# Supplementary materials

Supplementary Table 1 Terms used to search Embase and Embase Alert databases

* Search type: free-text
* Limits: 2010 onward
* Search date: 25 May 2016

|  |  |  |
| --- | --- | --- |
| Search number | Terms searched | Hits |
| S1 | innovat\* NEAR/3 defin\* | 308° |
| S2 | innovat\* NEAR/3 label\* | 84° |
| S3 | innovat\* NEAR/3 designat\* | 16° |
| S4 | innovat\* NEAR/3 class\* | 425° |
| S5 | innovat\* NEAR/3 consider | 130° |
| S6 | innovat\* NEAR/3 considered | 343° |
| S7 | S6 OR S5 OR S4 OR S3 OR S2 OR S1 | 1288° |
| S8 | health or care or healthcare | 8279531\* |
| S9 | drug\* or pharmaceutical\* or pharmacological\* | 11330074\* |
| S10 | therap\* or intervention\* or treat\* | 11887577\* |
| S11 | medic\* or biologic\* | 17017495\* |
| S12 | S11 OR S10 OR S9 OR S8 | 26166904\* |
| S13 | S12 AND S7 | 1165° |
| TOTAL | (S12 AND S7) AND yr (2010–2019) | 719° |

\* Duplicates are removed from the search, but included in the result count.

° Duplicates are removed from the search and from the result count.

Supplementary Table 2 Terms used to search Embase and Embase Alert databases

* Search type: controlled vocabulary
* Limits: 2010 onward
* Search date: 25 May 2016

|  |  |  |
| --- | --- | --- |
| Search number | Terms searched | Hits |
| S1 | health or care or healthcare | 8279531\* |
| S2 | drug\* or pharmaceutical\* or pharmacological\* | 11330074\* |
| S3 | therap\* or intervention\* or treat\* | 11887577\* |
| S4 | medic\* or biologic\* | 17017495\* |
| S5 | S25 OR S24 OR S23 OR S22 | 26166904\* |
| S6 | mjemb.exact("innovation" OR "innovation policy" OR "innovation decision process" OR "innovative device" OR "innovative drug" OR "innovative medicine" OR "innovative medicines initiative" OR "innovative new drug" OR "innovative medical technology" OR "innovative pharmaceutical" OR "innovative platform" OR "innovative technology" OR "innovator drug" OR "innovator agent") | 79° |
| S7 | emb.exact("innovation" OR "innovate" OR "innovation characteristics" OR "innovation policy" OR "innovative" OR "innovative biotechnology" OR "innovative drug" OR "innovative medicine" OR "innovative new drug" OR "innovative pharmaceutical" OR "innovative technology" OR "innovativeness" OR "innovator" OR "innovator agent" OR "innovator drug") | 115° |
| S8 | defin\* | 1521242\* |
| S9 | S28 OR S27 | 125° |
| S10 | S30 AND S29 AND S26 | 8° |
| TOTAL | (S30 AND S29 AND S26) AND yr(2010-2019) | 5° |

\* Duplicates are removed from the search, but included in the result count.

° Duplicates are removed from the search and from the result count.

Supplementary Table 3 Terms used to search MEDLINE database

* Search type: free-text
* Limits: 2010 onward
* Search date: 25 May 2016

|  |  |  |
| --- | --- | --- |
| Search number | Terms searched | Hits |
| S1 | innovat\* NEAR/3 defin\* | 224° |
| S2 | innovat\* NEAR/3 label\* | 68° |
| S3 | innovat\* NEAR/3 designat\* | 6° |
| S4 | innovat\* NEAR/3 class\* | 326° |
| S5 | innovat\* NEAR/3 consider | 100° |
| S6 | innovat\* NEAR/3 considered | 272° |
| S7 | S6 OR S5 OR S4 OR S3 OR S2 OR S1 | 983° |
| S8 | health or care or healthcare | 4632717\* |
| S9 | drug\* or pharmaceutical\* or pharmacological\* | 5381764\* |
| S10 | therap\* or intervention\* or treat\* | 7680464\* |
| S11 | medic\* or biologic\* | 22189913\* |
| S12 | S11 OR S10 OR S9 OR S8 | 23351488\* |
| S13 | S12 AND S7 | 948° |
| TOTAL | (S12 AND S7) AND yr (2010–2019) | 536° |

\* Duplicates are removed from the search, but included in the result count.

° Duplicates are removed from the search and from the result count.

