

Melanoma: assessment and management

Search strategies

NICE guideline <number>

Search strategies

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1 Scoping search strategies

Scoping searches

Scoping searches were undertaken on the following websites and databases (listed in alphabetical order) in September/October 2019 to provide information for scope development and project planning. Browsing or simple search strategies were employed.

Guidelines/website	Systematic review/economic evaluations
Audit Commission (archived site)	Campbell Collaboration
Canadian Medical Association Infobase	Cochrane Database of Systematic Reviews (CDSR)
Canadian Paediatric Society	Database of Abstracts of Reviews of Effects (DARE) – last updated April 2015
Care Quality Commission	Health Technology Assessment (HTA) Database – last updated October 2016
Core Outcome Measures in Effectiveness Trials (COMET)	NHS Economic Evaluation Database (NHS EED) – last updated April 2015
Cross Borders Patient Registries Initiative (PARENT)	NIHR Health Technology Assessment Programme
Cure Together	NIHR Health Services and Delivery Research (HS&DR) Programme
Department of Health & Social Care	PROSPERO
European Centre for Disease Prevention and Control	TRIP Database
General Medical Council	
Guidelines & Audit Implementation Network (GAIN)	
Guidelines International Network (GIN)	
Health and Social Care Information Centre	
Health Foundation	
Healthcare Quality Improvement Partnership	
Healthtalk Online	
International Guideline Library	
Joint Committee on Vaccination and Immunisation	
Map of Medicine	
Medicines and Healthcare Products Regulatory Agency (MHRA)	
National Audit Office	
National Clinical Audit and Patient Outcomes Programme	
National Health and Medical Research Council (Australia)	
National Institute for Health and Care Excellence (NICE) - published & in development guidelines	
National Prescribing Centre	
National Quality Board	
National Voices	
NHS Choices	

Guidelines/website	Systematic review/economic evaluations
<p>NHS Digital NHS England NHS Quality Improvement Scotland NHS Scotland NICE Clinical Knowledge Summaries (CKS) NICE Evidence Search Office for National Statistics Patient Experience Library Patient UK Patients Like Me PatientVoices PCORNet Public Health England Office for National Statistics Royal College of General Practitioners Royal College of Midwives Royal College of Nursing Royal College of Obstetricians and Gynaecologists Royal College of Paediatrics and Child Health Royal College of Physicians Scottish Government Scottish Intercollegiate Guidelines Network (SIGN) Treato UK Data Service UK National Statistics UK Research and Innovation US National Guidelines Clearinghouse Welsh Government World Health Organisation (WHO) YouthHealthTalk</p>	

2. Main searches

Bibliographic databases searched for the guideline

- Cochrane Database of Systematic Reviews – CDSR (Wiley)
- Cochrane Central Register of Controlled Trials – CENTRAL (Wiley)
- Database of Abstracts of Reviews of Effects – DARE (CDR)
- HTA (CDR)
- EMBASE (Ovid)
- MEDLINE (Ovid)
- MEDLINE Epub Ahead of Print (Ovid)
- MEDLINE In-Process (Ovid)
- INAHTA (for RQs 4.1 and 4.2)

Identification of evidence for review questions

A NICE information specialist conducted the literature searches for the evidence reviews. The searches were originally run between August 2020 and April 2021. The searches were updated in July 2021.

The principal search strategy was developed in MEDLINE (Ovid interface) and adapted, as appropriate, for use in the other sources listed in the protocol, taking into account their size, search functionality and subject coverage.

The MEDLINE strategies below were quality assured (QA) by trained NICE information specialist. All translated search strategies were peer reviewed to ensure their accuracy. Both procedures were adapted from the [2016 PRESS Checklist](#).

The search results were managed in EPPI-Reviewer v5. Duplicates were removed in EPPI-R5 using a two-step process. First, automated deduplication is performed using a high-value algorithm. Second, manual deduplication is used to assess 'low-probability' matches. All decisions made for the review can be accessed via the deduplication history.

English language limits were applied in adherence to standard NICE practice and the review protocol.

The limit to remove animal studies in the searches was the standard NICE practice, which has been adapted from: Dickersin, K., Scherer, R., & Lefebvre, C. (1994). [Systematic Reviews: Identifying relevant studies for systematic reviews](#). *BMJ*, 309(6964), 1286.

Review question search strategies

Population terms

Table 1: Population terms used for all searches

Medline Strategy
1. exp Melanoma/
2. melanoma\$.tw.
3. (maligna\$ adj1 lentigo\$).tw.
4. (hutchinson\$ adj1 (freckle\$ or melano\$)).tw.
5. dubreuilh.tw.
6. LMM.tw.
7. or/1-6

Review Question 1

1.1 What is the role and optimal timing of genetic testing of the tumour after diagnosis for a person with stage 2C-3 melanoma?

