

National Institute for Health and Care Excellence

Surveillance programme

Surveillance proposal consultation document

Psoriasis: assessment and management NICE guideline CG153 – 4-year surveillance review

Background information

Guideline issue date: October 2012

2-year surveillance review: no update

Surveillance proposal for consultation

We propose to not update the NICE guideline on [psoriasis](#) at this time.

During surveillance editorial or factual amendments were identified. Details are included in the [amendments](#) section of appendix A: summary of evidence from surveillance.

Reason for the proposal

Assessing the evidence

We found 76 relevant studies in a search for randomised controlled trials and systematic reviews published between 1 June 2014 and 12 July 2016. We also included 3 relevant studies from a total of 12 identified by members of the guideline committee who originally worked on this guideline.

We also considered evidence identified in previous surveillance 2 years after publication of the guideline. This included 12 studies identified by search.

From all sources, we considered 91 studies to be relevant to the guideline.

We found evidence in the following areas that could potentially add to existing recommendations: the effect of weight loss through diet and exercise on psoriasis; a medicated adhesive plaster containing betamethasone valerate (a potent corticosteroid); and a foam formulation of calcipotriol monohydrate plus betamethasone dipropionate. However, we have decided to await further evidence before considering an update. In making this decision, it was noted that the guideline in its current form does not preclude the use of these interventions. Additionally, the interventions are broadly covered by existing recommendations to offer healthy lifestyle information in line with NICE guidance on obesity and physical activity, to offer a potent corticosteroid, and to offer a combined product containing calcipotriol monohydrate and betamethasone dipropionate.

We also found evidence that could affect NICE's recommendations on the use of biological agents for psoriasis. However, recommendations on the first-line use of biological agents are covered by NICE technology appraisals. Review of technology appraisals is outside the remit of the surveillance process, therefore information has been passed to the NICE technology appraisals team for consideration as part of a review proposal process. Knowing the outcome of this process would be beneficial before any updates to the NICE guideline on psoriasis are considered.

We also identified other areas where evidence was not consistent with, or not covered by, current recommendations, but the evidence was not considered to impact on the guideline at this time. See [appendix A](#) for full details of all evidence considered and a discussion of the impact on recommendations.

We did not find any evidence related to risk of skin cancer with coal tar, phototherapy, or systemic non-biological or biological therapy.

For any evidence relating to published or ongoing NICE technology appraisals, the guideline surveillance review deferred to the technology appraisal decision. This included evidence on apremilast, adalimumab, briakinumab, brodalumab, dimethyl fumarate, etanercept, infliximab, ixekizumab, secukinumab, tildrakizumab, tofacitinib and ustekinumab.

All other evidence was deemed consistent with current recommendations.

Research recommendations

At 4-year and 8-year surveillance reviews of guidelines published after 2011, we assess progress made against prioritised research recommendations. See the [research recommendations](#) section of appendix A for further information.

For this surveillance review we assessed 5 prioritised research recommendations, and proposed that none should be removed from the NICE version of the guideline and the [NICE research recommendations database](#).

Equalities

No equalities issues were identified during the surveillance process.

Overall proposed decision

After considering all the evidence and views of topic experts, we propose to not update this guideline. However, we propose to make a number of editorial and factual amendments to the guideline, including links and referrals to NICE and non-NICE guidance, and drug safety and prescribing information. See the [amendments](#) section of appendix A for details.

Further information

See [appendix A](#): summary of evidence from surveillance below for further information.

For details of the process and update decisions that are available, see [ensuring that published guidelines are current and accurate](#) in developing NICE guidelines: the manual.

Appendix A: summary of evidence from surveillance

4-year surveillance – [Psoriasis: assessment and management](#) (2012) NICE guideline CG153

Summary of evidence from surveillance

[Principles of care](#)

153 – 01 What strategies can best support people with psoriasis (all types) to self-manage the condition effectively?