Supplementary Table 4 Terms used to search MEDLINE database

* Search type: controlled vocabulary
* Limits: 2010 onward
* Search date: 25 May 2016

|  |  |  |
| --- | --- | --- |
| Search number | Terms searched | Hits |
| S1 | health or care or healthcare | 4632717\* |
| S2 | drug\* or pharmaceutical\* or pharmacological\* | 5381764\* |
| S3 | therap\* or intervention\* or treat\* | 7680464\* |
| S4 | medic\* or biologic\* | 22189913\* |
| S5 | S11 OR S10 OR S9 OR S8 | 23351488\* |
| S6 | mjmesh.exact("Diffusion of Innovation") OR mjmesh.exact("Organizational Innovation") OR mjmesh.exact("Innovative Therapies") | 11433\* |
| S7 | mesh.exact("Diffusion of Innovation") OR mesh.exact("Organizational Innovation") OR mesh.exact("Innovative Therapies") | 35855\* |
| S8 | S16 OR S15 | 35855\* |
| S9 | defin\* | 981446\* |
| S10 | S19 AND S18 AND S12 | 1265° |
| TOTAL | (S19 AND S18 AND S12) | 370° |

\* Duplicates are removed from the search, but included in the result count.

° Duplicates are removed from the search and from the result count.

Supplementary Table 5 Terms used to search EconLit database

* Limits: English language, journal articles, 2010 onward
* Search date: 25 May 2016

|  |  |  |
| --- | --- | --- |
| Search number | Terms searched | Hits |
| S1 | Innovation AND definition | 192 |
| S2 | Innovation AND health | 551 |
| S3 | Innovative AND health | 218 |
| S4 | Innovation AND drug | 358 |
| S5 | Innovative AND drug | 82 |
| S6 | Innovation AND pharmaceutical | 188 |
| S7 | Innovative AND pharmaceutical | 45 |
| S8 | Innovation AND medicine | 48 |
| S9 | Innovative AND medicine | 20 |
| TOTAL | (Without duplicate removal) | 1702 |
| TOTAL | (After duplicate removal) | 1214 |

Supplementary Table 6 List of studies excluded at full-text review stage

|  |  |
| --- | --- |
| Study | Exclusion reason |
| Blanchet and James 2014 (57) | Does not define innovation |
| Ciani *et al.* 2016 (58) | Definition of innovation specifically for devices |
| Cicchetti 2012 (59) | Refers to previous paper only |
| Del Santo *et al.* 2011 (60) | Refers to previous paper only |
| Erdem and Thompson 2014 (61) | Does not define innovation |
| Flory and Reinhardt 2013 (62) | Does not define innovation |
| Henshall and Schuller 2013 (63) | Does not define innovation |
| Janssen *et al.* 2015 (64) | Does not define innovation in pharmaceutical products |
| Martelli *et al.* 2016 (65) | Medical devices not drugs |
| Mather 2006 (66) | Describes organisational innovation |
| Mennini *et al.* 2016 (67) | Does not define innovation |
| Page 2014 (68) | Does not define innovation in pharmaceutical products |
| Taboulet 2008 (69) | No specific definition of innovation with respect to drugs |
| Wardell *et al.* 1980 (70) | Refers to previous paper only |
| Willeme and Dumont 2015 (71) | Does not define innovation |
| Woollett 2012 (72) | Does not define innovation |

## References

57. Blanchet K, James P. Can international health programmes be sustained after the end of international funding: the case of eye care interventions in Ghana. BMC Health Serv Res. 2014;14:77.

58. Ciani O, Armeni P, Boscolo PR*, et al.* De innovatione: The concept of innovation for medical technologies and its implications for healthcare policy-making. Health Policy and Technology. 2016;5(1):47-64.

59. Cicchetti A. Definition of "innovative drug" in the Health Technology Assessment perspective. PharmacoEcon Ital Res Artic. 2012;14(1):66-8.

60. Del Santo F, Maratea D, Messori A. Definition of innovative drugs: Revisited in a context of limited resources. PharmacoEcon Ital Res Artic. 2011;13(2):121-4.

61. Erdem S, Thompson C. Prioritising health service innovation investments using public preferences: a discrete choice experiment. BMC Health Serv Res. 2014;14:360.

62. Flory E, Reinhardt J. European regulatory tools for advanced therapy medicinal products. Transfus Med Hemother. 2013;40(6):409-12.

63. Henshall C, Schuller T. Health technology assessment, value-based decision making, and innovation. Int J Technol Assess Health Care. 2013;29(4):353-9.

64. Janssen M, Stoopendaal AMV, Putters K. Situated Novelty: Introducing a Process Perspective on the Study of Innovation. Research Policy. 2015;44(10):1974-84.

