Supplementary Table S1. Full reproducible search strategy across databases.

Database	Search Strategy
PubMed / MEDLINE	(("Peripherally Acting Mu-Opioid Receptor Antagonists"[Mesh] OR "PAMORA" OR "naldemedine" OR "methylnaltrexone" OR "alvimopan" OR "naloxegol" OR "bevenopran" OR "axelopran") AND ("Opioid-Induced Constipation"[Mesh] OR "OIC") AND ("Randomized Controlled Trial"[ptyp] OR "randomized" OR "placebo"))
Embase	('peripherally acting mu opioid receptor antagonist'/exp OR 'PAMORA':ti,ab OR 'naldemedine':ti,ab OR 'methylnaltrexone':ti,ab OR 'alvimopan':ti,ab OR 'naloxegol':ti,ab OR 'bevenopran':ti,ab OR 'axelopran':ti,ab) AND ('opioid induced constipation'/exp OR 'OIC':ti,ab) AND ('randomized controlled trial'/exp OR 'placebo'/exp)
Cochrane (CENTRAL)	("PAMORA" OR "naldemedine" OR "methylnaltrexone" OR "alvimopan" OR "naloxegol" OR "bevenopran" OR "axelopran") AND ("opioid-induced constipation" OR "OIC") in Title Abstract Keyword

Table S2. Assessment of Risk of Bias for Included Randomized Controlled Trials

Study	Drug	Population	Random Sequence Generation	Allocation Concealment	Blinding (Participants/Personnel)	Blinding (Outcome Assessment)	Incomplete Outcome Data	Selective Outcome Reporting	Other Bias	Overall Risk
Compose 1	Naldemedine	Non-cancer	Low	Low	Low	Low	Low	Low	High	Low
Compose 2	Naldemedine	Non-cancer	Low	Low	Low	Low	Low	Low	High	Low
Compose 3	Naldemedine	Non-cancer	Low	Low	Low	Low	Low	Low	High	Low
Compose 4	Naldemedine	Cancer	Low	Low	Low	Low	Low	Low	High	Low
Katakami 2017	Naldemedine	Cancer	Low	Low	Low	Low	Low	Low	Unclear	Low
Webster (2017)	Naldemedine	Non-cancer	Low	Low	Low	Low	Low	Low	Unclear	Low
Hamano	Naldemedine	Cancer	Low	Low	Low	Low	Low	Low	Low	Low
Bull	Methylnaltrexone	Cancer	Low	Unclear	Low	Low	Low	Low	High	Low
Michna	Methylnaltrexone	Non-cancer	Low	Low	Low	Low	Low	Low	High	Low
Portenoy	Methylnaltrexone	Cancer	Low	Unclear	Low	Low	Unclear	Low	Unclear	Unclear
Irving	Alvimopan	Non-cancer	Low	Low	Low	Low	Low	Low	High	Low
Jansen	Alvimopan	Non-cancer	Low	Low	Low	Low	Low	Low	High	Low

Study	Drug	Population	Random Sequence Generation	Allocation Concealment	Blinding (Participants/Personnel)	Blinding (Outcome Assessment)	Incomplete Outcome Data	Selective Outcome Reporting	Other Bias	Overall Risk
Paulson	Alvimopan	Non-cancer	Low	Low	Low	Low	Low	Low	Unclear	Low
Webster (2013)	Naloxegol	Non-cancer	Low	Low	Low	Low	Unclear	Low	High	Low
KODIAC-04	Naloxegol	Non-cancer	Low	Low	Low	Low	Low	Low	Low	Low
KODIAC-05	Naloxegol	Non-cancer	Low	Low	Low	Low	Low	Low	Low	Low
Singla	Bevenopran	Non-cancer	Low	Unclear	Low	Low	Unclear	Low	Low	Low
Vickery	Axelopran	Non-cancer	Low	Unclear	Low	Low	Low	Low	Unclear	Unclear
Ross	Axelopran	Non-cancer	Low	Unclear	Low	Low	Low	Low	Unclear	Unclear

Figure S1.