Recommendations derived from this review question

- 1.1.1.1 Offer people with any type of psoriasis (and their families or carers), support and information tailored to suit their individual needs and circumstances, in a range of different formats so they can confidently understand:
- their diagnosis and treatment options
 - relevant lifestyle risk factors
 - when and how to treat their condition
 - how to use prescribed treatments safely and effectively (for example, how to apply topical treatments, how to minimise the risk of side effects through monitoring for safety of medicines)
 - when and how to seek further general or specialist review
 - strategies to deal with the impact on their physical, psychological and social wellbeing.
- 1.1.1.2 When offering treatments to a person with any type of psoriasis:
- ensure the treatment strategy is developed to meet the person's health goals so that the impact of their condition is minimised and use relevant assessment tools to ensure these goals are met
 - take into account the age and individual circumstances of the person, disease phenotype, severity and impact, co-existing psoriatic arthritis, comorbidities and previous treatment history
 - discuss the risks and benefits of treatment options with the person (and their families or carers where appropriate). Where possible use absolute risk and natural frequency^a
 - discuss the importance of adherence to treatment for optimising outcomes.
- For more information about involving patients in decisions and supporting adherence see [Medicines adherence](#) (NICE clinical guideline 76).
- 1.1.1.3 Assess whether support and information need updating or revising at every review or interaction with the person, in particular:
- during transition from children's services to adult services
 - when new interventions become available
 - when the person's disease severity or circumstances (for example, in terms of comorbidities or lifestyle) change.
- 1.1.1.4 Provide a single point of contact to help people with all types of psoriasis (and their families or carers where appropriate) access appropriate information and advice about their condition and the services available at each stage of the care pathway.

1.1.1.5 NICE has produced guidance on the components of good patient experience in adult NHS services. All healthcare professionals should follow the recommendations in [Patient experience in adult NHS services](#) (NICE clinical guideline 138).

a See [appendix B](#) for details of the risk-benefit profiles of interventions recommended in this guideline.

Surveillance decision

This review question should be not updated.

Decision aids

2-year Evidence Update

No relevant evidence was identified.

4-year surveillance summary

No relevant evidence was identified.

Topic expert feedback

Topic experts noted the use of decision aids to support guideline implementation, and the importance of providing accessible data for use by clinicians/patients to support recommendations and treatment choice.

They also noted that the table on risk/benefit of treatments in CG153 ([Appendix B](#) of the NICE version/[Appendix S](#) of the full version) does not include information on the latest technology appraisals of biologics. They also noted that visibility of and access to the risk/benefit table could be improved – for example, by linking to it from recommendations about the individual interventions whose risks and benefits are discussed in the table.

Impact statement

Topic experts raised the issue of decision aids and accessible data to help clinicians and patients with treatment choice. Evidence for decision aids (in the form a decision board) was examined during the development of CG153 but the single study was non-randomised and had several limitations. The full version of CG153 stated that: 'Decision boards may help patients to weigh up the risks and benefits of different treatments. However, they could also be misused as a substitute for a proper discussion with the patient. Additionally, the patient may not be engaged by this type of intervention.'

CG153 does not, therefore, make recommendations on decision aids. It does

however state 'For more information about involving patients in decisions and supporting adherence see [Medicines adherence](#) (NICE clinical guideline 76)'. Since CG153 was published, NICE has now also published NG5 'Medicines optimisation', in which section 1.6 provides generic recommendations on patient decision aids used in consultations involving medicines. A cross-referral to NG5, alongside the referral to CG76, should be made from CG153.

CG153 also recommends discussing the risks and benefits of treatment options with the person (and their families or carers where appropriate), where possible using absolute risk and natural frequency. This recommendation then refers to [Appendix B](#) of the NICE version of CG153, which provides a table to facilitate discussion of risks and benefits of treatments for people with psoriasis. Although technology appraisals have published since CG153 was originally published (namely TA350 secukinumab; and TA419 apremilast) that do not feature in the current risk/benefit table, NICE is not able to keep this table continuously up to date. NICE is also currently reviewing its approach to decision aids as part of guideline development. A new chapter of the NICE guidelines manual is being drafted on this subject. As such, any amendments to guidance related to decision aids would be more suitably examined at a future date.