65. Martelli N, Van Den Brink H, Borget I. New French Coverage with Evidence Development for innovative medical devices: Improvements and unresolved issues. Value in Health. 2016;19(1):17-9.

66. Mather CM. Medical innovation, unmet medical needs, and the drug pipeline. Can J Clin Pharmacol. 2006;13(1):e85-91.

67. Mennini FS, Gitto L, Scrivo R*, et al.* The promotion of drug innovation in Italy: Critical aspects and unsolved problems. Global and Regional Health Technology Assessment. 2016;3(1):42-7.

68. Page T. Notions of Innovation in Healthcare Services and Products. Int J of Innovation and Sustainable Development. 2014;8(3):217-31.

69. Taboulet F. Les « médicaments innovants » destinés aux patients ambulatoires : quelle spécificité en droit français ? Médecine & Droit. 2008;2008(93):172-80.

70. Wardell WM, DiRaddo J, Weintraub M. The measurement of therapeutic value. J Clin Pharmacol. 1980;20(2-3):77-90.

71. Willeme P, Dumont M. Machines That Go 'Ping': Medical Technology and Health Expenditures in OECD Countries. Health Economics. 2015;24(8):1027-41.

72. Woollett GR. Innovation in biotechnology: current and future states. Clin Pharmacol Ther. 2012;91(1):17-20.

Supplementary Table 7 Mapping of definition terms to dimensions of innovation

| Definition term | Dimension |
| --- | --- |
| adherence | Administration |
| change of venue | Administration |
| convenience | Administration |
| availability of existing treatment | Availability of existing treatment |
| clinical study design | Clinical evidence |
| comparator | Clinical evidence |
| use of active comparator | Clinical evidence |
| use of adequate comparator | Clinical evidence |
| acceptable cost | Cost |
| cost | Cost |
| cost-effectiveness | Cost |
| cost-saving | Cost |
| newness | Newness |
| period of time on market | Newness |
| level of technology | Novelty |
| molecular novelty | Novelty |
| new indications | Novelty |
| new modes of action | Novelty |
| new molecular entity | Novelty |
| new type or mechanism | Novelty |
| novelty | Novelty |
| pharmacological or technological differences | Novelty |
| significant breakthrough | Novelty |
| source of innovation (revolution/evolution) | Novelty |
| technical innovation | Novelty |
| impact on population health | Other |
| market share | Other |
| societal or commercial success | Other |
| adverse effect profiles | Safety |
| degree of invasiveness | Safety |
| improvement in safety | Safety |
| safety | Safety |
| added therapeutic value | Therapeutic benefit |
| additional benefit | Therapeutic benefit |
| additional benefits | Therapeutic benefit |
| advantages over existing methods | Therapeutic benefit |
| amount of life gained | Therapeutic benefit |
| benefit–harm ratio | Therapeutic benefit |
| benefit–risk balance | Therapeutic benefit |
| clinical benefit | Therapeutic benefit |
| clinical improvements | Therapeutic benefit |
| clinical relevance of endpoints | Therapeutic benefit |
| comparative effectiveness | Therapeutic benefit |
| effectiveness | Therapeutic benefit |
| efficacy | Therapeutic benefit |
| evidence of superiority | Therapeutic benefit |
| favourable risk–benefit profile | Therapeutic benefit |
| health gains | Therapeutic benefit |
| health outcomes | Therapeutic benefit |
| important advance over existing therapies | Therapeutic benefit |
| improved outcomes | Therapeutic benefit |
| improvement in efficacy | Therapeutic benefit |
| improvement in patient health | Therapeutic benefit |
| improvement in quality of patient management and outcomes | Therapeutic benefit |
| improvement on existing interventions | Therapeutic benefit |
| improvement over existing therapies | Therapeutic benefit |
| improvements in patient condition | Therapeutic benefit |
| increased effectiveness | Therapeutic benefit |
| patient benefits | Therapeutic benefit |
| step-change | Therapeutic benefit |
| substantial benefit | Therapeutic benefit |
| substantial therapeutic benefit | Therapeutic benefit |
| targeting of population | Therapeutic benefit |
| therapeutic advance | Therapeutic benefit |
| therapeutic benefit | Therapeutic benefit |
| therapeutic effect | Therapeutic benefit |
| therapeutic improvement | Therapeutic benefit |
| therapeutic potential | Therapeutic benefit |
| therapeutic value | Therapeutic benefit |
| usefulness | Therapeutic benefit |
| active in patients resistant to current therapies | Unmet Need |
| disease severity | Unmet Need |
| serious or life-threatening disease | Unmet Need |
| unmet need | Unmet Need |

