Determinants of Opioid Use Disorder Relapse from the Biopsychosocial Perspective: A Systematic Review

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Developing a Risk Prediction Engine for Relapse in Opioid Use Disorder

Background and Objectives

Opioid use disorder (OUD) is a chronic condition and relapses are common. OUD poses significant challenges to public health systems worldwide [1]. Despite advances in treatment modalities, relapse remains a pervasive issue, undermining long-term recovery efforts.

Relapse in OUD is influenced by an interplay of various factors and is broadly understood as a biopsychosocial disorder [2]. The determinants of OUD relapse can be categorized into biological, psychological, social, and spiritual domains. **This systematic review aims to comprehensively examine the current literature on the determinants of opioid relapse across the biopsychosocial-spiritual domains.**

Objectives

(1) Identify statistically significant determinants and protective elements that influence relapse in OUD
(2) Utilize findings to inform the development of digital health technologies for supporting relapse prevention efforts.

Methods: Study Design

This systematic review, adhering to PRISMA guidelines, explored determinants of opioid relapse through a search of PubMed, PsycINFO, and Web of Science (2003–2023), using refined search terms related to "opioid use disorder" and "relapse" (Figure 1).

Inclusion Criteria: Studies published in English identifying specific relapse factors in adult populations.

Exclusion Criteria: Dissertations, books, systematic reviews, qualitative studies, and treatment-centric papers unless they examined independent relapse risk factors.

Relapse was defined as positive toxicological tests or patient-reported use among individuals willingly attempting recovery.

PRISMA Flow Diagram

- Database Search (n=2515) → Duplicates Removed (n=813)
- Title and Abstract Screening (n=1702) → Studies Excluded (n=1404)
- Full Text Review (n=298) → Studies Excluded (n=226), Studies Not Retrieved (n=6)
- Data Extraction (n=66)

Figure 1. The abbreviated PRISMA diagram shows the systematic review process. During the retrieval of full-text papers for full text review, 6 papers could not be found or accessed and were removed from the study.

Results

Data extraction captured study methods, relapse definitions, and statistical analyses, while quality assessment considered transparency, sample size, and bias.

A total of **682 determinants** were analyzed using hypothesis testing and regression methods, with **results grouped under high-level categories to identify significant patterns** and prioritize determinants studied in six or more papers (Table 1).

Determinants of OUD Relapse Outcomes

High-Level Determinant Category	Total # of Participants across Studies Where The Determinant was Statistically Significant	Total # of Participants across Studies Where The Determinant was Not Statistically Significant	Total # of Studies Assessed in Systematic Review	Percentage of Reviewed Studies that were Determined to be Significant by the Investigator
Biological				
Age	4218	5727	34	41%
Brain	240	58	7	86%
Gender (Male)	29	7383	24	4%
Overall Health	1508	953	7	71%
Psychiatric Comorbidities (Diagnosis)	3036	1223	10	50%
Race & Ethnicity	941	2095	10	20%
Psychological				
Anxiety (Symptoms)	31	341	7	14%
Craving	1517	597	16	81%
Depression (Symptoms)	1654	438	11	36%
Pain	793	1031	10	40%
Self-Efficacy	1293	323	7	71%
Social				
Adverse Life Events	1226	1818	7	29%
Education	100	3003	19	5%
Employment Status	589	4070	10	20%
History of Incarceration	3162	172	7	71%
Marital Status	772	2686	10	20%
Social Support	2219	0	7	100%
Spiritual				

Table 1. The determinants table shows the findings for all determinants where at least 6 studies independently assessed the statistical significance of the determinant on opioid relapse outcomes. No Spiritual determinants were examined by 6 or more studies.

Conclusion

This systematic review highlights key determinants of opioid relapse, emphasizing the multifaceted nature of opioid use disorder and the importance of considering biological, psychological, and social factors in relapse prevention. By synthesizing findings from 66 studies, it underscores the value of robust statistical analysis in identifying significant relapse predictors, which can inform targeted interventions and policy decisions. Future research should address gaps in the literature, including underrepresented populations and the integration of digital biomarkers, to enhance the precision and scalability of relapse prevention strategies.