NICE also has information on [shared decision making](#) on its website.

New evidence is unlikely to change guideline recommendations.

Telephone-based motivational interviewing

2-year Evidence Update

No relevant evidence was identified.

4-year surveillance summary

An RCT¹ (n=169) compared a 3-month telephone-based motivational interviewing intervention (after heliotherapy) with usual care for self-management of psoriasis. There were significant overall treatment effects for the primary outcomes of Self-Administered Psoriasis Area and Severity Index (SAPASI) score, 3 self-management domains of the Health Education Impact Questionnaire (heiQ) and self-efficacy scores. For secondary outcomes, the study group had significantly better lifestyle change parameters, illness perception at 3 months, and psoriasis knowledge at 6 months.

A cost-utility analysis² of the above RCT was also done. A within-trial analysis compared costs and quality-adjusted life years (QALYs). Utilities were measured with the 15D instrument, supplemented with the Dermatological Life Quality Index (DLQI). A time-integrated summary score defined the clinical effects. QALYs were adjusted for baseline differences. Compared with usual care, motivational interviewing provided

equivalent quality of life and utility on both the 15D instrument and the DLQI, at lower cost. The authors stated that motivational interviewing was cost-effective (although the result for lower cost was not significant).

Topic expert feedback

No topic expert feedback was relevant to this evidence.

Impact statement

The new evidence suggests that a 3-month motivational interviewing intervention after heliotherapy could have a positive and potentially cost-effective effect on disease severity, self-efficacy, psoriasis knowledge and health behaviour change. CG153 makes general recommendations to offer people with psoriasis (and their families or carers), support and information tailored to suit their individual needs and circumstances, in a range of different formats. It does not make recommendations specifically about motivational interviewing, but the evidence for this was from a single small trial therefore is currently unlikely to impact on the guideline.

New evidence is unlikely to change guideline recommendations.

Smartphone apps

2-year Evidence Update

No relevant evidence was identified.

4-year surveillance summary

No relevant evidence was identified.

Topic expert feedback

Topic experts drew attention to 'MyPso' (a Pharma-sponsored app for personal tracking of psoriasis progress) and queried if there had been any follow up work or feedback from users to examine whether this is an effective tool.

Impact statement

Topic experts highlighted the MyPso app, however no evidence was identified for this intervention. [An RCT](#) began in January 2017 to examine the effect of the app on adherence to topical treatment, but currently no impact on CG153 is expected.

New evidence is unlikely to change guideline recommendations.

Assessment and referral

153 – 02 In people with psoriasis (all types), which are the most effective tools to assess the (a) severity and (b) impact of disease across all levels of healthcare provision and at any stage of the disease journey?

Recommendations derived from this review question

1.2.1 Assessment tools for disease severity and impact and when to refer for specialist care

1.2.1.1 For people with any type of psoriasis assess:

- disease severity
- the impact of disease on physical, psychological and social wellbeing
- whether they have psoriatic arthritis
- the presence of comorbidities.

1.2.1.2 Assess the severity and impact of any type of psoriasis:

- at first presentation
- before referral for specialist advice and at each referral point in the treatment pathway
- to evaluate the efficacy of interventions.

1.2.1.3 When assessing the disease severity in any healthcare setting, record:

- the results of a static Physician's Global Assessment (classified as clear, nearly clear, mild, moderate, severe or very severe)^a
- the patient's assessment of current disease severity, for example, using the static Patient's Global Assessment (classified as clear, nearly clear, mild, moderate, severe or very severe)
- the body surface area affected
- any involvement of nails, high-impact and difficult-to-treat sites (for example, the face, scalp, palms, soles, flexures and genitals)
- any systemic upset such as fever and malaise, which are common in unstable forms of psoriasis such as erythroderma or generalised pustular psoriasis.

1.2.1.4 In specialist settings, use a validated tool to assess severity of psoriasis, for example the [Psoriasis Area and Severity Index](#) (PASI)^b (in addition to the assessments indicated in recommendation 1.2.1.3).