Table 2: search strategy

Medline Strategy, searched 12/08/2020
Database: Ovid MEDLINE(R) 1946 to August 11, 2020
1 exp Melanoma/ (95112)
2 Skin Neoplasms/ (121069)
3 (melanoma* or melanocarcinoma* or naevocarcinoma* or nevocarcinoma*).tw. (103532)
4 ((skin or derm* or cutaneous* or epitheli* or epiderm*) adj1 (adenocarcinoma* or cancer* or carcinoma* or malignan* or neoplas* or oncolog* or tumor* or tumour*)).tw. (61495)
5 ((maligna* or melano*) adj2 (freckle* or lesion* or mole* or nev* or naev*)).tw. (24915)
6 (hutchinson* adj2 (freckle* or melano\$)).tw. (69)
7 dubreuilh*.tw. (72)
8 (maligna* adj2 lentigo*).tw. (1065)
9 LMM.tw. (868)
10 or/1-9 (251058)
11 Genetic Testing/ (38160)

Medline Strategy, searched 12/08/2020

Database: Ovid MEDLINE(R) 1946 to August 11, 2020

- 12 Molecular Diagnostic Techniques/ (11164)
- 13 DNA Mutational Analysis/ (60177)
- 14 exp *Immunohistochemistry/ (39074)
- 15 In Situ Hybridization, Fluorescence/ (42639)
- 16 (fluorescence* adj2 (hybridisation* or hybridization*)).tw. (602)
- 17 ((genetic* or genomic* or immunohistochem* or "immuno histochem*" or IHC or FISH or fluorescen* or immunofluorescen* or "immuno fluorescen*" or molecular* or somatic*) adj2 (analys* or test* or techni*)).tw. (249959)
- 18 ((braf* or b raf or v600* or dna) adj4 mutat* adj4 (analys* or test* or techni*)).tw. (2722)
- 19 or/11-18 (401966)
- 20 Proto-Oncogene Proteins B-raf/ (8767)
- 21 (braf* or b raf or v600*).tw. (12772)
- 22 or/20-21 (13843)
- 23 Mutation/ (428586)
- 24 (gene* adj2 (alter* or chang* or modif*)).tw. (113586)
- 25 (mutation* or mutated or mutating).tw. (603697)
- 26 or/23-25 (870250)
- 27 (sensitiv: or predictive value:).mp. or accurac:..tw. (1884066)
- 28 22 and 26 and 27 (1798)
- 29 19 or 28 (402913)
- 30 10 and 29 (8313)
- 31 limit 30 to english language (7890)
- 32 animals/ not humans/ (4691424)
- 33 31 not 32 (7389)
- 34 limit 33 to (letter or historical article or comment or editorial or news or case reports) (1280)
- 35 33 not 34 (6109)
- 36 limit 35 to ed=20131009-20200812 (2235)

Filters used (see section 3): McMaster optimal diagnostic filter

Review Question 2.1 and 6.1-6.4

RQ 2.1 What is the most accurate method of staging melanoma in people preliminarily assigned: (a) clinicopathological stage 1A melanoma? (b) clinicopathological stage 1B to 2C melanoma (including, but not limited to, sentinel lymph node biopsy)? (c) clinicopathological stage 3 melanoma? (d) clinicopathological stage 4 melanoma?

RQ 6.1 What is the optimal method, frequency, setting and duration of follow-up for stage I-III melanoma?

RQ 6.2 What is the diagnostic accuracy of body imaging for re-staging during the follow-up of people with stage 2C (with no sentinel lymph node biopsy) and stage 3 melanoma?

RQ 6.3 Should brain imaging be included for people with melanoma who are undergoing body imaging as part of follow-up, and who have no neurological signs or symptoms?

RQ 6.4 What is the effectiveness of body imaging for the follow-up of people with stage 4 (and unresectable stage 3) melanoma after concluding treatment, including the optimal frequency and duration?

