

Systematic Review of Probabilistic Sensitivity Analysis Methods in Microsimulation Models of Chronic Diseases

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Background and objectives

- Monte-Carlo microsimulation models (MSMs) are generally defined as those modeling individual patients one at a time, without interaction between patients.¹
- MSM models have been increasingly applied to address health policy decisions in the post-approval space.
- Methodologies in MSMs include general Markov-based microsimulation, discrete-event simulation (DES), and more recent agent-based models.^{2,3}
- Probabilistic sensitivity analysis (PSA) is defined as conducting a separate analysis from the expected value model and allowing for a range of input parameters to run the model in an iterative manner to capture the uncertainty in input parameters within the model outcome.²
- While PSA is described and used as a requirement for cohort-based models in health economics, there is ambiguity on the requirement and approaches for PSA in MSMs for health policy decision-making. Specifically, the computational time required for conducting PSA often prevents analysts from conducting PSA in MSMs.²
- **The objectives were to systematically identify studies that conducted MSMs in chronic diseases and review PSA methods from 2010 to 2021.**

Methods: Screening strategy

- **Assessment criteria:** Assessment criteria included: policy questions, types of MSM and software used, modeling of patient characteristics/patient history, PSA methodology, justification for number of runs and sample sizes for PSA and convergence analysis, limitation noted for PSA and approximation methods used based on previously published comparisons and validations of MSM models, and PSA approaches in chronic diseases.² The assessment criteria were adapted according to a consensus session with experts from the disciplines of health economics and biostatistics with a focus on health policy assessment.
- **Inclusion and exclusion criteria:** All studies published in English between January 1, 2010 to March 1, 2021 were considered for inclusion. Studies limited to infectious diseases (influenza models, human immunodeficiency virus [HIV], coronavirus disease [COVID], and sexually transmitted diseases [STDs]) and fiscal policies and taxation policies (non-health interventions) were excluded. The PICOS criteria is provided in Table 1.
- **Data extraction:** Microsoft Office Excel (Microsoft Corp, Redmond, WA) was used. Data were extracted independently by two reviewers (L.R and R.M.). Each reviewer verified the other reviewer’s data entries. These data entries were also verified by a third reviewer (S.B.). Recorded study characteristics, PSA methods, baseline patient and operative characteristics, and outcomes were extracted.

Abbreviations: COVID, coronavirus disease; DES, discrete-event simulation; HIV, human immunodeficiency virus; MSM, microsimulation model; PICOS, population, interventions, comparators, outcomes, and study design; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; PSA, probabilistic sensitivity analysis; STD, sexually transmitted disease

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Table 1. PICOS statement

Criteria	Included
Population	Chronic disease Non-communicable chronic disease Non-infectious disease
Interventions	Any health intervention Any health policy
Comparators	No restrictions
Outcomes	No restrictions
Study design	"microsimulation" or "patient-level" or " individual-level" "discrete-event" "agent-based"

Results

- The systematic literature search identified 62 publications, of which 31 were microsimulation/patient-level models, 28 were DES, and 3 were agent-based models (**Figure 1**).
- Out of these 62 publications, a total of 13 publications were included in the final extraction of studies with PSA in MSM (**Figure 2**).
- Results suggest a trend of an increasing number of MSMs conducted in chronic disease areas, from five identified studies between 2010-2012 to 23 between 2019-2021 (**Figure 3**). Among the models identified, there has been an increasing number of studies conducting PSA, from zero between 2010-2012 to six between 2019-2021.
- The majority (n=13) of studies in which PSA was conducted were microsimulations (patient-level Markov model or cohort-based; n=8) and the rest were DES (n=5).
- Nine of these 13 studies conducted first-order Monte Carlo without any inner loops, while the remaining four studies conducted second-order Monte Carlo analysis (inner loops).

