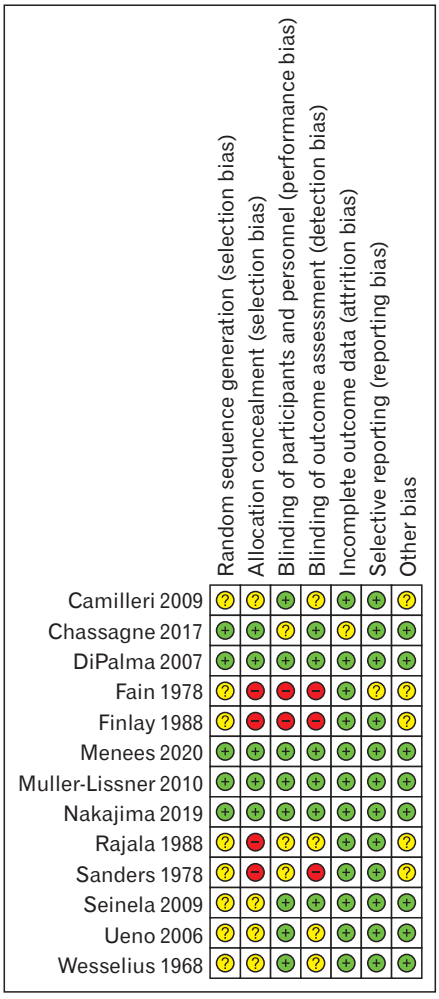
**Supplementary Table 1.** Characteristics of Excluded Studies

| No | Study | Reason for exclusion |
|---|---|---|
| 1 | Stern 1966 | Medication is not on the list of FDA formulate |
| 2 | MacLennan 1968 | Definition of constipation was not clear |
| 3 | Williamson 1975 | Full-text article was not available |
| 4 | Wojcicki 1975 | Full-text article was not available |
| 5 | Marchesi 1982 | Written in Italy. Full-text article was not available |
| 6 | Doffoel 1990 | Written in French |
| 7 | Snustad 1991 | Full-text article was not available |
| 8 | Ling 1992 | Not a randomize controlled trial |
| 9 | Teuri 1998 | Not pharmacologic intervention (prebiotics) |
| 10 | Howard 2000 | Not pharmacologic intervention (dietary supplements) |
| 11 | Kim 2005 | Not pharmacologic intervention (abdominal massage) |
| 12 | Wisten 2005 | Not pharmacologic intervention (fruit and fiber) |
| 13 | Bub 2006 | Not pharmacologic intervention (herbal supplements) |
| 14 | Chin 2006 | Not pharmacologic intervention (physical training) |
| 15 | Ueno 2006 | No control arm |
| 16 | Hale 2007 | Not pharmacologic intervention (natural mixture) |
| 17 | Pitaka 2007 | Not pharmacologic intervention (fermented cereal) |
| 18 | Sairanen 2007 | Not pharmacologic intervention (yoghurt with prebiotics) |
| 19 | Simon 2009 | Not pharmacologic intervention (behavioral therapy) |
| 20 | Schnelle 2010 | Endpoint was improvement in fecal incontinence<br>Intervention are not clearly described |
| 21 | Huang 2011 | Not pharmacologic intervention (herbal medication) |
| 22 | Marteau 2011 | Not pharmacologic intervention (chicory inulin supplement) |
| 23 | Mun 2011 | Not pharmacologic intervention (carbonated water) |
| 24 | Yen 2011 | Not pharmacologic intervention (isomalto-oligosaccharide) |
| 25 | Yen 2011 | Not pharmacologic intervention (fructo-oligosaccharide) |
| 26 | Hunag 2012 | Not pharmacologic intervention (herbal medication) |
| 27 | Kondo 2013 | Different inclusion criteria (tube feeding patients) |
| 28 | Li 2014 | Not pharmacologic intervention (auricular pressure) |
| 29 | Yeun 2016 | Not pharmacologic intervention (probiotics) |
| 30 | Konradsen 2017 | Not pharmacologic intervention (home care nursing) |
| 31 | Fang 2017 | Written in Chinese |
| 32 | Simon 2017 | Not pharmacologic intervention (biofeedback therapy) |

FDA, Food and Drug Administration.

**Supplementary Table 2.** Quality Assessment for Cross-over Study

| Study | Appropriate cross-over design | Randomized treatment order | Carry-over effect | Unbiased data | Allocation concealment | Blinding | Incomplete outcome data | Selective outcome reporting | Other bias |
|---|---|---|---|---|---|---|---|---|---|
| Ewerth et al,[18] 1980 | Low | Unclear | Low | Unclear | High | Low | Low | Low | Unclear |
| Cheskin et al,[21] 1995 | Low | Unclear | Unclear | Unclear | High | High | Unclear | Low | Unclear |
| Chokhavatia et al,[22] 1988 | Low | Unclear | Unclear | Unclear | Unclear | High | Unclear | Low | Unclear |
| Vanderdonckt et al,[25] 1990 | Low | Unclear | Unclear | Unclear | High | Low | Unclear | Low | Unclear |
| Lederle et al,[27] 1990 | Low | Unclear | Unclear | Unclear | High | High | Low | Low | Unclear |
| Hyland and Foran,[30] 1968 | Unclear | Unclear | Unclear | High | High | Low | Low | Low | Unclear |
| Kinnunen and Salokannel,[32] 1987 | Low | Unclear | Unclear | Unclear | High | Unclear | Low | Low | Unclear |
| Kinnunen et al,[33] 1993 | Low | Unclear | Unclear | Low | High | High | Low | Low | Unclear |
| Passmore et al,[34] 1993 | Low | Low | Unclear | Unclear | Unclear | Low | Low | Low | Unclear |
| Pers and Pers,[35] 1983 | Low | Unclear | High | Low | Unclear | Unclear | Low | Low | Unclear |




**Supplementary Figure.** Risk of bias of included studies.