3-year scoping report

Topic: Cutaneous melanoma: literature published since SIGN 146 was published in 2017

Date of search: September 2019

Searched by: Julie Calvert

Key concepts: melanoma

Summary of findings

The purpose of this 3-year scoping is to establish what evidence has been published since the publication of SIGN 146, 2017, that could effect the existing recommendations or require the addition of recommendations and whether any sections of the guideline require updating. A rapid search of the literature was conducted, using a predefined list of resources.

Relevant evidence and implications for SIGN recommendations

Relevant evidence is organised by SIGN section in the tables below.

SIGN section 4.5 Biopsy of suspicious lesions

Reference	Details	How does this potentially change current recommendations?
GUIDELINE Coit et al. Melanoma. Version 3.2018. In National Comprehensive	For an initial biopsy for suspicious lesions there should be a narrow excision of entire suspicious lesion with 1-3 mm borders of normal skin and cuff of fat	SIGN recommends that a suspected melanoma should be excised with a 2 mm margin and a cuff of fat.

Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (2018). Reported in Dynamed, Melanoma		*SIGN should consider whether the recommended excision size needs to be changed.*

SIGN section 5.2 Staging melanoma

Reference	Details	How does this potentially change current recommendations?
GUIDANCE Amin et al, eds AJCC Cancer Staging Manual. 8th ed. New York: Springer International Publishing; 2017. Reported in: 2019 NICE surveillance of Melanoma: assessment and management (NICE guideline NG14, 2015)	To update the melanoma staging system of the American Joint Committee on Cancer (AJCC) a large database was assembled comprising >46,000 patients from 10 centers worldwide with stages I, II, and III melanoma diagnosed since 1998. Based on analyses of this new database, the existing seventh edition AJCC stage IV database, and contemporary clinical trial data, the AJCC Melanoma Expert Panel introduced several important changes to the Tumor, Nodes, Metastasis (TNM) classification and stage grouping criteria. Key changes in the eighth edition AJCC Cancer Staging Manual include: 1) tumor thickness measurements to be recorded to the nearest 0.1 mm, not 0.01 mm; 2) definitions of T1a and T1b are revised (T1a, <0.8 mm without ulceration; T1b, 0.8-1.0 mm with or without ulceration or <0.8 mm with ulceration), with mitotic rate no longer a T category criterion; 3) pathological (but not clinical) stage IA is revised to include T1b N0 M0 (formerly pathologic stage IB); 4) the N category descriptors "microscopic" and "macroscopic" for regional node metastasis are redefined as "clinically occult" and "clinically apparent"; 5) prognostic stage III groupings are based on N category criteria and T category criteria (ie, primary tumor thickness and ulceration) and increased from 3 to 4 subgroups (stages IIIA-IIID); 6) definitions of N subcategories are revised, with the presence of microsatellites, satellites, or in-transit metastases now categorized as N1c, N2c, or N3c based on the number of tumor-involved regional lymph nodes, if any; 7) descriptors are added to	This was also highlighted by the chair of the guideline group: ‘New TNM staging classification has been released which makes changes to previous version with resulting change in practice’ *SIGN should consider the new staging system and whether or not it should be included in the guideline.*

	each M1 subcategory designation for lactate dehydrogenase (LDH) level (LDH elevation no longer upstages to M1c); and 8) a new M1d designation is added for central nervous system metastases.	

SIGN section 5.3.2 Management of non-palpable lymph nodes

Reference	Details	How does this potentially change current recommendations?
Amin et al, eds AJCC Cancer Staging Manual. 8th ed. New York: Springer International Publishing; 2017.	New melanoma staging system of the American Joint Committee on Cancer (AJCC) Described above	Highlighted by chair *SIGN should consider the indication for SLNB to match new TNM*
GUIDELINE SURVEILLANCE REPORT 2019 NICE surveillance of melanoma: assessment and management (NICE guideline NG14, 2015).	The NICE document reports new evidence around survival following CLND, which has been published in the last few years These studies indicated that CLND may be of only limited survival benefit. The findings from several observational studies also comparing CLND with observation, were more variable. Included evidence on completion lymphadenectomy published after 2016 in the surveillance report are listed below. **Secondary** Delgado, 2017: This systematic review and meta-analysis estimated survival after immediate complete lymph node dissection (CLND) compared to observation only (OO) or delayed CLND in patients with melanoma and lymph node metastasis. The 4 included RCTs demonstrated no significant difference in melanoma-specific survival (MSS) (HR=0.91, 95% CI=0.77-1.08, p=0.29). In a sensitivity analysis, MSS was higher after immediate CLND compared to delayed CLND in patients with nodal	SIGN 146 states there is 'no good-quality evidence …to determine whether completion lymphadenectomy provides better survival than clinical observation with or without serial ultrasound.' The recommendation is that 'patients with a positive sentinel lymph node should be offered appropriate counselling regarding the advantages and disadvantages of completion lymphadenectomy. This recent meta-analysis suggested that CLND appears to have no additional survival benefit after SNB compared to OO. However, subgroup analysis suggests a time-dependent benefit for early surgical lymph node removal compared to delayed or none.

