



eAPPENDIX 1 Search strategy

We searched Medical Literature Analysis and Retrieval System Online (MEDLINE), Excerpta Medica database (Embase), American College of Physicians (ACP) Journal Club, and Cochrane Central Register of Controlled Trials (CENTRAL) electronic databases via Ovid interface from inception to Jan 31, 2019. We also searched Evidence Based Medicine (EBM) Reviews' selected subset of Economic Evaluation databases (Database of Abstracts of Reviews of Effects (DARE) and NHS Economic Evaluation Database (NHS EED)) from inception to first quarter of 2016 (latest date of creation for all records within database-archived version).

A sensitive search strategy (Appendix 1) identified relevant economic evaluation studies using of probiotics for prophylaxis in hospitalized adults (age ≥ 18 years) and was based on a combination of the following subject headings and free-text keywords using alternative word spellings and endings: *probiotics, synbiotics, costs, cost analysis, economics, economic analysis/evaluation, critical illness, intensive care units, hospital units, inpatients, and hospitalization.*

Database: Ovid MEDLINE(R) ALL <1946 to Jan 31, 2019> (Jan 31th, 2019)

Search Strategy:

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- 1 probiotics/ or synbiotics/ or exp Lactobacillus/ or exp Bifidobacterium/ (36082)
 - 2 (probiotic\$ or synbiotic\$ or bifidus\$ or bifidogenic\$ or bifido\$ or bifidobacter\$ or bifidobacter\$ or lactobacill\$).mp. or (beneficial adj3 bacter\$).tw,kw. (52541)
 - 3 or/1-2 (52541)
 - 4 exp "Costs and Cost Analysis"/ or exp Economic Evaluation/ or exp Pharmacoeconomics/ or exp Economics, hospital/ or exp Economics, medical/ or Economics/ or exp models, economic/ or "Value of Life"/ or ec.fs. (491561)
 - 5 (cost\$ or economic\$ or reimburs\$ or pharmacoeconomic\$).tw,kw. (709720)
 - 6 ((value or values or valuation) adj2 (money or monetary or life or lives)).tw,kw. (4462)
 - 7 (((willingness adj1 pay) or sensitivity) adj analys?s) or quality adjusted life expectanc\$).tw,kw. (26864)
 - 8 or/4-7 (1015053)
 - 9 3 and 8 (1330)
 - 10 (decision adj1 (tree\$ or analy\$ or model\$)).ti,ab. (14725)
 - 11 "Quality of Life"/ or (QOL or QOLY or QOLYs or HRQOL or QALY or QALYs).ti,ab. or (quality\$ adj2 life\$).tw. (285029)
 - 12 quality-adjusted life years/ or (life year\$ adj3 (adjusted\$ or quality-adjusted\$)).tw. (16544)
 - 13 or/10-12 (301202)
 - 14 3 and 13 (502)
 - 15 limit 3 to "economics (best balance of sensitivity and specificity)" (803)

- 16 9 or 14 or 15 (1781)
- 17 critical\$.jw,ja,jn. or critically\$.tw. or exp Critical Care/ or intensive care units/ or *Critical Illness/ or ((critical\$ or intensive) adj care).mp. or (intensive care unit\$ or ICU or intensive therapy unit\$).mp. or apache/ or apache.tw. (350663)
- 18 exp Respiration, Artificial/ or exp Ventilators, Mechanical/ or Pneumonia, Ventilator-Associated/ (78012)
- 19 (ventilat\$ adj2 (artificial\$ or mechanical\$ or pneumon\$)).tw. (52385)
- 20 (respirat\$ adj2 (artificial\$ or assisted\$ or mechanical\$)).tw. (2920)
- 21 (respirat\$ adj2 failure\$).tw. (27352)
- 22 (ventilat\$ adj3 patient\$).mp. or (ventilat\$ and patient\$).ti. or (ventilat\$ and patient\$).ab. /freq=3 (32607)
- 23 (PPV and (pressure or ventilat\$)).tw. (1058)
- 24 (positive adj3 pressure adj5 (ventilat\$ or respir\$)).tw. (8862)
- 25 or/18-24 [ventilated patients search concept] (134664)
- 26 or/17,25 (444844)
- 27 16 and 26 (61)
- 28 exp Hospitalization/ or exp hospital units/ or exp hospitals/ or patients/ or inpatients/ or outpatients/ or pharmacy service, hospital/ or exp Drug Prescriptions/ or hospital\$.mp. or (patients\$ or inpatient\$ or outpatient\$ or in-patient\$ or out-patient\$ or tertiary\$ or (out\$ adj2 hospital\$) or ambulat\$ or same day or same-day or admission\$ or admitted\$).tw,kw. (6080532)
- 29 28 and (9 or 15) (247)
- 30 27 or 29 (280)
- 31 limit 30 to "all adult (19 plus years)" (49)
- 32 limit 30 to "all child (0 to 18 years)" (58)
- 33 30 not (32 not (31 and 32)) (237)
- 34 33 and adult\$.ti. (14)
- 35 33 and (pediatr\$ or paediatr\$ or child\$ or adolescent\$ or infan\$ or newborn\$ or boy\$1 or neonat\$).ti. (14)
- 36 33 not (35 not (34 and 35)) (226)
- 37 remove duplicates from 36 (221)