Figure 1. PRISMA flowchart

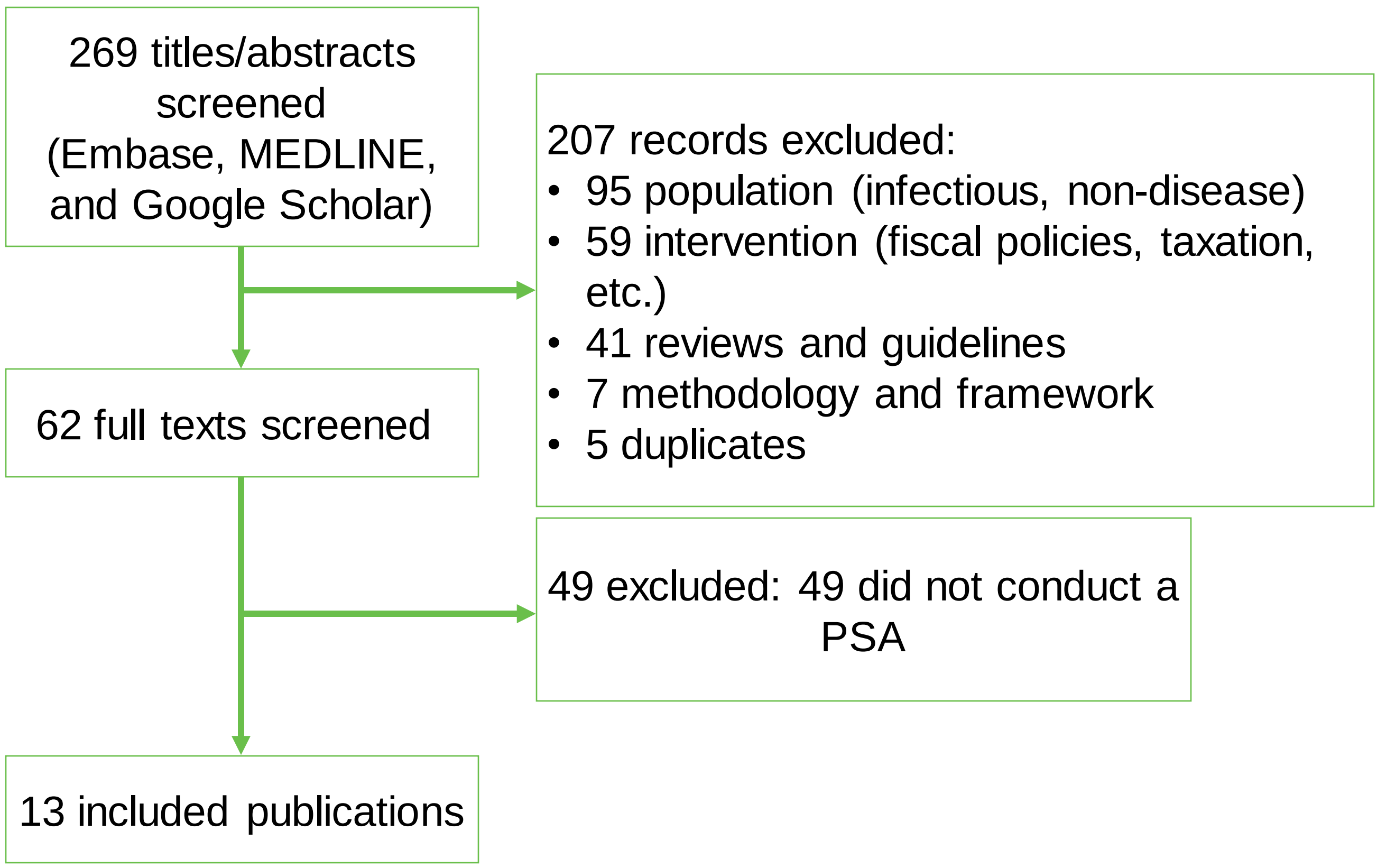


Figure 2. Proportion of studies conducting PSA

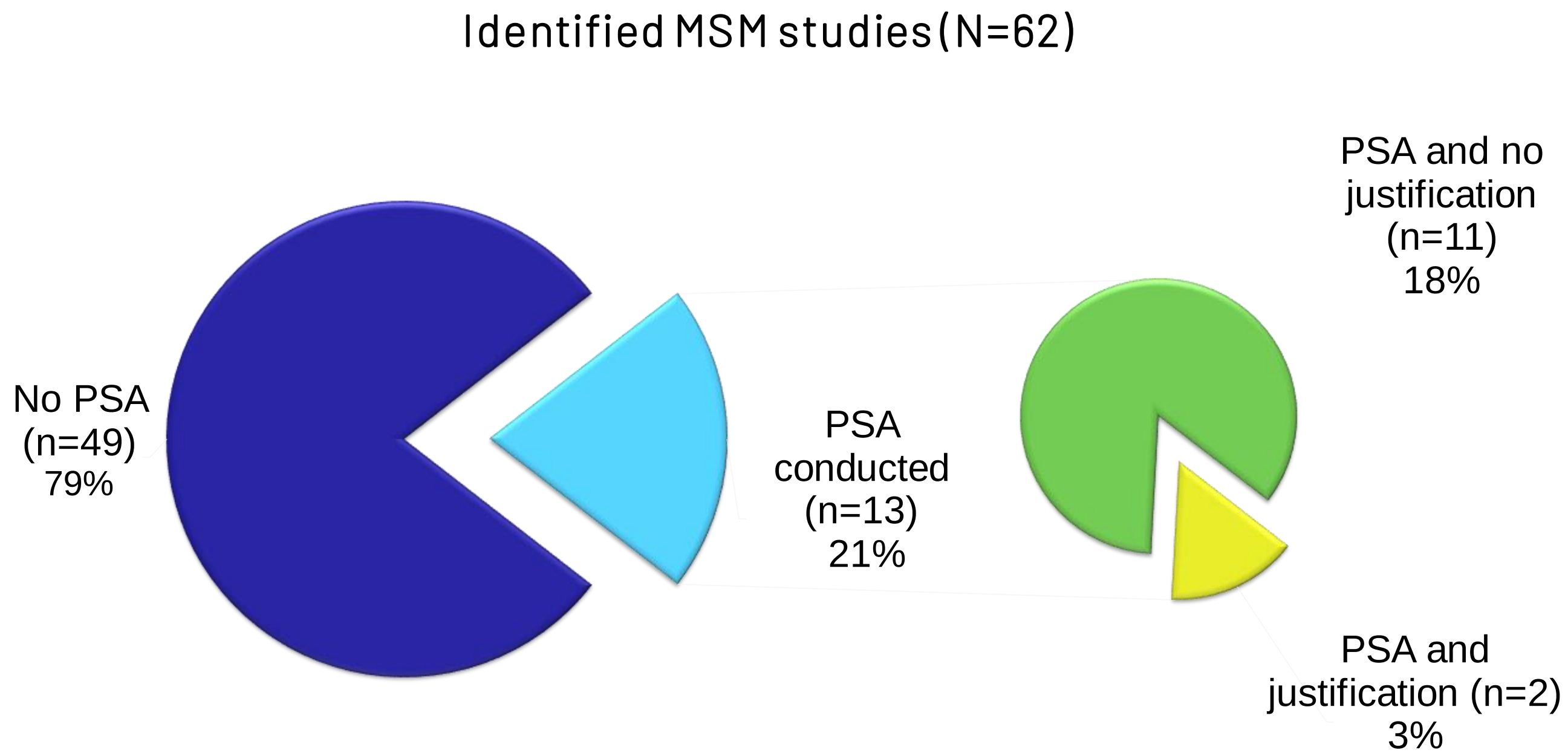
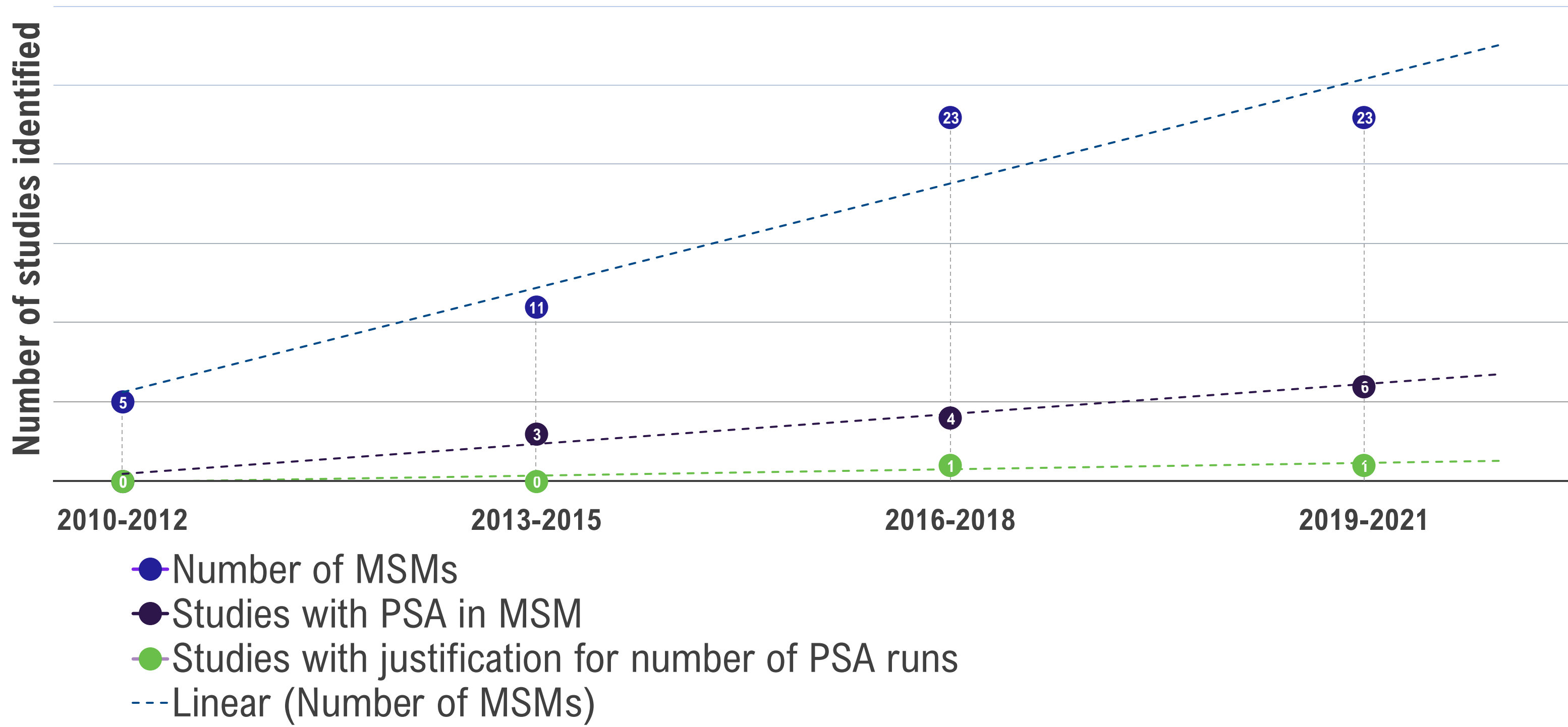


Figure 3. Number of studies by study type



Conclusion

- There has been an increasing number of studies using MSMs in healthcare policy evaluation in chronic diseases, from 5 studies in 2010-2012 to 23 in 2019-2021.
- Among the identified MSMs, few conducted PSA (13 out of 62 studies), and very few justified the PSA approach used (2 out of 13 studies).
- There is a need for a uniform framework on sample size estimation in conducting PSA in MSMs.

References

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