# Primer: Problems with Case Series

## Definition
A group of patients receives an intervention and outcomes are assessed. There is no appropriate comparison group. (Historical controls are sometimes used, but this is not an appropriate comparison group.)

## Key Points
Case series is not evidence – unless you have “all-or-none results” which is rare — and there is still potential for bias. Case series can be useful for hypothesis generation.

## Key Problem: There is no appropriate comparison group.
Patients frequently improve after a medical visit, but outcomes might otherwise be the same whether a treatment is administered or not (see Observational Bias below). Comparisons reveal associations by exposing differences. Lack of a comparison group can make it appear as if there is an association between an intervention and an outcome when, in fact, there is not.

## Conclusions
Case series can be useful in describing a clinical condition or to generate ideas for study. However, because of the above mentioned biases, case series can almost never be relied upon to draw conclusions between interventions and outcomes. Rarely, conditions where morbidity or mortality is nearly 100 percent and, with the intervention, is decreased dramatically, case series may be sufficient to draw conclusions about the effect of the intervention on outcomes – but it has to be emphasized that this is extremely rare.

## Discussion
Bias will always be present in case series.

- **Selection bias will always be present in case series.**
  There are usually no criteria for patient selection. • Frequently cases are not consecutively selected. • Clinicians usually report on those patients with the best outcomes.

- **Observation bias will always be present in case series.**
  When there is no blinding, clinician beliefs in, or hopes for, an intervention can affect outcomes – resulting in performance bias. • Assessment bias often occurs because lack of consecutively selected patients can result in selective reporting favoring the intervention.

- **Key Point — Patients frequently improve after a medical visit, but outcomes might otherwise be the same whether a treatment is administered or not (see above). Therefore, without a comparison group, almost any intervention will appear to be beneficial and attributed to medical care when, in fact, improvement may be due to –**
  a) The self-limited nature of the condition,
  b) Placebo effect,
  c) Regression-to-the-mean – meaning that extreme test values are statistically likely to move to an average over time. When patients present with extreme values and then seem to have improvement, it may be falsely attributed to an intervention. A comparison group with no intervention can help expose this effect. OR
  d) Coincidence (chance).

- **There are reporting problems resulting from case series.**
  o Due to publication bias, negative results are almost never reported (the reporting of which would still present its own problems since a negative-finding case series would be highly prone to bias for the above reasons). Authors of case series frequently compare their results to those of other case series. There is always the possibility that the authors will select case series for comparison that show their results in the best light.