Table 3: search strategy

Medline Strategy, searched 09/12/2020

Database: Ovid MEDLINE(R) 1946 to December 02, 2020

Search Strategy:

- 1 exp Melanoma/ (96197)
- 2 Skin Neoplasms/ (122179)
- 3 (melanoma* or melanocarcinoma* or naevocarcinoma* or nevocarcinoma*).tw. (104932)
- 4 ((skin or derm* or cutaneous* or epitheli* or epiderm*) adj1 (adenocarcinoma* or cancer* or carcinoma* or malignan* or neoplas* or oncolog* or tumor* or tumour*)).tw. (62202)
- 5 ((maligna* or melano*) adj2 (freckle* or lesion* or mole* or nev* or naev*)).tw. (25240)
- 6 (hutchinson* adj2 (freckle* or melano*)).tw. (69)
- 7 dubreuilh*.tw. (74)
- 8 (maligna* adj2 lentigo*).tw. (1077)
- 9 LMM.tw. (896)
- 10 or/1-9 (253749)
- 11 diagnostic imaging/ (41253)
- 12 (diagnos* adj imag*).tw. (14491)

Medline Strategy, searched 09/12/2020

Database: Ovid MEDLINE(R) 1946 to December 02, 2020

Search Strategy:

- 13 exp Ultrasonography/ (442717)
- 14 (ultraso* or sonogra* or echogra* or echoscop* or echosound* or echotomogra*).tw. (358379)
- 15 exp Tomography, X-Ray Computed/ (439691)
- 16 ((CT or CAT) adj (electron beam or examination* or imag* or scan* or x ray*)).tw. (113134)
- 17 cine-ct.tw. (154)
- 18 ((comput* or electron beam) adj3 tomogra*).tw. (259726)
- 19 tomodensitometr*.tw. (945)
- 20 exp Tomography, Emission-Computed/ (114564)
- 21 (PET adj (CT or examination* or imag* or scan*)).tw. (39193)
- 22 (positron adj2 tomograph*).tw. (49323)
- 23 spect.tw. (25116)
- 24 exp Magnetic Resonance Imaging/ (461319)
- 25 magnet* resonance.tw. (290200)
- 26 (fMRI or MRI or MR*2 or NMR*1 or MP-MR* or MPMR*).tw. (1006485)
- 27 ((magnet* or MR*) adj (examination* or imag* or scan* or tomograph*)).tw. (83271)
- 28 ((diffusion or planar or echoplanar or echo-planar or functional) adj1 (imag* or scan* or tomogra*)).tw. (16480)
- 29 Whole Body Imaging/ (5062)
- 30 (whole body adj (imag* or mr* or radiograph* or scan* or screen* or tomograph*)).tw. (4543)
- 31 wbm*.tw. (93)
- 32 or/11-31 (2288055)
- 33 Follow-Up Studies/ (651891)
- 34 (follow-up or followup).tw. (877661)
- 35 (checkup*1 or check-up*1).tw. (13118)
- 36 surveillance.tw. (156194)
- 37 (re-examin* or reexamin*).tw. (24666)
- 38 ((aftercare or after-care or post-care or post-hospital* or post-operat* or post-surg* or post-therap* or post-treat*) adj1 (assess* or examin* or evaluat* or monitor* or screen*)).tw. (2652)
- 39 or/33-38 (1407445)

Medline Strategy, searched 09/12/2020

Database: Ovid MEDLINE(R) 1946 to December 02, 2020

Search Strategy:

- 40 32 or 39 (3469441)
- 41 Neoplasm Staging/ (176383)
- 42 Neoplasm Recurrence, Local/ (119904)
- 43 exp Neoplasm Metastasis/ (206033)
- 44 (disseminat* or metasta* or migration or spread* or stage* or staging or recurr* or relaps* or restag* or re-stag* or upstag* or up-stag* or TNM).tw. (2246242)
- 45 ((AJCC or UICC) adj4 (classification* or system*)).tw. (2111)
- 46 (sensitiv: or predictive value:).mp. or accurac:.tw. (1913345)
- 47 prognosis.sh. (518913)
- 48 prognos:.tw. (527238)
- 49 or/41-48 (4479075)
- 50 10 and 40 and 49 (29926)
- 51 limit 50 to english language (26589)
- 52 animals/ not humans/ (4728824)
- 53 51 not 52 (25661)
- 54 limit 53 to (letter or historical article or comment or editorial or news or case reports) (5688)
- 55 53 not 54 (19973)
- 56 limit 55 to ed=20141001-20201209 (6216)

Filters used (see section 3) The McMaster optimal diagnostic filter and an adapted version of the McMaster prognosis optimal/sensitive filter was used for part of the search in all databases except Cochrane (Wiley) and CRD

Review Question 2.1

2.1 What is the most accurate method of staging melanoma in people preliminarily assigned: (a) clinicopathological stage 1A melanoma? (b) clinicopathological stage 1B to 2C melanoma (including, but not limited to, sentinel lymph node biopsy)? (c) clinicopathological stage 3 melanoma? (d) clinicopathological stage 4 melanoma?