Supplementary Table 8 Additional website searches

| Organisation | Acronym | Country | Website | Search method | Keywords |
| --- | --- | --- | --- | --- | --- |
| National Institute of Health and Care Excellence | NICE | England | <https://www.nice.org.uk/> | 1) Search box 2) "Guide to the methods of technology appraisal 2013" pdf 3) "Single technology appraisal: User guide for company evidence submission template" pdf | Innov\* |
| Haute Autorité de Santé | HAS | France | <http://www.has-sante.fr/portail/> | 1) Search box 2) "Choix méthodologiques pour l’évaluation économique à la HAS" pdf 3) "Guide méthologique pour la mise en place d’une analyse d’impact budgétaire" | Innovation, innovative, innovant |
| Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen | IQWiQ | Germany | <https://www.iqwig.de/> | 1) Search box 2) General Methods 4.2 (English) pdf 3) Google search engine | 1, 2) Innovat 3) IQWiG definition of innovation |
| Agenzia Italiana del Farmaco | AIFA | Italy | <http://www.agenziafarmaco.gov.it/> | 1) Search box 2) Glossary 3) Google search engine | 1, 2) Innovation, innovazione 3) AIFA definition of innovation |
| Agencia de Evaluación de Tecnologías Sanitarias | AETS | Spain | http://www.isciii.es/ | 1) Search box 2) Google search engine | 1, 2) Innovation, innovac 3) AETS definition of innovation |
| Tandvårds- och läkemedelsförmånsverket | TLV | Sweden | <http://www.tlv.se/In-English/in-english/> | 1) Search box 2) Google search engine | 1) Innovation 2) TLV definition of innovation |
| Scottish Medicines Consortium | SMC | Scotland | <https://www.scottishmedicines.org.uk/> | 1) Search box 2) SMC policy statements 3) "Guide to the Scottish Medicines Consortium" pdf 4) "NHS Scotland Patient Access Scheme (PAS) Guidance" pdf 5) Glossary 6) Google search engine | 1–5) Innovative, Innovation 6) Scottish Medicines Consortium definition of innovation |
| Zorginstituut Nederland | ZINL | Netherlands | <https://www.zorginstituutnederland.nl/> | 1) Search box 2) Guideline for economic evaluations in healthcare pdf 3) Toekomstscenario’s voor de ontwikkeling en prijszetting van geneesmiddelen odf 4) Investigation of the accessibility and affordability of medicines in specialist medical care pdf 5) Google search engine | 1–4) innovative, innovatie 5) ZINL definition of innovation |
| International Society For Pharmacoeconomics and Outcomes Research | ISPOR | International | <http://www.ispor.org/> | 1) Search box 2) ISPOR book of terms 3) ISPOR TASK FORCE REPORT: Budget Impact Analysis—Principles of Good Practice | 1–3) Innovative, Innovation, Definition 4) ISPOR definition of innovation |
| American Society of Clinical Oncology | ASCO | USA | <https://www.asco.org/> | 1) Search box 2) American Society of Clinical Oncology Value Framework (2016) 3) Google search engine | 1, 2) Innovative, Innovation, Definition 3) ASCO definition of innovation |
| European Society for Medical Oncology | ESMO | Europe | <http://www.esmo.org/> | 1) Search box 2) European Society for Medical Oncology Magnitude of Clinical Benefit Scale pdf 3) ESMO Patient Guide Personalised Cancer Medicine pdf 3) Google search engine | 1–3) Innovative, Innovation, Definition 4) ESMO definition of innovation |
| European Medicines Agency | EMA | Europe | <http://www.ema.europa.eu/> | 1) Document library search 2) Site-wide search | 1) Innovative, Innovation, Definitions 2) Definitions |
| National Health Service, England | NHS England | England | <https://www.england.nhs.uk/> | 1) Search box 2) Technical definitions for commissioners 3) Technical definitions for clinical commissioning groups 4) Google search engine | 1–3) Innovative, Innovation, Definitions 4) "NHS England definition of innovation" |
| World Health Organization | WHO | International | http://www.who.int/en/ | 1) Search box  2) Glossary of terms used  3) Google search engine | 1) “Innovative medicine”  2) Innovative, Innovation  3) “WHO definition of innovation”, “World Health Organization definition of innovation” |

No definitions were identified in searches of IQWiQ, AETS, ISPOR, ASCO, ESMO, EMA or WHO websites