

Table 1 Risk of bias ratings by study reporting safety outcomes for non-randomised evidence

Author Year	RSG	AC	BPP	BOA	IOD	SR	OB	Overall
Barrueco 2005 ¹	-	-	-	-	+	?	+	-
Bars 2006 ²	-	-	-	-	?	?	?	-
Cartin-Ceba 2011 ³	-	-	-	-	?	?	+	-
Cunningham 2016 ⁴	-	-	-	-	?	?	?	-
Davies 2015 ⁵	-	-	-	-	?	+	+	-
Demir 2004 ⁶	-	-	-	-	?	?	+	-
Deniz 2016 ⁷	-	-	-	-	?	?	+	-
Dhelaria 2012 ⁸	-	-	-	-	?	?	+	-
Dollerup 2017 ⁹	-	-	-	-	?	+	+	-
Ebbert 2009 ¹⁰	-	-	-	-	?	?	?	-
Ferketich 2013 ¹¹	-	-	-	-	?	?	+	-
Garcia-Portilla 2016 ¹²	-	-	-	-	-	?	+	-
Gomez-Bastero 2012 ¹³	-	-	-	-	?	?	+	-
Graham 2014 ¹⁴	-	-	-	-	?	?	+	-
Gunnell 2009 ¹⁵	-	-	-	-	?	?	+	-
Hodgkin 2013 ¹⁶	-	-	-	-	?	?	+	-
Hsueh 2014 ¹⁷	-	-	-	-	?	?	+	-
Hsueh 2015 ¹⁸	-	-	-	-	?	?	+	-
JimenezRuiz 2000 ¹⁹	-	-	-	-	+	?	+	-
JimenezRuiz 2012 ²⁰	-	-	-	-	?	?	+	-
Jimenez-Ruiz 2018 ²¹	-	-	-	-	?	?	?	-
Kaduri 2015 ²²	-	-	-	-	?	?	+	-
Kerr 2016 ²³	-	-	-	-	?	?	+	-
Kocak 2015 ²⁴	-	-	-	-	?	?	+	-
Korzeniowska 2013 ²⁵	-	-	-	-	?	?	+	-
Kotz 2015 ²⁶	-	-	-	-	?	?	+	-
Kotz 2017 ²⁷	-	-	-	-	?	?	+	-
Lee 2007 ²⁸	-	-	-	-	?	?	+	-
Mainar 2011 ²⁹	-	-	-	-	?	?	+	-
Manzoli 2015 ³⁰	-	-	+	+	+	+	+	-
Meine 2005 ³¹	-	-	-	-	?	?	+	-
Meyer 2013 ³²	-	-	-	-	?	?	+	-
Molero 2015 ³³	-	-	-	-	?	?	+	-
Orsel 2005 ³⁴	-	-	-	-	?	?	+	-
Ossip 2009 ³⁵	-	-	-	-	?	?	+	-
Panos 2010 ³⁶	-	-	-	-	?	?	+	-
Pasternak 2013 ³⁷	-	-	-	-	?	?	+	-

Author Year	RSG	AC	BPP	BOA	IOD	SR	OB	Overall
Pena 2013 ³⁸	-	-	-	-	?	?	+	-
Politis 2018 ³⁹	-	-	-	-	-	?	+	-
Postolache 2013 ⁴⁰	-	-	-	-	?	?	+	-
Roth 2005 ⁴¹	-	-	-	-	?	?	+	-
Sachs 2012 ⁴²	-	-	-	-	+	?	+	-
Saxon 2003 ⁴³	-	-	-	-	-	?	+	-
Shiltz 2011 ⁴⁴	-	-	-	-	?	?	+	-
Stapleton 2008 ⁴⁵	-	-	-	-	?	?	+	-
Steinberg 2011 ⁴⁶	-	-	-	-	?	?	+	-
Svanstrom 2012 ⁴⁷	-	-	-	-	?	?	+	-
Thomas 2013 ⁴⁸	-	-	-	-	?	?	+	-
Williams 2012 ⁴⁹	-	-	-	-	-	?	+	-
Wolfenden 2008 ⁵⁰	-	+	-	+	+	?	+	-
Woolf 2012 ⁵¹	-	-	-	-	?	?	+	-
Xiao 2014 ⁵²	-	-	-	-	+	?	+	-
Xu 2018 ⁵³	-	-	-	-	?	?	+	-

Note. "+" = low risk of bias; "?" = unclear risk of bias; "-" = high risk of bias; RSG, random sequence generation; AC, allocation concealment; BPP, blinding of participants and personnel; BOA, blinding of outcome assessment; IOD, incomplete outcome data; SR, selective reporting; OB, other bias; Overall, overall risk of bias.