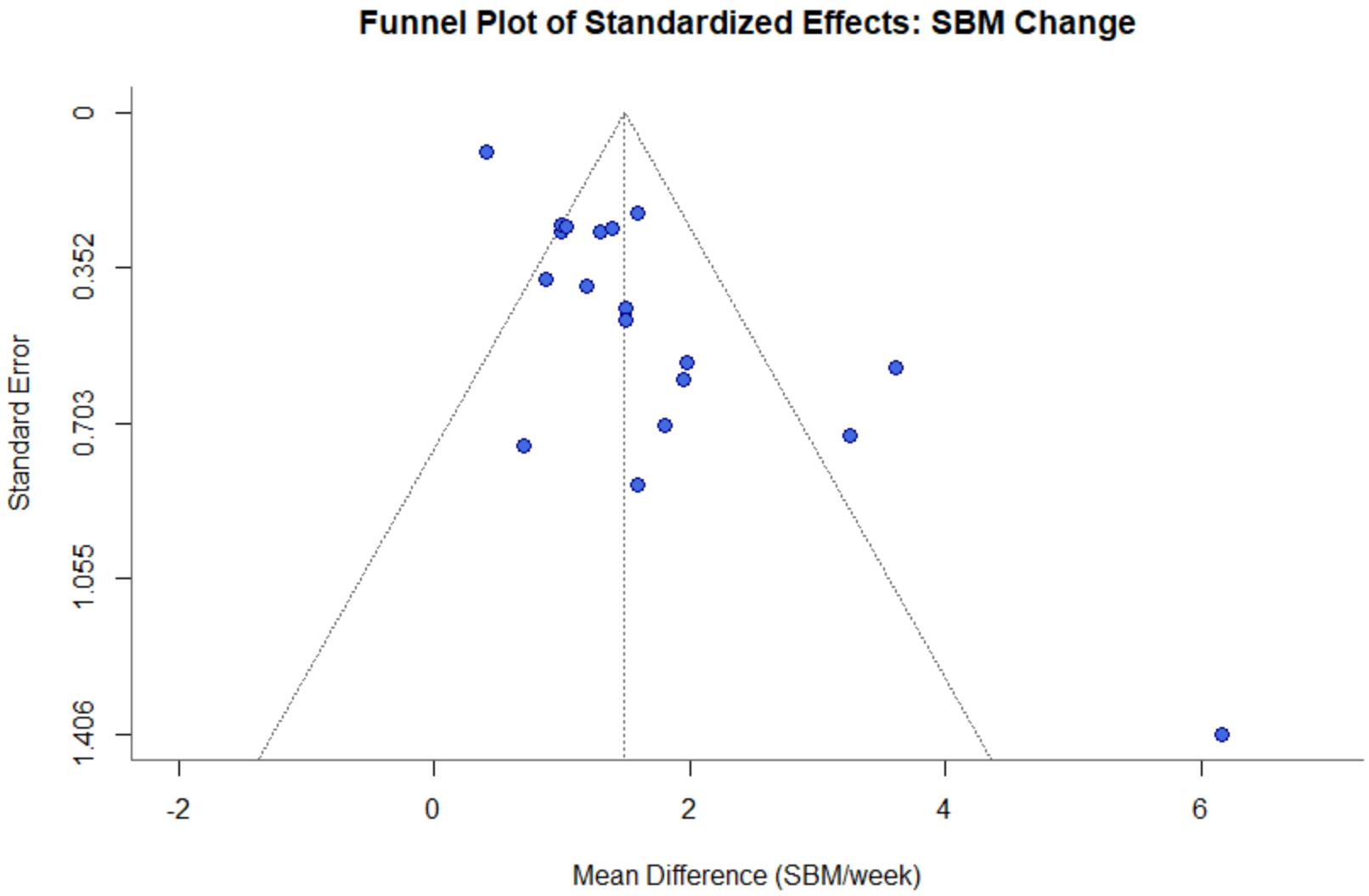
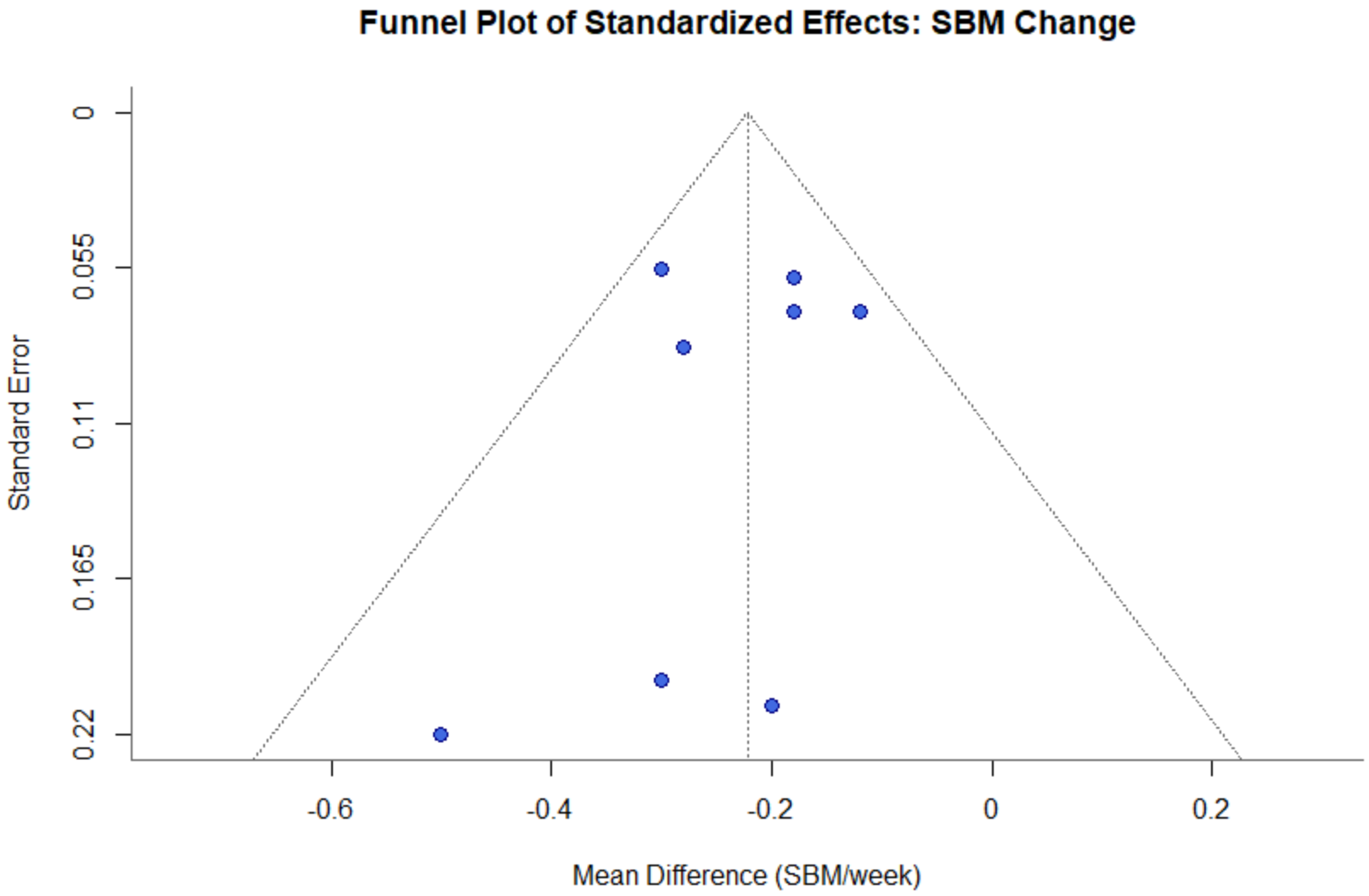

Funnel Plot of Standardized Effects: SBM Change
Standard Error
0
0.352
0.703
1.055
1.406
-2
0
2
4
6
Mean Difference (SBM/week)

Figure S2.


Funnel Plot of Standardized Effects: SBM Change
Standard Error
0
0.055
0.11
0.165
0.22
-0.6
-0.4
-0.2
0
0.2
Mean Difference (SBM/week)