Database: Embase Classic+Embase <1947 to Jan 31, 2019> (Jan 31, 2019)

Search Strategy:

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- 1 probiotic agent/ or synbiotic agent/ or exp *Lactobacillus/ or exp *Bifidobacterium/ (43323)
 - 2 (probiotic\$ or synbiotic\$ or bifidus\$ or bifidogenic\$ or bifido\$ or bifidobacter\$ or bifidobacter\$ or lactobacill\$ or (beneficial adj3 bacter\$)).tw,kw. (55137)
 - 3 or/1-2 (64150)
 - 4 exp *Economic Aspect/ or exp *Cost/ or *Reimbursement/ or pe.fs. [Pharmacoeconomics] (499919)
 - 5 (cost\$ or economic\$ or reimburs\$ or pharmacoeconomic\$).tw,kw. (928773)
 - 6 ((value or values or valuation) adj2 (money or monetary or life or lives)).ti,ab. (6098)
 - 7 (((willingness adj1 pay) or sensitivity) adj analys?s) or quality adjusted life expectanc\$).ti,ab. (40333)

8 or/4-7 (1279874)
 9 3 and 8 (1994)
 10 (decision adj1 (tree\$ or analy\$ or model\$)).ti,ab. (21203)
 11 *"Quality of Life"/ or (QOL or QOLY or QOLYs or HRQOL or QALY or QALYs).ti,ab.
 or (quality\$ adj2 life\$).tw. (377968)
 12 *quality adjusted life year/ or "quality of life index"/ or (life year\$ adj3 (adjusted\$ or
 quality-adjusted\$)).tw. (20840)
 13 or/10-12 (397483)
 14 3 and 13 (899)
 15 limit 3 to "economics (best balance of sensitivity and specificity)" (1045)
 16 9 or 14 or 15 (2772)
 17 *critically ill patient/ or critically\$.tw. or *Critical Illness/ or exp *intensive care/ or
 *intensive care unit/ or ((critical\$ or intensive) adj care).mp. or icu.tw. or (intensive care unit\$ or
 ICU or intensive therapy unit\$).mp. or *apache/ or apache.tw. (601767)
 18 exp *artificial ventilation/ or exp *assisted ventilation/ or (ventilat\$ adj2 (artificial\$ or
 mechanical\$)).tw. or ventilator associated pneumonia/ (142764)
 19 (ventilat\$ adj2 (artificial\$ or mechanical\$ or pneumon\$)).tw. (81176)
 20 (respirat\$ adj2 (artificial\$ or assisted\$ or mechanical\$)).tw. (5520)
 21 (respirat\$ adj2 failure\$).tw. (45637)
 22 (ventilat\$ adj3 patient\$).mp. or (ventilat\$ and patient\$).ti. or (ventilat\$ and patient\$).ab.
 /freq=3 (53824)
 23 (PPV and (pressure or ventilat\$)).tw. (1962)
 24 (positive adj3 pressure adj5 (ventilat\$ or respir\$)).tw. (12752)
 25 or/18-24 [ventilated patients search concept] (200715)
 26 or/17,25 (696858)
 27 16 and 26 (91)
 28 exp *hospital care/ or exp *hospital/ or *hospitalization/ or exp *"hospital cost"/ or exp
 *hospital infection/ or exp *hospital patient/ or exp *hospital management/ or (hospital\$ or
 inpatient\$ or in-patient\$).tw,kw. (4094480)
 29 28 and (9 or 15) (334)
 30 27 or 29 (373)
 31 limit 30 to (adult <18 to 64 years> or aged <65+ years>) (90)
 32 limit 30 to (embryo or infant or child) (61)
 33 30 not (32 not (31 and 32)) (323)
 34 33 and adult\$.ti. (22)
 35 33 and (pediatr\$ or paediatr\$ or child\$ or adolescent\$ or infan\$ or newborn\$ or boy\$1 or
 neonat\$).ti. (25)
 36 33 not (35 not (34 and 35)) (303)
 37 remove duplicates from 36 (292)