- Barrueco M, Otero MJ, Palomo L, Jimenez-Ruiz C, Torrecilla M, Romero P, et al. Adverse effects of pharmacological therapy for nicotine addiction in smokers following a smoking cessation program. *Nicotine Tob Res.* 2005;7(3):335-42.
- Bars MP, Banauch GI, Appel D, Andreachi M, Mouren P, Kelly KJ, et al. "Tobacco Free With FDNY": the New York City Fire Department World Trade Center Tobacco Cessation Study. *Chest.* 2006;129(4):979-87.
- Cartin-Ceba R, Warner DO, Hays JT, Afessa B. Nicotine replacement therapy in critically ill patients: a prospective observational cohort study. *Crit Care Med.* 2011;39(7):1635-40.
- Cunningham FE, Hur K, Dong D, Miller DR, Zhang R, Wei X, et al. A comparison of neuropsychiatric adverse events during early treatment with varenicline or a nicotine patch. *Addiction.* 2016;111(7):1283-92.
- Davies NM, Taylor GMJ, Taylor AE, Jones T, Martin RM, Munafò MR, et al. The effects of prescribing varenicline on two-year health outcomes: an observational cohort study using electronic medical records. *Addiction.* 2018;113(6):1105-16.
- Demir T, Tutluoglu B, Koc N, Bilgin L. One-year follow up results of Smoking Cessation Outpatient Clinic. [Turkish]. *Tuberkuloz ve Toraks.* 2004;52(1):63-8.
- Deniz S, Emre JC, Ozdemir O, Baysak A. Two-Years Follow-up Results of a Smoking Cessation Clinic in a State Hospital. *Eurasian Journal of Pulmonology.* 2016;18(2):80-4.
- Dhelaria RK, Friderici J, Wu K, Gupta E, Khan C, Rothberg MB. Effectiveness of varenicline for smoking cessation at 2 urban academic health centers. *Eur J Intern Med.* 2012;23(5):461-4.
- Dollerup J, Vestbo J, Murray-Thomas T, Kaplan A, Martin RJ, Pizzichini E, et al. Cardiovascular risks in smokers treated with nicotine replacement therapy: a historical cohort study. *Clin Epidemiol.* 2017;9:231-43.
- Ebbert JO, Burke MV, Hays JT, Hurt RD. Combination treatment with varenicline and nicotine replacement therapy. *Nicotine Tob Res.* 2009;11(5):572-6.
- Ferketich AK, Diaz P, Browning KK, Lu B, Koletar SL, Reynolds NR, et al. Safety of varenicline among smokers enrolled in the lung HIV study. *Nicotine Tob Res.* 2013;15(1):247-54.