	metastasis (HR=0.63, 95% CI=0.35-0.74, p=0.0004) without evidence of heterogeneity. **Primary** Leiter, 2016: The DeCOG-SLT multicentre phase III RCT compared CLND (intention to treat n=240) with observation (intention to treat n=233) in patients with cutaneous melanoma following positive SLNB. The primary endpoint was distant metastasis free survival, with a median follow-up of 35 months. The trial was stated by the study authors to be underpowered as it closed early (December 2014) due to enrolment difficulties and a low event rate. Three-year distant metastasis-free survival was similar between people who had CLND compared with those in the observation group. Faries, 2017: CLND was not associated with increased melanoma-specific survival among 1934 patients with data that could be evaluated in an intention-to-treat analysis or among 1755 patients in the per-protocol analysis. In the per-protocol analysis, the mean (±SE) 3-year rate of melanoma-specific survival was similar in the dissection group and the observation group (86±1.3% and 86±1.2%, respectively; P=0.42 by the log-rank test) at a median follow-up of 43 months. The rate of disease-free survival was slightly higher in the dissection group than in the observation group (68±1.7% and 63±1.7%, respectively; P=0.05 by the log-rank test) at 3 years, based on an increased rate of disease control in the regional nodes at 3 years (92±1.0% vs. 77±1.5%; P<0.001 by the log-rank test); these results must be interpreted with caution. Nonsentinel-node metastases, identified in 11.5% of the patients in the dissection group, were a strong, independent prognostic factor for	This recent RCT suggested that CLND appears to have no additional survival benefit compared to OO. However, there were methodological difficulties associated with this study including being underpowered. This recent RCT suggested that CLND increased the rate of regional disease control and provided prognostic information but did not increase melanoma-specific survival among patients with melanoma and sentinel-node metastases.

	recurrence (hazard ratio, 1.78; P=0.005). Lymphedema was observed in 24.1% of the patients in the dissection group and in 6.3% of those in the observation group. Immediate completion lymph-node dissection increased the rate of regional disease control and provided prognostic information but did not increase melanoma-specific survival among patients with melanoma and sentinel-node metastases Mosquedo, 2017: A retrospective observational study (n=2172) compared CLND and observation in melanoma patients with intermediate thickness tumours and positive SLNB. Survival analysis and Cox regression analysis showed that CLND was not associated with improved survival. Lee, 2016: An observational study compared the survival of people with SLNB-positive melanoma who received immediate CLND (n=375) and an observation group who did not have immediate CLND (n=96). The immediate CLND group was younger and had more sentinel lymph nodes removed. Compared with observation, people who had undergone CLND had significantly better 5-year nodal recurrence-free survival. Five-year and 10-year distant metastasis-free survival did not differ between groups. However, people who had CLND had better 5-year and 10-year melanoma-specific survival than those who did not have the procedure. Persa, 2018: A single centre retrospective observational study examined the effect of CLND compared with observation following SLNB in melanoma patients with multiple positive (n=78) and one positive (n=197) sentinel lymph nodes. Among those with multiple positive sentinel	This recent observational study suggested that CLND was not associated with improved survival. This recent observational study suggested that CLND was associated with improved 5-year and 10-year melanoma specific survival. This recent RCT suggested that CLND was not associated with improved survival.

