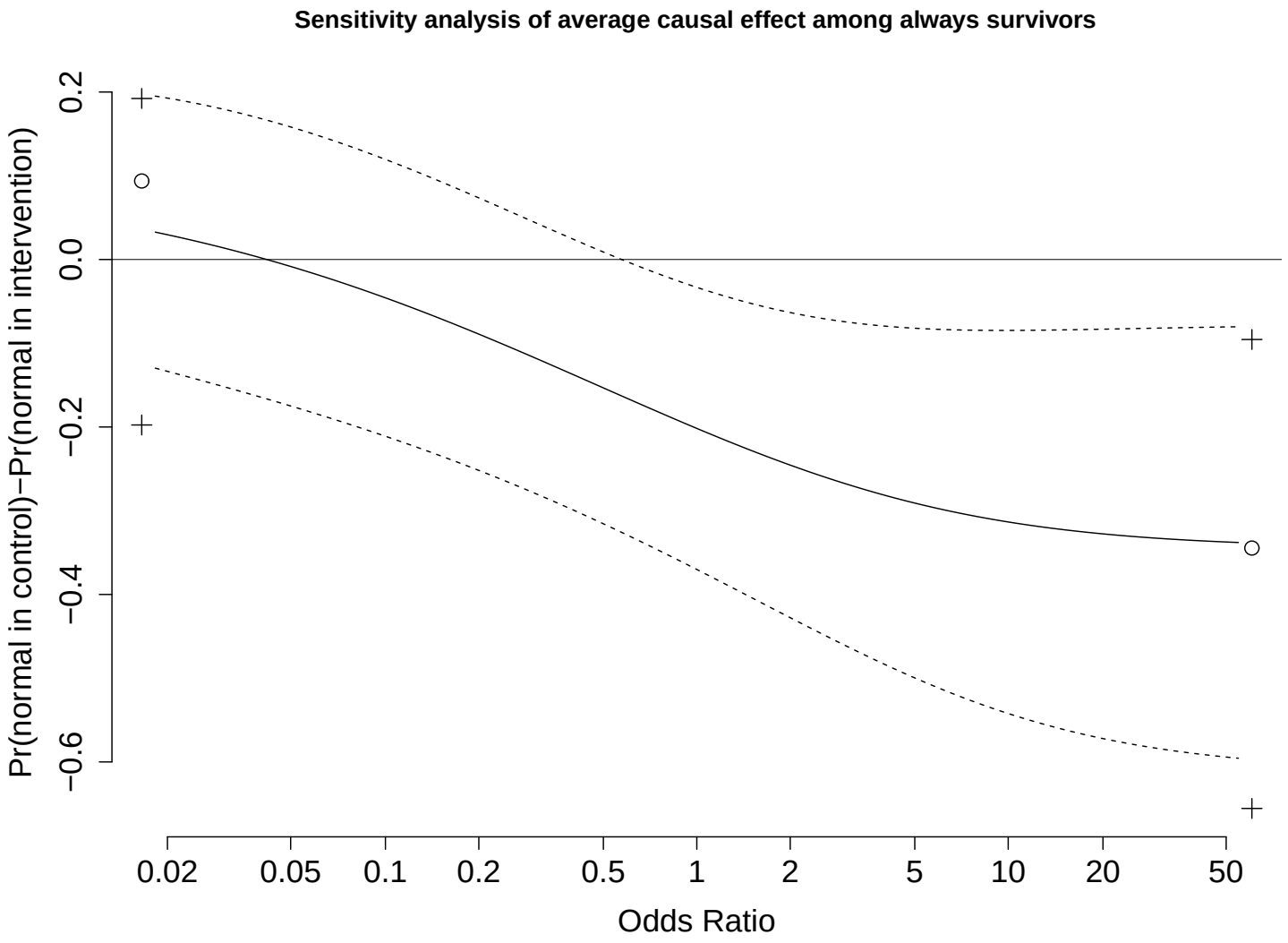
Example 2. Clinical Trial of spontaneous breathing treatment in ICU

- 336 mechanically ventilated patients in intensive care
- 168 randomized to intervention (spontaneous awakening through interruption of sedatives)
- 168 randomized to standard of care
- intervention protected against death during the year after enrollment
    - hazard ratio = 0.68, 95% CI 0.50 to 0.92, p=0.01

Girard TD, et al. (2008). *Lancet* 371: 126-34.

A follow-up study submitted to *American Journal of Respiratory and Critical Care Medicine*

- Goal to assess effect of intervention on cognitive function.
- Original submission used combined endpoint of death and abnormal cognitive function.
- Editor and a referee critical of this endpoint:
  - "The use of an endpoint combining death and abnormal cognitive function is not appropriate. Your group has already nicely demonstrated the effect of the intervention on long-term survival. The combined endpoint will need to be dropped as the correct (and novel) analysis throughout is the effect of the intervention on cognitive outcomes among evaluable survivors. This analysis may lead to differential censoring, ie, a bias toward worse late outcomes in the intervention arm because some ill patients are saved by the intervention – you should acknowledge this limitation."


Sensitivity analysis of average causal effect among always survivors
Pr(normal in control)−Pr(normal in intervention)
0.2
0.0
−0.2
−0.4
−0.6
0.02
0.05
0.1
0.2
0.5
1
2
5
10
20
50
Odds Ratio