12. Garcia-Portilla MP, Garcia-Alvarez L, Sarramea F, Galvan G, Diaz-Mesa E, Bobes-Bascaran T, et al. It is feasible and effective to help patients with severe mental disorders to quit smoking: An ecological pragmatic clinical trial with transdermal nicotine patches and varenicline. *Schizophr Res.* 2016;176(2-3):272-80.
13. Gomez-Bastero A, Almadana V, Romero C, Luque E, Vega A, Montserrat S, et al. Differences between the recommended and real dose in a smoking cessation practice. *European Respiratory Journal.* 2012;40(no pagination).
14. Graham DJ, By K, McKean S, Mosholder A, Kornegay C, Racoosin JA, et al. Cardiovascular and mortality risks in older Medicare patients treated with varenicline or bupropion for smoking cessation: an observational cohort study. *Pharmacoepidemiol Drug Saf.* 2014;23(11):1205-12.
15. Gunnell D, Irvine D, Wise L, Davies C, Martin RM. Varenicline and suicidal behaviour: a cohort study based on data from the General Practice Research Database. *BMJ.* 2009;339(7729):b3805.
16. Hodgkin JE, Sachs DP, Swan GE, Jack LM, Titus BL, Waldron SJ, et al. Outcomes from a patient-centered residential treatment plan for tobacco dependence. *Mayo Clin Proc.* 2013;88(9):970-6.
17. Hsueh KC, Hsueh SC, Chou MY, Pan LF, Tu MS, McEwen A, et al. Varenicline versus transdermal nicotine patch: a 3-year follow-up in a smoking cessation clinic in Taiwan. *Psychopharmacology (Berl).* 2014;231(14):2819-23.
18. Hsueh SC, Hsueh KC, Chou MY, Tu MS. A comparison of the effectiveness of varenicline and transdermal nicotine patch in outpatients following a standardized smoking cessation program in Southern Taiwan. *Eval Health Prof.* 2015;38(1):115-25.
19. Jimenez Ruiz CA, Cisneros C, Perello Bosch O, Barruero Ferrero M, Hernandez Mezquita MA, Solano Reina S. [Individual treatment of smoking addiction. Results using 2 and 4 mg nicotine gum]. *Arch Bronconeumol.* 2000;36(3):129-32.
20. Jimenez Ruiz CA, Ramos Pinedo A, Cicero Guerrero A, Mayayo Ulibarri M, Cristobal Fernandez M, Lopez Gonzalez G. Characteristics of COPD smokers and effectiveness and safety of smoking cessation medications. *Nicotine Tob Res.* 2012;14(9):1035-9.
21. Jimenez-Ruiz CA, Pascual-Lledo JF, Cicero-Guerrero A, Cristobal-Fernandez M, Mayayo-Ulibarri M, Villar-Laguna C. Effectiveness and safety of varenicline and nicotine replacement therapy among mental health patients: A retrospective cohort study. *Pulmonology.* 2017;24(1):10-5.
22. Kaduri P, Voci S, Zawertailo L, Chaiton M, McKenzie K, Selby P. Real-world effectiveness of varenicline versus nicotine replacement therapy in patients with and without psychiatric disorders. *J Addict Med.* 2015;9(3):169-76.
23. Kerr A, McVey JT, Wood AM, Van Haren F. Safety of nicotine replacement therapy in critically ill smokers: a retrospective cohort study. *Anaesth Intensive Care.* 2016;44(6):758-61.
24. Kocak ND, Eren A, Boga S, Akturk UA, Ozturk UA, Arinc S, et al. Relapse Rate and Factors Related to Relapse in a 1-Year Follow-Up of Subjects Participating in a Smoking Cessation Program. *Respir Care.* 2015;60(12):1796-803.
25. Korzeniowska K, Cieslewicz A, Jablecka A. [Safety of nicotine addiction treatment]. [Polish]. *Przegląd Lekarski.* 2013;70(10):839-41.
26. Kotz D, Viechtbauer W, Simpson C, van Schayck OC, West R, Sheikh A. Cardiovascular and neuropsychiatric risks of varenicline: a retrospective cohort study. *Lancet Respir Med.* 2015;3(10):761-8.
27. Kotz D, Viechtbauer W, Simpson CR, van Schayck OCP, West R, Sheikh A. Cardiovascular and neuropsychiatric risks of varenicline and bupropion in smokers with chronic obstructive pulmonary disease. *Thorax.* 2017;72(10):905-11.
28. Lee AH, Afessa B. The association of nicotine replacement therapy with mortality in a medical intensive care unit. *Crit Care Med.* 2007;35(6):1517-21.
29. Sicras Mainar A, Navarro Artieda R, Diaz Cerezo S, Marti Sanchez B, Sanz De Burgoa V. [Abstinence rates with varenicline compared to bupropion and nicotine replacement therapy for quitting smoking in primary care]. *Aten Primaria.* 2011;43(9):482-9.
30. Manzoli L, Flacco ME, Fiore M, La Vecchia C, Marzuillo C, Gualano MR, et al. Electronic Cigarettes Efficacy and Safety at 12 Months: Cohort Study. *PLoS One.* 2015;10(6):e0129443.
31. Meine TJ, Patel MR, Washam JB, Pappas PA, Jollis JG. Safety and effectiveness of transdermal nicotine patch in smokers admitted with acute coronary syndromes. *Am J Cardiol.* 2005;95(8):976-8.
32. Meyer TE, Taylor LG, Xie S, Graham DJ, Mosholder AD, Williams JR, et al. Neuropsychiatric events in varenicline and nicotine replacement patch users in the Military Health System. *Addiction.* 2013;108(1):203-10.
33. Molero Y, Lichtenstein P, Zetterqvist J, Gumpert CH, Fazel S. Varenicline and risk of psychiatric conditions, suicidal behaviour, criminal offending, and transport accidents and offences: population based cohort study. *BMJ.* 2015;350:h2388.