	lymph nodes, CLND did not result in significantly better melanoma-specific survival or progression free survival. Fritsch, 2016: A retrospective database analysis compared 5-year disease-specific survival between people with sentinel lymph node positive cutaneous melanoma of the head and neck who underwent CLND (n=210) and those who deferred the procedure (n=140). In the subgroup with the lowest risk of non-sentinel lymph node metastasis, younger people who received CLND had significantly better survival than people who received SLNB only. However, among those with a higher risk of nonsentinel lymph node metastasis, survival was similar between groups.	This recent database analysis suggested that CLND was associated with improved 5-year and 10-year melanoma specific survival. *SIGN may wish to review this evidence and consider including it in the guideline.* *SIGN may wish to consider which patient groups would benefit from CLND treatment and which would have no benefit.*
SYSTEMATIC REVIEW AND META-ANALYSIS Angeles et al. Meta-analysis of completion lymph node dissection in sentinel lymph node-positive melanoma. Br J Surg 2019 May;106(6):672 Reported in Dynamed, Melanoma	This systematic review and meta-analysis included 15 studies, 3 of which were reported in the 2019 NICE surveillance reported above (Leiter, 2016; Faries, 2017; Lee, 2016) and only 2 other included studies were 2016 or later. In patients with sentinel lymph node-positive melanoma, completion lymph node dissection may not decrease mortality or risk of recurrence compared to nodal basin observation alone based on systematic review limited by significant heterogeneity systematic review of 13 observational studies and 2 randomized trials (MSLT-II and DeCOG-SLT trials) comparing completion lymph node dissection vs. nodal basin observation alone in 10,096 patients with sentinel lymph node-positive melanoma follow-up ranged from 23 to 80 months reporting data all results limited by significant heterogeneity no significant differences in mortality (risk	SIGN 146 states there is 'no good-quality evidence …to determine whether completion lymphadenectomy provides better survival than clinical observation with or without serial ultrasound.' The recommendation is that 'patients with a positive sentinel lymph node should be offered appropriate counselling regarding the advantages and disadvantages of completion lymphadenectomy. This recent meta-analysis suggests that completion lymph node dissection may not decrease mortality or risk of recurrence compared to nodal basin observation.

	ratio 0.85, 95% CI 0.71-1.02) in analysis of 7 cohort studies and 1 trial with 4,649 patients risk of recurrence (risk ratio 0.91, 95% CI 0.79-1.05) in analysis of 8 cohort studies and 2 trials with 4,337 patients	*SIGN may wish to include this evidence in the guideline.*
GUIDELINE Wong et al. Sentinel Lymph Node Biopsy and Management of Regional Lymph Nodes in Melanoma: American Society of Clinical Oncology and Society of Surgical Oncology Clinical Practice Guideline Update. Ann Surg Oncol 2018 Feb;25(2):356 Reported in Dynamed, Melanoma	American Society of Clinical Oncology and Society of Surgical Oncology recommendations on sentinel lymph node biopsy (SLNB) after cutaneous melanoma diagnosis: • perform SLN biopsy on patients with cutaneous melanomas of Breslow thickness 1-4 mm • SLN biopsy may be recommended for T4 melanomas (> 4 mm in Breslow thickness) after discussion of risks and benefits • SLN biopsy may be recommended for T1b melanomas (0.8 to 1.0 mm Breslow thickness or < 0.8 mm Breslow thickness with ulceration) after discussion of risks and benefits • routine SLN biopsy is not recommended for T1a melanomas (< 0.8 mm in Breslow thickness and nonulcerated) • for positive SLN biopsy with low-risk micrometastatic disease, options include completion lymph node dissection (CLND) or careful observation	SIGN states that SLNB should not be offered to patients with stage 1B melanoma where Breslow thickness is ≤1mm *SIGN may wish to consider this guideline and the evidence underpinning this recommendation.*

SIGN section 6.1 Imaging techniques

Reference	**Details**	**How does this potentially change current recommendations?**
Amin et al, eds AJCC Cancer Staging Manual. 8th ed. New York: Springer International Publishing; 2017.	New melanoma staging system of the American Joint Committee on Cancer (AJCC) Described above	Highlighted by chair *SIGN could consider reviewing this section to match new TNM*