Secondary Findings

Participants were assessed for relapse (patient-reported and/or urine testing) at varying frequencies.
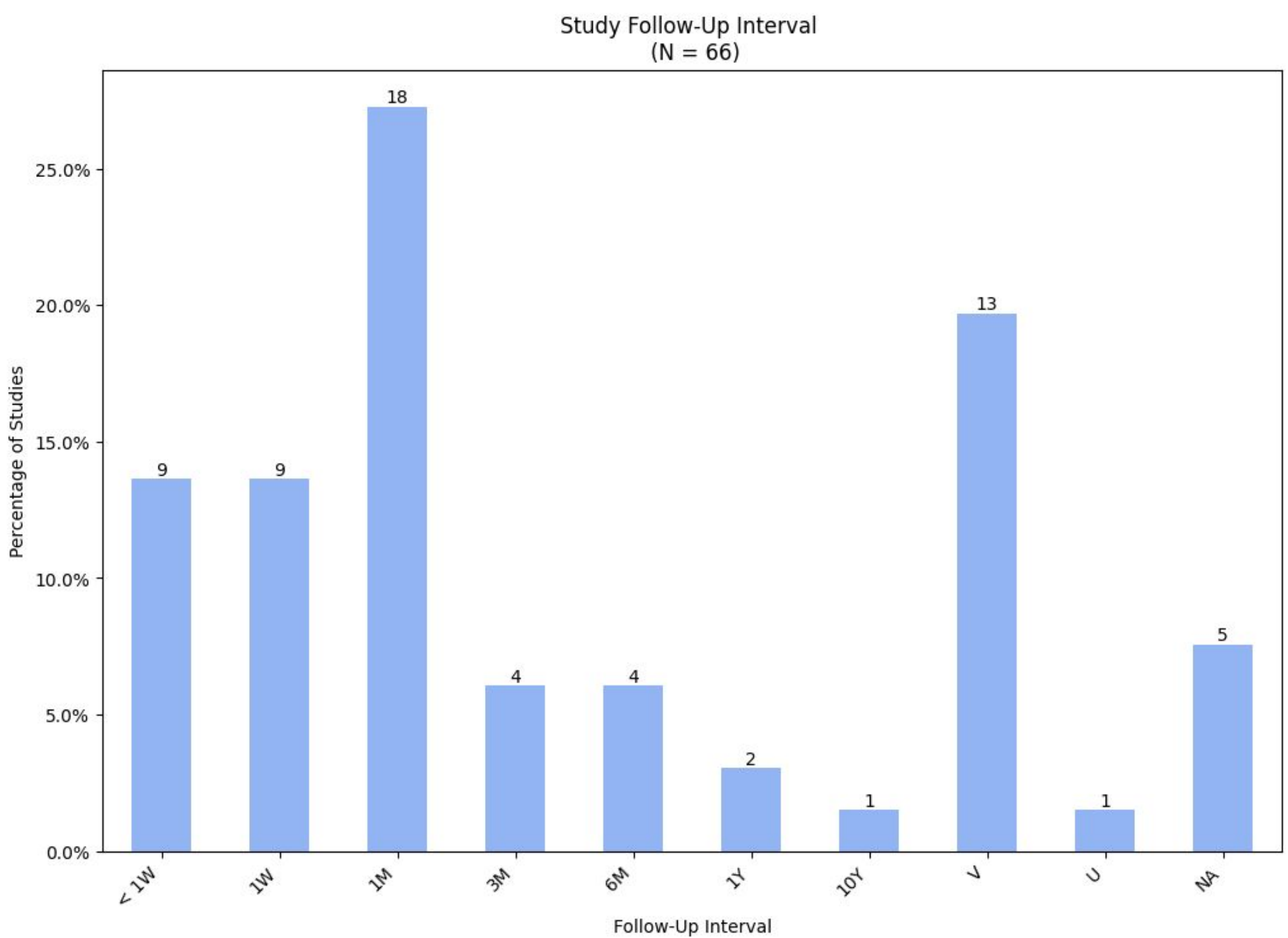

Figure 2. Study Follow-Up Interval per publication. Follow-up assessment frequencies in studies on OUD relapse. The figure displays how often relapse was assessed, ranging from hourly to 10-year follow-up, across the included studies. This includes studies that evaluated relapse using both urinalysis and patient-reported outcomes.