34. Orsel O, Orsel S, Alpar S, Ucar N, Sipit T, Kurt B. The comparison of nicotine replacement therapy and behavioral education in smoking cessation: a study of naturalistic follow-up. [Turkish]. *Tuberkuloz ve Toraks*. 2005;53(4):354-61.
35. Ossip DJ, Abrams SM, Mahoney MC, Sall D, Cummings KM. Adverse effects with use of nicotine replacement therapy among quitline clients. *Nicotine Tob Res*. 2009;11(4):408-17.
36. Panos NG, Tesoro EP, Kim KS, Mucksavage JJ. Outcomes associated with transdermal nicotine replacement therapy in a neurosurgery intensive care unit. *Am J Health Syst Pharm*. 2010;67(16):1357-61.
37. Pasternak B, Svanstrom H, Hviid A. Use of varenicline versus bupropion and risk of psychiatric adverse events. *Addiction*. 2013;108(7):1336-43.
38. Pena P, Zagolin M, Acuna M, Navarrete S, Bustamante P, Suarez C, et al. [Results of a multidisciplinary program to quit smoking]. *Rev Med Chil*. 2013;141(3):345-52.
39. Politis A, Ioannidis V, Gourgoulialis KI, Daniil Z, Hatzoglou C. Effects of varenicline therapy in combination with advanced behavioral support on smoking cessation and quality of life in inpatients with acute exacerbation of COPD, bronchial asthma, or community-acquired pneumonia: A prospective, open-label, preference-based, 52-week, follow-up trial. *Chron Respir Dis*. 2018;15(2):146-56.
40. Postolache P, Cojocar DC, Olaru M, Todea D, Nemes RM. Pharmacotherapy for Smoking Cessation - the Experience of a Smoking Cessation Center. 2013 E-Health and Bioengineering Conference (Ehb). 2013.
41. Roth MT, Andrus MR, Westman EC. Outcomes from an outpatient smoking-cessation clinic. *Pharmacotherapy*. 2005;25(2):279-88.
42. Sachs R, Wild TC, Thomas L, Hammal F, Finegan BA. Smoking cessation interventions in the pre-admission clinic: assessing two approaches. *Can J Anaesth*. 2012;59(7):662-9.
43. Saxon AJ, Baer JS, Davis TM, Sloan KL, Malte CA, Fitzgibbons K, et al. Smoking cessation treatment among dually diagnosed individuals: preliminary evaluation of different pharmacotherapies. *Nicotine Tob Res*. 2003;5(4):589-96.
44. Shiltz D, Paniagua A, Hastings JE. A Retrospective Comparison of Varenicline Monotherapy Versus the Combination of Varenicline and Bupropion or Bupropion and Nicotine Patches in a VA Tobacco Cessation Clinic. *Journal of Smoking Cessation*. 2012;6(1):65-73.
45. Stapleton JA, Watson L, Spirling LI, Smith R, Milbrandt A, Ratcliffe M, et al. Varenicline in the routine treatment of tobacco dependence: a pre-post comparison with nicotine replacement therapy and an evaluation in those with mental illness. *Addiction*. 2008;103(1):146-54.
46. Steinberg MB, Bover MT, Richardson DL, Schmelzer AC, Williams JM, Foulds J. Abstinence and psychological distress in co-morbid smokers using various pharmacotherapies. *Drug Alcohol Depend*. 2011;114(1):77-81.
47. Svanstrom H, Pasternak B, Hviid A. Use of varenicline for smoking cessation and risk of serious cardiovascular events: nationwide cohort study. *BMJ*. 2012;345:e7176.
48. Thomas KH, Martin RM, Davies NM, Metcalfe C, Windmeijer F, Gunnell D. Smoking cessation treatment and risk of depression, suicide, and self harm in the Clinical Practice Research Datalink: prospective cohort study. *BMJ*. 2013;347(f5704):f5704.
49. Williams JH, Jones TE. Smoking cessation post-discharge following nicotine replacement therapy use during an inpatient admission. *Intern Med J*. 2012;42(2):154-9.
50. Wolfenden L, Wiggers J, Campbell E, Knight J. Pilot of a preoperative smoking cessation intervention incorporating post-discharge support from a Quitline. *Health Promot J Austr*. 2008;19(2):158-60.
51. Woolf KJ, Zabad MN, Post JM, McNitt S, Williams GC, Bisognano JD. Effect of nicotine replacement therapy on cardiovascular outcomes after acute coronary syndromes. *Am J Cardiol*. 2012;110(7):968-70.
52. Xiao D, Zhong N, Bai C, Xiu Q, Xie C, Hu D, et al. Nicotine gum or patch treatment for smoking cessation and smoking reduction: a multi-centre study in Chinese physicians. *Front Med*. 2014;8(1):84-90.
53. Xu Z, Fujiwara R, Fucito L, Bernstein S, Hsia HC. 30(th) Annual Meeting of the Wound Healing Society SAWC-Spring/WHS Joint Meeting: Charlotte Convention Center, Charlotte, North Carolina, USA April 25-29, 2018. *Wound Repair Regen*. 2018;26(1):A1-A42.