SIGN guideline section 7.2 Immunotherapy

Reference	Details	How does this potentially change current recommendations?
RCT Eggermont et al. Adjuvant Pembrolizumab versus Placebo in Resected Stage III Melanoma. N Engl J Med. 2018 May 10;378(19):1789-1801. Epub 2018 Apr 15. Reported in: BMJ Best practice, Melanoma.	A BMJ BP document reported a phase 3 double-blind trial to evaluate pembrolizumab as adjuvant therapy in patients with resected, high-risk stage III melanoma. Pembrolizumab (514 patients) or placebo (505 patients) was given intravenously every 3 weeks for a total of 18 doses (approximately 1 year) or until disease recurrence or unacceptable toxic effects occurred. At a median follow-up of 15 months, pembrolizumab was associated with significantly longer recurrence-free survival than placebo in the overall intention-to-treat population (1-year rate of recurrence-free survival, 75.4% [95% confidence interval {CI}, 71.3 to 78.9] vs. 61.0% [95% CI, 56.5 to 65.1]; hazard ratio for recurrence or death, 0.57; 98.4% CI, 0.43 to 0.74; P<0.001) and in the subgroup of 853 patients with PD-L1-positive tumors (1-year rate of recurrence-free survival, 77.1% [95% CI, 72.7 to 80.9] in the pembrolizumab group and 62.6% [95% CI, 57.7 to 67.0] in the placebo group; hazard ratio, 0.54; 95% CI, 0.42 to 0.69; P<0.001). Adverse events of grades 3 to 5 that were related to the trial regimen were reported in 14.7% of the patients in the pembrolizumab group and in 3.4% of patients in the placebo group. There was one treatment-related death due to myositis in the pembrolizumab group.	SIGN currently states that a number of well-designed trials of adjuvant immunotherapy (including ipilmumab, nivolumab and pembrolizumab) are ongoing (for adjuvant treatment of stage II and III melanoma). This is a recent RCT which showed a benefit of pembrolizumab. NB it was a phase 3 trial. *SIGN could consider adding Pembrolizumab for the treatment of completely resected Stage III melanoma in adults.*
NICE TA Pembrolizumab for adjuvant treatment of resected	Pembrolizumab is recommended for use within the Cancer Drugs Fund as an option for the adjuvant treatment of stage III melanoma with lymph node involvement in adults who have had complete resection.	SIGN currently states that a number of well-designed trials of adjuvant immunotherapy (including ipilmumab, nivolumab and pembrolizumab) are

melanoma with high risk of recurrence Technology appraisal guidance [TA553] Published date: 19 December 2018	SMC (May 2019) approved Pembrolizumab as monotherapy for the adjuvant treatment of adults with Stage III melanoma and lymph node involvement who have undergone complete resection.	ongoing (for adjuvant treatment of stage II and III melanoma). *SIGN could consider adding Pembrolizumab for the treatment of completely resected melanoma in adults with lymph node involvement.*
RCT Weber J et al. Adjuvant Nivolumab versus Ipilimumab in Resected Stage III or IV Melanoma. N Engl J Med. 2017 Nov 9;377(19):1824-1835. Epub 2017 Sep 10. Reported in: BMJ Best practice, Melanoma.	A BMJ BP document reported a double-blind, phase 3 trial to determine the efficacy of nivolumab versus ipilimumab for adjuvant therapy in patients with resected advanced melanoma. 906 patients (≥15 years of age) who were undergoing complete resection of stage IIIB, IIIC, or IV melanoma received an intravenous infusion of either nivolumab at a dose of 3 mg per kilogram of body weight every 2 weeks (453 patients) or ipilimumab at a dose of 10 mg per kilogram every 3 weeks for four doses and then every 12 weeks (453 patients). The patients were treated for a period of up to 1 year or until disease recurrence, a report of unacceptable toxic effects, or withdrawal of consent. The primary end point was recurrence-free survival in the intention-to-treat population. At a minimum follow-up of 18 months, the 12-month rate of recurrence-free survival was 70.5% (95% confidence interval [CI], 66.1 to 74.5) in the nivolumab group and 60.8% (95% CI, 56.0 to 65.2) in the ipilimumab group (hazard ratio for disease recurrence or death, 0.65; 97.56% CI, 0.51 to 0.83; P<0.001). Treatment-related grade 3 or 4 adverse events were reported in 14.4% of the patients in the nivolumab group and in 45.9% of those in the ipilimumab group; treatment was discontinued because of any adverse event in 9.7% and 42.6% of the patients, respectively. Two deaths (0.4%) related to toxic effects were reported in the ipilimumab group more than 100 days after treatment. Among patients undergoing resection of stage IIIB, IIIC, or IV melanoma, adjuvant therapy with nivolumab resulted in significantly longer recurrence-free survival and a lower rate of	SIGN 146 states that a number of well-designed trials of adjuvant immunotherapy are ongoing. This is a recent RCT which showed a benefit of nivolumab compared to ipilimumab. NB it was a phase 3 trial. *SIGN may wish to include*

