The article reviewed is an article review about the differential outcome procedure from basic literature to humans research, trying to go further in the study of translational research.

The review article is well-written, and the main goal is to provide an excellent theoretical base of the DOP and summarise valuable previous studies carried out in both animals and human research.

These are some comments and suggestions:

- I have some doubts about the order of the subtitle, The differential outcomes procedure: Principal and mechanism (page 3), specifically when first demonstrations in animals and humans are explained, in the human studies there are some overlap with the later studies detailed in the subtitle, From animal to human studies, I suggest to integrated both subtitles in one, after the underlying mechanism subsection. When human studies were described, it will be interesting to further develop the main results of the systematic review carried out by McCornamck et al. (2019) of the effects of the DOP in humans, study briefly mentioned on page 18.

- Moreover, I have some suggestions about subsection (“Applications of the differential outcomes procedure to adherences to medical treatment, page 16). In my point of view, paragraph developed in pages 16 and 17 until page 18, it may help to the reader to sum up the epidemiological information about different chronic clinical conditions and the economic impact of them in our society.