Table 4: search strategy

Medline Strategy, searched 27 October 2020

Database: Ovid MEDLINE(R) 1946 to October 26, 2020

Search Strategy:

- 1 exp Melanoma/ (95782)
- 2 Skin Neoplasms/ (121708)
- 3 (melanoma* or melanocarcinoma* or naevocarcinoma* or nevocarcinoma*).tw. (104386)
- 4 ((skin or dermat* or cutaneous* or epitheli* or epiderm*) adj1 (adenocarcinoma* or cancer* or carcinoma* or malignan* or neoplas* or oncolog* or tumor* or tumour*)).tw. (61895)
- 5 ((maligna* or melano*) adj2 (freckle* or lesion* or mole* or nev* or naev*)).tw. (25092)
- 6 (hutchinson* adj2 (freckle* or melano*)).tw. (69)
- 7 dubreuilh*.tw. (73)
- 8 (maligna* adj2 lentigo*).tw. (1071)
- 9 LMM.tw. (887)
- 10 or/1-9 (252664)
- 11 Sentinel Lymph Node Biopsy/ (11246)
- 12 (sentinel adj2 node*).tw. (13111)
- 13 (sentinel adj2 lymphadenectom*).tw. (356)
- 14 SLNB.tw. (1623)
- 15 or/11-14 (14975)
- 16 (breslow adj2 (thick* or depth* or scale* or level* or measur*)).tw. (1573)
- 17 Mitotic Index/ (5834)
- 18 ((mitosis or miotic or mitotic) adj2 (activit* or index* or indices or number* or rate* or ratio*)).tw. (16464)
- 19 ((neutrophil* or lymphocyte*) adj1 ratio*).tw. (5725)
- 20 NLR.tw. (5020)
- 21 Skin Ulcer/ (8877)
- 22 ulcer*.tw. (184391)
- 23 or/16-22 (215582)
- 24 exp Ultrasonography/ (440796)
- 25 (ultraso* or sonogra* or echogra* or echoscop* or echosound* or echotomogra*).tw. (356488)
- 26 Tomography, X-Ray Computed/ (383251)
- 27 ((CT or CAT) adj (scan* or imag* or examination* or x ray*)).tw. (112322)
- 28 (cine adj ct).tw. (154)

Medline Strategy, searched 27 October 2020
Database: Ovid MEDLINE(R) 1946 to October 26, 2020
Search Strategy:

29 ((comput* or electron beam) adj3 tomogra*).tw. (258004)
30 tomodensitometr*.tw. (941)
31 Positron Emission Tomography Computed Tomography/ (9816)
32 (PET adj (CT or scan* or imag* or examination*)).tw. (38793)
33 (positron adj2 tomograph*).tw. (49045)
34 or/24-33 (1089140)
35 10 and 15 and 23 (917)
36 10 and 34 (14665)
37 35 or 36 (15520)
38 limit 37 to english language (13256)
39 animals/ not humans/ (4715700)
40 38 not 39 (12822)
41 limit 40 to (letter or historical article or comment or editorial or news or case reports) (4890)
42 40 not 41 (7932)
43 limit 42 to ed=20141001-20201027 (2461)

Filters used (see section 3) - None

Review Question 3.1

3.1 What are the most effective surgical and histological excision margins for stage 0 to 2 melanoma?

Table 5: Population terms used for all searches

Medline Strategy, searched: 07/04/2021
Database: Ovid MEDLINE(R) <1946 to April 06, 2021>
Search strategy:

1 exp Melanoma/ (97661)
2 Skin Neoplasms/ (123732)
3 (melanoma* or melanocarcinoma* or naevocarcinoma* or nevocarcinoma*).tw. (106805)

Medline Strategy, searched: 07/04/2021
Database: Ovid MEDLINE(R) <1946 to April 06, 2021>
Search strategy:

- 4 ((skin or derm* or cutaneous* or epitheli* or epiderm*) adj1 (adenocarcinoma* or cancer* or carcinoma* or malignan* or neoplas* or oncolog* or tumor* or tumour*)).tw. (63123)
- 5 ((maligna* or melano*) adj2 (freckle* or lesion* or mole* or nev* or naev*)).tw. (25578)
- 6 (hutchinson* adj2 (freckle* or melano*)).tw. (69)
- 7 dubreuilh*.tw. (74)
- 8 (maligna* adj2 lentigo*).tw. (1088)
- 9 LMM.tw. (932)
- 10 or/1-9 (257387)
- 11 "Margins of Excision"/ (2849)
- 12 (excis* or margin* or surg* or remov* or resect*).tw. (2487124)
- 13 or/11-12 (2487248)
- 14 10 and 13 (43300)
- 15 animals/ not humans/ (4776418)
- 16 14 not 15 (41454)
- 17 limit 16 to "english language" (35325)
- 18 limit 17 to ed=20150101-20210407 (9408)
- 19 randomized controlled trial.pt. (526157)
- 20 randomi?ed.mp. (832300)
- 21 placebo.mp. (201160)
- 22 or/19-21 (885067)
- 23 18 and 22 (385)