	grade 3 or 4 adverse events than adjuvant therapy with ipilimumab.	
NICE TA Nivolumab for adjuvant treatment of completely resected melanoma with lymph node involvement or metastatic disease Technology appraisal guidance [TA558] Published date: 23 January 2019	Nivolumab is recommended for use within the Cancer Drugs Fund as an option for the adjuvant treatment of completely resected melanoma in adults with lymph node involvement or metastatic disease. SMC (Dec, 2018) approved nivolumab As monotherapy for the adjuvant treatment of adults with melanoma with involvement of lymph nodes or metastatic disease who have undergone complete resection.	SIGN recommends nivolumab monotherapy or ipilimumab/nivolumab combination therapy are recommended for patients with unresectable stage IIIC and IV melanoma. *As above, SIGN could consider adding nivolumab for the treatment of completely resected melanoma in adults with lymph node involvement or metastatic disease.*

8.7.2 Surveillance Imaging

Reference	Details	How does this potentially change current recommendations?
References above relating to the use of adjuvant therapy	As above	The chair highlighted: *Should SIGN recommend now that adjuvant therapy is used?*

SIGN section 9.3.1 BRAF AND MEK inhibitors

Reference	Details	How does this potentially change current recommendations?
NICE TA Dabrafenib with trametinib for adjuvant treatment of resected BRAF V600 mutation-positive melanoma Technology appraisal	Dabrafenib with trametinib is recommended as an option for the adjuvant treatment of resected stage III BRAF V600 mutation-positive melanoma in adults SMC (Feb, 2019) approved dabrafenib In combination with trametinib for the adjuvant treatment of adult	SIGN recommends that Trametinib in combination with dabrafenib is recommended for patients with unresectable stage IIIC or stage IV melanoma with a BRAF V600 mutation.

guidance Published: 17 October 2018	patients with Stage III melanoma with a BRAF V600 mutation, following complete resection.	*SIGN could consider adding this combination for the treatment of resected stage III BRAF V600 mutation-positive melanoma*

SIGN section 9.3 systemic therapy

Reference	Details	How does this potentially change current recommendations?
RCT Ascierto et al. Ipilimumab 3 mg/kg in patients with unresectable or metastatic melanoma: a randomised, double-blind, multicentre, phase 3 trial. Lancet Oncol 2017 May;18(5):611 Reported in: Dynamed, Melanoma	Ipilimumab 10 mg/kg improves overall survival but increases risk of serious adverse events compared to ipilimumab 3 mg/kg in patients with advanced melanoma based on randomized trial 727 adults (mean age 62 years, 62% men) with treated or untreated unresectable stage III or IV melanoma and no previous treatment with BRAF inhibitors, CTLA-4 or PD-1 antagonists, or PD-L1 or CD137 agonists were randomized to ipilimumab 10 mg/kg vs. 3 mg/kg IV every 3 weeks for 12 weeks or until disease progression, unacceptable toxicity, or withdrawal of consent, patients with brain metastases with symptoms or requiring treatment, primary ocular melanoma, history of autoimmune disease, uncontrolled infectious disease, immunodeficiency disease, splenectomy, splenic irradiation, or previous allogenic stem cell transplantation were excluded. Patients who progressed after first 12 weeks of treatment were eligible for retreatment with study drug per original dosing scheme crossover or reduction of ipilimumab dose not permitted health-related quality of life was assessed using European Organisation for Research and Treatment of Cancer (EORTC) QLQ-C30 questionnaire version 3 (scale 0-100 points, with higher scores indicating improved quality of life; minimum clinically important difference 10 points) median follow-up 14.5 months in 10 mg/kg group and 11.2 months in 3 mg/kg group	SIGN recommends that ipilimumab, pembrolizumab and nivolumab monotherapy or ipilimumab/nivolumab combination therapy are recommended for patients with unresectable stage IIIC and IV melanoma. *SIGN do not mention dose in the text or recommendation and may wish to consider adding this information to recommendations*