The majority of identified studies followed patients to assess opioid outcomes for less than 1 year.
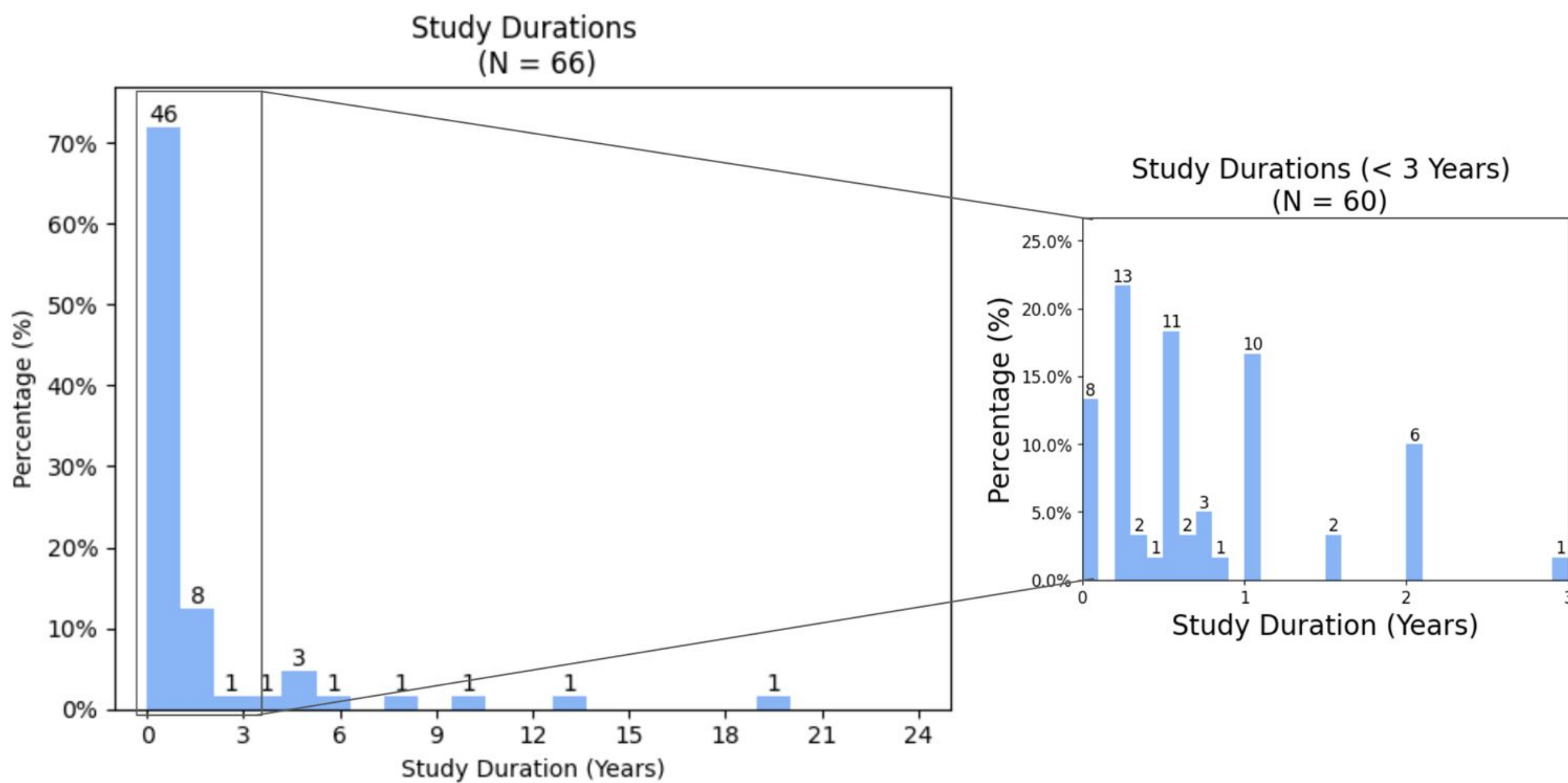

Figure 3. Duration of study follow-up periods across the included studies on opioid use disorder (OUD) relapse determinants. The figure shows the range of time patients were followed, highlighting short-term versus long-term study designs. Two studies included in the review did not specify study duration.

References

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