Filters used (see section 3) - McMaster Balanced RCT Filter was applied to Ovid searches

Review Question 4.1

4.1 What is the most effective surgical treatment for stage 3 melanoma?

Table 5: search strategy

Medline Strategy, searched 26/04/2021

Database: Ovid MEDLINE(R) <1946 to April 23, 2021>

Search strategy:

- 1 exp Melanoma/ (97886)
- 2 Skin Neoplasms/ (123938)
- 3 (melanoma* or melanocarcinoma* or naevocarcinoma* or nevocarcinoma*).tw. (107117)
- 4 ((skin or dermat* or cutaneous* or epitheli* or epiderm*) adj1 (adenocarcinoma* or cancer* or carcinoma* or malignan* or neoplas* or oncolog* or tumor* or tumour*)).tw. (63259)
- 5 ((maligna* or melano*) adj2 (freckle* or lesion* or mole* or nev* or naev*)).tw. (25649)
- 6 (hutchinson* adj2 (freckle* or melano*)).tw. (69)
- 7 dubreuilh*.tw. (74)
- 8 (maligna* adj2 lentigo*).tw. (1090)
- 9 LMM.tw. (934)
- 10 or/1-9 (257928)
- 11 Lymph Node Excision/ (34194)
- 12 exp Lymph Nodes/ (91576)
- 13 (surg* or resect* or remov* or ablat* or operat* or excision* or excised or dissection* or lymphadenectom* or CLND* or TLND*).tw. (3034192)
- 14 or/11-13 (3106687)
- 15 10 and 14 (50104)
- 16 animals/ not humans/ (4782806)
- 17 15 not 16 (47673)
- 18 limit 17 to "english language" (40599)
- 19 randomized controlled trial.pt. (527406)
- 20 randomi?ed.mp. (834943)
- 21 placebo.mp. (201653)
- 22 or/19-21 (887781)
- 23 18 and 22 (1450)
- 24 limit 23 to ed=20150101-20210426 (440)

Filters used (see section 3) - McMaster Balanced RCT Filter was applied to Ovid searches

Review Question 4.2

4.2 Sentinel lymph node biopsy for people with stage 3 melanoma and micro-satellite lesions

Table 6: search strategy

Medline Strategy, searched 27/04/2021		
Database: Ovid MEDLINE(R) 1946 to April 23, 2021		
Search strategy:		
1	exp Melanoma/	97786
2	Skin Neoplasms/	123844
3	(melanoma* or melanocarcinoma* or naevocarcinoma* or nevocarcinoma*).tw.	106964
4	((skin or derm* or cutaneous* or epitheli* or epiderm*) adj1 (adenocarcinoma* or cancer* or carcinoma* or malignan* or neoplas* or oncolog* or tumor* or tumour*)).tw.	63197
5	((maligna* or melano*) adj2 (freckle* or lesion* or mole* or nev* or naev*)).tw.	25629
6	(hutchinson* adj2 (freckle* or melano*)).tw.	69
7	dubreuilh*.tw.	74
8	(maligna* adj2 lentigo*).tw.	1088
9	LMM.tw.	933
10	or/1-9	257674
11	Sentinel Lymph Node Biopsy/	11522
12	(sentinel adj2 node*).tw.	13465
13	(sentinel adj2 lymphadenectom*).tw.	363
14	(SLNB or SNB).tw.	3442
15	or/11-14	16534
16	(Microsatellit* or micro-satellit*).tw.	36790
17	Satellit*.tw.	24729
18	(In-transit* or Intransit* or In-tralymphatic* or Intralymphatic*).tw.	9264
19	((Small* or tiny or micro* or thin* or subcutan* or aggressive*) adj4 (lesion* or nodal* or nodule* or recurren* or re-curren* or structure* or tumour* or tumor* or deposit*)).tw.	198339
20	SITM.tw.	3
21	(Metasta* or advanc*).tw.	1083173
22	("Stage-3" or "stage3" or stage-iii or stageiii or stage-three).tw.	40982
23	or/16-22	1327299
24	10 and 15 and 23	2568
25	limit 24 to english language	2347
26	animals/ not humans/	4779874
27	25 not 26	2312
28	limit 27 to (letter or historical article or comment or editorial or news or case reports)	280
29	27 not 28	2032
30	randomized controlled trial.pt.	526759
31	randomi?ed.mp.	833628
32	placebo.mp.	201387
33	or/30-32	886424
34	Observational Studies as Topic/	6111