	all patients included in analysis survival outcomes comparing ipilimumab 10 mg/kg vs. ipilimumab 3 mg/kg median overall survival 15.7 months vs. 11.5 months (hazard ratio for death 0.84, 95% CI 0.7-0.99) 1-year overall survival 54.3% vs. 47.6% (no p value reported) 2-year overall survival 38.5% vs. 31% (no p value reported) 3-year overall survival 31.2% vs. 23.2% (no p value reported) mean reduction in EORTC QLQ-C30 score at 12 weeks 13.26 points with ipilimumab 10 mg/kg vs. 8.07 points with ipilimumab 3 mg/kg (no p value reported) adverse events comparing ipilimumab 10 mg/kg vs. ipilimumab 3 mg/kg any treatment-related adverse event in 79% vs. 63% (no p value reported) treatment-related serious adverse events in 37% vs. 18% (no p value reported) treatment discontinuation due to adverse events in 31% vs. 19% (no p value reported) most common adverse events were diarrhea, colitis, increased aminotransferase levels, and hypophysitis	

Evidence sources

Resource	Results
Previous HIS projects on this topic	None
BMJ Best Practice	Melanoma https://bestpractice.bmj.com/topics/en-us/268
Dynamed	Melanoma https://www.dynamed.com/condition/melanoma/
TRIP	Melanoma https://www.tripdatabase.com/search?criteria=melanoma
UK guidance	
NICE	Surveillance of melanoma: assessment and management (NICE guideline NG14, 2015). 2019

	https://www.nice.org.uk/guidance/ng14/evidence/appendix-a1-and-a2-summary-of-evidence-from-surveillance-ng14-and-csg8-pdf-6782714462 Dabrafenib with trametinib for adjuvant treatment of resected BRAF V600 mutation-positive melanoma Technology appraisal guidance Published: 17 October 2018 https://www.nice.org.uk/guidance/TA544 Nivolumab for adjuvant treatment of completely resected melanoma with lymph node involvement or metastatic disease Technology appraisal guidance [TA558] Published date: 23 January 2019 https://www.nice.org.uk/guidance/ta558 Pembrolizumab for adjuvant treatment of resected melanoma with high risk of recurrence Technology appraisal guidance [TA553] Published date: 19 December 2018 https://www.nice.org.uk/guidance/ta553
Guidelines International Network (GIN)	None
Other	For information, as recommended by chair of guideline group The Current Role of Sentinel Lymph Node Biopsy in the Management of Cutaneous Melanoma – a UK Consensus Statement based on a multi-disciplinary meeting held in Cambridge, UK on 17 May 2018 https://melanomafocus.com/wp-content/uploads/2019/01/SNB-Consensus-Final-1.pdf
Secondary literature and economic evaluations	
Cochrane library	None

Concluding remarks

The literature search has identified a recent NICE surveillance report as well as a Dynamed summary, and BMJ Practice report that provided some recent evidence which may influence changes to SIGN's recommendations. In particular, the new TNM staging classification and survival following CLND as well as the recent trials on adjuvant immunotherapy and BRAF AND MEK inhibitors should be considered.

Consultation

Specialist review

This topic exploration was reviewed by the group responsible for developing SIGN146 *Cutaneous melanoma*, who were asked to comment primarily on the comprehensiveness and accuracy of the summary of findings and whether there is sufficient new evidence to warrant a refresh of the guideline. Guideline development group membership can be found in section 14.2 of the guideline.

In addition to the evidence included above, one former GDG member also stated that SIGN should consider the evidence on imaging for staging and the surveillance of melanoma contained in the recently updated National Comprehensive Cancer Network guideline.

Conclusion

In conclusion, the 3-year scoping review has highlighted a number of topics (biopsy of suspicious lesions, a new staging classification for melanoma, management of non-palpable lymph nodes, imaging techniques and staging, immunotherapy, BRAF and MEK inhibitors, and systemic therapy with ipilimumab) for which there is new evidence that could potentially change existing recommendations within the guideline or add new recommendations. This new evidence requires consideration with a view to updating SIGN 146. Most of these topics were also identified independently by the Chair of the previous SIGN guideline development group who considered that an update was required.

Outcome

The recommendation to the Guideline Programme Advisory Group is that SIGN 146 is that some recommendations will change in the light of the new evidence and selected elements of the guideline should be reviewed.

Decision

The recommendation was ratified by the Guideline Programme Advisory Group on 19 February 2020.

This guideline is in need of review and has been accepted onto the new Evidence directorate topic selection process