- **Lack of control over data quality.**

- Lack of control over what is being collected; lack of data on practice patterns; lack of data on initial conditions; lack of data on all outcomes of interest for guideline evaluation.

- Difficulty with the measure of correlated data.

- Limited availability of statistical methods to deal with ecological exposures in individual level studies.

- Limited number of diagnoses amenable to be studied through this method.

- Outcomes research works when natural experiments can be observed. Only for a few conditions, the argument is as follows: treatments are so varied, and the doctor’s choice so unpredictable, that database records approximate those obtained from arbitrary assignment in clinical trials.