Medline Strategy, searched 27/04/2021	
Database: Ovid MEDLINE(R) 1946 to April 23, 2021	
Search strategy:	
35	Observational Study/ 96272
36	Epidemiologic Studies/ 8612
37	exp Case-Control Studies/ 1158898
38	exp Cohort Studies/ 2114576
39	Cross-Sectional Studies/ 360004
40	Controlled Before-After Studies/ 604
41	Historically Controlled Study/ 197
42	Interrupted Time Series Analysis/ 1183
43	Comparative Study.pt. 1887335
44	case control\$.tw. 117417
45	case series.tw. 63760
46	(cohort adj (study or studies)).tw. 188717
47	cohort analy\$.tw. 7389
48	(follow up adj (study or studies)).tw. 46419
49	(observational adj (study or studies)).tw. 94767
50	longitudinal.tw. 217345
51	prospective.tw. 520610
52	retrospective.tw. 476397
53	cross sectional.tw. 309343
54	or/34-53 4535891
55	33 or 54 5055154
56	29 and 55 1080

Filters used (see section 3) –

McMaster Balanced RCT Filter was applied to Ovid searches

Observational filter was applied to Ovid searches

Review Question 5.1

5.1 Sequencing. What is the most effective systemic and localised anticancer treatment for people with stage 4 (+ unresectable stage 3) melanoma?

Table 7: Search strategies

Medline Strategy, searched 03/12/2020	
Database: Ovid MEDLINE(R) <1946 to December 02, 2020>	
Search strategy:	
1	exp Melanoma/ (96197)
2	Skin Neoplasms/ (122179)
3	(melanoma* or melanocarcinoma* or naevocarcinoma* or nevocarcinoma*).tw. (104932)
4	((skin or derm* or cutaneous* or epitheli* or epiderm*) adj1 (adenocarcinoma* or cancer* or carcinoma* or malignan* or neoplas* or oncolog* or tumor* or tumour*)).tw. (62202)
5	((maligna* or melano*) adj2 (freckle* or lesion* or mole* or nev* or naev*)).tw. (25240)

Medline Strategy, searched 03/12/2020

Database: Ovid MEDLINE(R) <1946 to December 02, 2020>

Search strategy:

6 (hutchinson* adj2 (freckle* or melano*)).tw. (69)
 7 dubreuilh*.tw. (74)
 8 (maligna* adj2 lentigo*).tw. (1077)
 9 LMM.tw. (896)
 10 or/1-9 (253749)
 11 nivolumab/ (2740)
 12 (nivolumab* or 31yo63lbn or bms 936558 or mdx 1106 or ono 4538 or opdivo*).tw. (2935)
 13 ipilimumab/ (1985)
 14 (ipilimumab* or 6t8c155666 or anti ctla 4 mab* or "mdx 010" or mdx ctla 4 or yervoy*).tw. (2292)
 15 Vemurafenib/ (1357)
 16 (vemurafenib* or zelboraf* or rg-7204 or plx 4032 or r05185426 or 207smy3fqt).tw. (1556)
 17 (pembrolizumab* or keytruda* or mk 3475 or sch 900475 or lambrolizumab*).tw. (2153)
 18 or/11-17 (8153)
 19 (encorafenib* or braftovi* or lgx 818 or nvp lgx 818).tw. (67)
 20 (binimetinib* or mektovi* or arry 162 or arry 438162 or balimek or mek 162).tw. (99)
 21 (trametinib* or mekinist* or gsk 1120212* or jtp 74057).tw. (785)
 22 (dabrafenib* or tafinlar* or gsk 2118436*).tw. (720)
 23 or/19-22 (1187)
 24 ((regional or locoregional or "isolated limb*") adj2 (chemotherap* or infusion* or perfusion*)).tw. (5567)
 25 (ili or ilp).tw. (2716)
 26 Electrochemotherapy/ (656)
 27 (electrochemotherap* or electroporation*).tw. (9601)
 28 tvec.tw. (22)
 29 "Talimogene laherparepvec*".tw. (129)
 30 Imlygic*.tw. (18)
 31 (diphencyprone* or diphenylcyclopropenone* or DPCP).tw. (315)
 32 or/24-31 (18053)
 33 18 or 23 (8910)
 34 10 and 33 (4411)
 35 10 and 32 (1436)
 36 animals/ not humans/ (4728824)
 37 34 not 36 (4367)
 38 35 not 36 (1283)
 39 limit 37 to english language (4163)
 40 limit 38 to english language (1182)
 41 limit 39 to (letter or historical article or comment or editorial or news or case reports) (1534)
 42 limit 40 to (letter or historical article or comment or editorial or news or case reports) (180)
 43 39 not 41 (2629)
 44 40 not 42 (1002)
 45 randomized controlled trial.pt. (518015)
 46 randomi?ed.mp. (814966)
 47 placebo.mp. (198182)
 48 or/45-47 (867208)
 49 Observational Studies as Topic/ (5662)
 50 Observational Study/ (88863)
 51 Epidemiologic Studies/ (8484)