Database: EBM Reviews - ACP Journal Club <1991 to Jan 31, 2019>, EBM Reviews - Cochrane Central Register of Controlled Trials <April 2018>, EBM Reviews - Database of Abstracts of

Reviews of Effects <1st Quarter 2016>, EBM Reviews - Health Technology Assessment <4th Quarter 2016>, EBM Reviews - NHS Economic Evaluation Database <1st Quarter 2016>
Search Strategy:

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- 1 (probiotic\$ or synbiotic\$ or bifidus\$ or bifidogenic\$ or bifido\$ or bifidobacter\$ or bifidobacter\$ or lactobacill\$).mp. or (beneficial adj3 bacter\$).tw,kw. (5067)
 - 2 ec.fs. (23293)
 - 3 (cost\$ or economic\$ or reimburs\$ or pharmacoeconomic\$).tw,kw. (75674)
 - 4 ((value or values or valuation) adj2 (money or monetary or life or lives)).ti,ab. (525)
 - 5 (((willingness adj1 pay) or sensitivity) adj analys?s) or quality adjusted life expectanc\$).ti,ab. (3092)
 - 6 or/2-5 (78940)
 - 7 1 and 6 (213)
 - 8 (decision adj1 (tree\$ or analy\$ or model\$)).ti,ab. (1245)
 - 9 (QOL or QOLY or QOLYs or HRQOL or QALY or QALYs).ti,ab. or (quality\$ adj2 life\$).tw. (60440)
 - 10 quality-adjusted life years/ or (life year\$ adj3 (adjusted\$ or quality-adjusted\$)).tw. (7742)
 - 11 or/8-10 (61488)
 - 12 1 and 11 (265)
 - 13 critical\$.jw,ja,jn. or critically\$.tw. or ((critical\$ or intensive) adj care).mp. or (intensive care unit\$ or ICU or intensive therapy unit\$).mp. or apache.tw. (24227)
 - 14 (ventilat\$ adj2 (artificial\$ or mechanical\$ or pneumon\$)).tw. (7105)
 - 15 (respirat\$ adj2 (artificial\$ or assisted\$ or mechanical\$)).tw. (522)
 - 16 (respirat\$ adj2 failure\$).tw. (2287)
 - 17 (ventilat\$ adj3 patient\$).mp. or (ventilat\$ and patient\$).ti. or (ventilat\$ and patient\$).ab. /freq=3 (7329)
 - 18 (PPV and (pressure or ventilat\$)).tw. (147)
 - 19 (positive adj3 pressure adj5 (ventilat\$ or respir\$)).tw. (1764)
 - 20 or/13-19 (31449)
 - 21 (7 or 12) and 20 (12)
 - 22 hospital\$.mp. or (patients\$ or inpatient\$ or outpatient\$ or in-patient\$ or out-patient\$ or tertiary\$ or (out\$ adj2 hospital\$) or ambulat\$ or same day or same-day or admission\$ or admitted\$).tw,kw. (721318)
 - 23 7 and 22 (163)
 - 24 21 or 23 (163)
 - 25 24 and adult\$.ti. (11)
 - 26 24 and (pediatr\$ or paediatr\$ or child\$ or adolescent\$ or infan\$ or newborn\$ or boy\$1 or neonat\$).ti. (39)
 - 27 24 not (26 not (25 and 26)) (124)
 - 28 7 and 27 (124)
 - 29 remove duplicates from 28 (120)
