**Figure 1.** This figure shows the RCT and analyses of medical claims as two extreme ends of the spectrum of study designs, with a low versus a high level of control. In between these two extremes, there are a number of alternative designs, and some of these have been included as examples here.

- **Left end of the spectrum**
  - Large number of patients
  - Long term follow-up
  - Representative of the general population
  - Cheap
  - Low attrition

- **Right end of the spectrum**
  - Controlled conditions reducing the impact of confounders
  - Randomization isolating a causal link

<table>
<thead>
<tr>
<th>Analyses of medical claims data</th>
<th>Prospective longitudinal cohort study</th>
<th>Registry based RCT</th>
<th>Pragmatic RCT</th>
<th>RCT</th>
</tr>
</thead>
</table>

**Increasingly controlled conditions**

- **Left end of the spectrum**
  - Potential confounding based on un-measured factors
  - No randomization (causality cannot be guaranteed)
  - No disease-specific outcomes (such as UPDRS scale)
  - Data quality not known, including measurement error

- **Right end of the spectrum**
  - Inclusion bias (not representative for general population)
  - Small number of patients
  - Limited follow-up
  - Costly and time consuming
  - Relatively high attrition

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*Measurement error refers to the fact that in medical claims, conditions are defined imprecisely and inaccurately, that measurement may vary in a biased way, and that little is known about how robust the measures are.*

*Attrition rate is a problem for any study design. RCTs actually perform reasonably well by comparison to other clinical studies.*