Medline Strategy, searched 03/12/2020
Database: Ovid MEDLINE(R) <1946 to December 02, 2020>
Search strategy:

52 exp Case-Control Studies/ (1123667)
53 exp Cohort Studies/ (2061901)
54 Cross-Sectional Studies/ (345417)
55 Controlled Before-After Studies/ (573)
56 Historically Controlled Study/ (192)
57 Interrupted Time Series Analysis/ (1050)
58 Comparative Study.pt. (1876925)
59 case control\$.tw. (114689)
60 case series.tw. (61390)
61 (cohort adj (study or studies)).tw. (179159)
62 cohort analy\$.tw. (7049)
63 (follow up adj (study or studies)).tw. (45782)
64 (observational adj (study or studies)).tw. (90368)
65 longitudinal.tw. (210803)
66 prospective.tw. (507642)
67 retrospective.tw. (459022)
68 cross sectional.tw. (296503)
69 or/49-68 (4450196)
70 43 and 48 (379)
71 44 and 69 (293)
72 limit 70 to ed=20130101-20201202 (330)
73 limit 71 to ed=20130101-20201202 (119)

Filters used (see section 3)

McMaster Balanced RCT Filter was applied to Lines 11-17 (Immunotherapies) and 19-22 (Combined targeted therapy for BRAF-positive melanoma) in Ovid searches

Observational filter was applied to lines 24-31 (Localised treatments for people with locoregional disease) in Ovid searches

3 Study Design Filters

Table 10: Study design filters

The study filters and limiting search strategies used as part of the literature searches are presented below.
<p>RCT</p> <ol style="list-style-type: none">1 randomized controlled trial.pt.2 randomi?ed.mp.3 placebo.mp.4 or/1-3 <p>Source: McMaster Therapy – Medline - “best balance of sensitivity and specificity” version.</p> <p>Haynes RB et al. (2005) Optimal search strategies for retrieving scientifically strong studies of treatment from Medline: analytical survey. <i>BMJ</i>, 330, 1179-1183.</p>
<p>Systematic Review</p> <ol style="list-style-type: none">1 MEDLINE or pubmed).tw.2 systematic review.tw.3 systematic review.pt.4 meta-analysis.pt.5 intervention\$.ti.6 or/1-5 <p>Source: Lee, E. et al. (2012) An optimal search filter for retrieving systematic reviews and meta-analyses. <i>BMC Medical Research Methodology</i>, 12(1), 51.</p> <p>In MEDLINE, the standard NICE modifications were used: pubmed.tw added; systematic review.pt added from MeSH update 2019.</p>
<p>Observational</p> <ol style="list-style-type: none">1. Observational Studies as Topic/2. Observational Study/3. Epidemiologic Studies/4. exp Case-Control Studies/5. exp Cohort Studies/6. Cross-Sectional Studies/7. Controlled Before-After Studies/8. Historically Controlled Study/9. Interrupted Time Series Analysis/10. Comparative Study.pt.11. case control\$.tw.12. case series.tw.13. (cohort adj (study or studies)).tw.14. cohort analy\$.tw.15. (follow up adj (study or studies)).tw.16. (observational adj (study or studies)).tw.17. longitudinal.tw.18. prospective.tw.19. retrospective.tw.20. cross sectional.tw.

The study filters and limiting search strategies used as part of the literature searches are presented below.

21. or/1-20

4 Health Economics Search Strategies

Economic evaluations and quality of life data

Sources searched to identify economic evaluations

- Econlit (Ovid)
- Embase (Ovid)
- HTA database (CRD)
- MEDLINE (Ovid)
- MEDLINE In-Process (Ovid)
- NHS EED (Wiley)

A single search to identify economic evidence was run on 12th February 2020 and re run on 13th April 2021.

Table 11: Economic evidence search

Medline Strategy, searched 10/08/2020	
Database: Ovid MEDLINE(R) ALL 1946 to August 07, 2020	
Search Strategy:	
1	exp Melanoma/ (95096)
2	Skin Neoplasms/ (121058)
3	(melanoma* or melanocarcinoma* or naevocarcinoma* or nevocarcinoma*).tw. (116860)
4	((skin or dermat* or cutaneous* or epitheli* or epiderm*) adj1 (adenocarcinoma* or cancer* or carcinoma* or malignan* or neoplas* or oncolog* or tumor* or tumour*)).tw. (68859)
5	((maligna* or melano*) adj2 (freckle* or lesion* or mole* or nev* or naev*)).tw. (28425)
6	(hutchinson* adj2 (freckle* or melano*)).tw. (71)
7	dubreuilh*.tw. (72)
8	(maligna* adj2 lentigo*).tw. (1159)
9	LMM.tw. (1078)
10	or/1-9 (272944)
11	Economics/ (27211)
12	exp "Costs and Cost Analysis"/ (237411)
13	Economics, Dental/ (1911)
14	exp Economics, Hospital/ (24592)
15	exp Economics, Medical/ (14208)
16	Economics, Nursing/ (3999)
17	Economics, Pharmaceutical/ (2942)

Medline Strategy, searched 10/08/2020
Database: Ovid MEDLINE(R) ALL 1946 to August 07, 2020
Search Strategy:

- 18 Budgets/ (11326)
- 19 exp Models, Economic/ (15090)
- 20 Markov Chains/ (14357)
- 21 Monte Carlo Method/ (28376)
- 22 Decision Trees/ (11152)
- 23 econom\$.tw. (294015)
- 24 cba.tw. (10291)
- 25 cea.tw. (22909)
- 26 cua.tw. (1217)
- 27 markov\$.tw. (24598)
- 28 (monte adj carlo).tw. (48506)
- 29 (decision adj3 (tree\$ or analys\$)).tw. (16667)
- 30 (cost or costs or costing\$ or costly or costed).tw. (575926)
- 31 (price\$ or pricing\$).tw. (40656)
- 32 budget\$.tw. (29438)
- 33 expenditure\$.tw. (57180)
- 34 (value adj3 (money or monetary)).tw. (2534)
- 35 (pharmacoeconomic\$ or (pharmacoeconomic\$)).tw. (4053)
- 36 or/11-35 (1124805)
- 37 "Quality of Life"/ (195373)
- 38 quality of life.tw. (278787)
- 39 "Value of Life"/ (5708)
- 40 Quality-Adjusted Life Years/ (12333)
- 41 quality adjusted life.tw. (13013)
- 42 (qaly\$ or qald\$ or qale\$ or qtime\$).tw. (10728)
- 43 disability adjusted life.tw. (3388)
- 44 daly\$.tw. (3073)
- 45 Health Status Indicators/ (23426)
- 46 (sf36 or sf 36 or short form 36 or shortform 36 or sf thirtysix or sf thirty six or shortform thirtysix or shortform thirty six or short form thirtysix or short form thirty six).tw. (25747)

Medline Strategy, searched 10/08/2020

Database: Ovid MEDLINE(R) ALL 1946 to August 07, 2020

Search Strategy:

- 47 (sf6 or sf 6 or short form 6 or shortform 6 or sf six or sfsix or shortform six or short form six).tw. (2157)
- 48 (sf12 or sf 12 or short form 12 or shortform 12 or sf twelve or sftwelve or shortform twelve or short form twelve).tw. (5880)
- 49 (sf16 or sf 16 or short form 16 or shortform 16 or sf sixteen or sfsixteen or shortform sixteen or short form sixteen).tw. (35)
- 50 (sf20 or sf 20 or short form 20 or shortform 20 or sf twenty or sftwenty or shortform twenty or short form twenty).tw. (406)
- 51 (euroqol or euro qol or eq5d or eq 5d).tw. (11200)
- 52 (qol or hql or hqol or hrqol).tw. (53514)
- 53 (hye or hyes).tw. (69)
- 54 health\$ year\$ equivalent\$.tw. (40)
- 55 utilit\$.tw. (209346)
- 56 (hui or hui1 or hui2 or hui3).tw. (1532)
- 57 disutili\$.tw. (469)
- 58 rosser.tw. (98)
- 59 quality of wellbeing.tw. (24)
- 60 quality of well-being.tw. (419)
- 61 qwbtw. (206)
- 62 willingness to pay.tw. (5677)
- 63 standard gamble\$.tw. (855)
- 64 time trade off.tw. (1179)
- 65 time tradeoff.tw. (251)
- 66 tto.tw. (1065)
- 67 or/37-66 (582670)
- 68 36 or 67 (1627056)
- 69 10 and 68 (9314)
- 70 limit 69 to english language (8670)
- 71 animals/ not humans/ (4690899)
- 72 70 not 71 (8322)
- 73 limit 72 to (letter or historical article or comment or editorial or news or case reports) (820)
- 74 72 not 73 (7502)

Medline Strategy, searched 10/08/2020
Database: Ovid MEDLINE(R) ALL 1946 to August 07, 2020
Search Strategy:

75 limit 74 to ed=20141010-20200810 (2482)