1.2.1.5 Be aware that:

- PASI and body surface area are not validated for use in children and young people
- erythema may be underestimated in people with darker skin types, such as skin types V and VI on the Fitzpatrick scale^c.

1.2.1.6 Use the Nail Psoriasis Severity Index^d to assess nail disease in specialist settings:

- if there is a major functional or cosmetic impact **or**
- before and after treatment is initiated specifically for nail disease.

1.2.1.7 Assess the impact of any type of psoriasis on physical, psychological and social wellbeing by asking:

- what aspects of their daily living are affected by the person's psoriasis
- how the person is coping with their skin condition and any treatments they are using
- if they need further advice or support
- if their psoriasis has an impact on their mood

- if their psoriasis causes them distress (be aware the patient may have levels of distress and not be clinically depressed)
- if their condition has any impact on their family or carers.

Ask children and young people age-appropriate questions.

1.2.1.8 In specialist settings, and if practical in non-specialist settings, use a validated tool to assess the impact of any type of psoriasis on physical, psychological and social wellbeing, for example the:

- [Dermatology Life Quality Index](#) (DLQI)^{e,f} for adults **or**
- [Children's Dermatology Life Quality Index](#) (CDLQI)^g for children and young people.

1.2.1.9 When using an assessment tool for a person with any type of psoriasis:

- take account of their age, any disabilities (such as physical, visual or cognitive impairment), and any language or other communication difficulties, and provide help and support if needed^e
- ensure that the chosen assessment tool continues to be a sufficiently accurate measure.

1.2.1.10 Following assessment in a non-specialist setting, refer people for dermatology specialist advice if:

- there is diagnostic uncertainty **or**
- any type of psoriasis is severe or extensive, for example more than 10% of the body surface area is affected **or**
- any type of psoriasis cannot be controlled with topical therapy **or**
- acute guttate psoriasis requires phototherapy (see recommendation [1.4.1.1](#)) **or**
- nail disease has a major functional or cosmetic impact **or**
- any type of psoriasis is having a major impact on a person's physical, psychological or social wellbeing.

1.2.1.11 People with generalised pustular psoriasis or erythroderma should be referred immediately for same-day specialist assessment and treatment.

1.2.1.12 Refer children and young people with any type of psoriasis to a specialist at presentation.

a See Feldman SR, Krueger GG (2005) Psoriasis assessment tools in clinical trials. *Annals of Rheumatic Disease* 64 (Suppl. 2): ii65–ii68.

b See [Psoriasis Area and Severity Index](#). The PASI is also available from the [British Association of Dermatologists](#) website.

c Fitzpatrick scale: type I: always burns, never tans; type II: usually burns, tans with difficulty, type III: sometimes mild burn, gradually tans; type IV: rarely burns, tans with ease; type V: very rarely burns, tans very easily; type VI: never burns, tans very easily.

d See Rich P, Scher RK (2003) Nail Psoriasis Severity Index: a useful tool for evaluation of nail psoriasis. *Journal of the American Academy of Dermatology* 49: 206–12.

e See [Dermatology Life Quality Index](#). The DLQI is also available from the [British Association of Dermatologists](#) website.

f See also recommendation 1.5.3.3.

g See [Children's Dermatology Life Quality Index](#).

Surveillance decision

This review question should not be updated.

Screening for anxiety and depression

2-year Evidence Update

No relevant evidence was identified.

4-year surveillance summary

Topic experts identified a cross sectional single-centre study³ (n=607 people with psoriasis; just over half on biologics) examined screening for anxiety and depression in a tertiary referral centre over a 10-month period. Patients completed the Patient Health Questionnaire Depression Scale (PHQ-9), Generalised Anxiety Disorder Scale (GAD-7) and DLQI. 10% screened positive for major depressive disorder and 13% for generalised anxiety disorder. Suicidal ideation was reported in 35% of major depressive disorder; whereas DLQI was <10 (suggestive of no to moderate effect of skin disease on quality of life) in 38% and 46% cases of major depressive disorder and generalised anxiety disorder respectively. After adjusting for covariates, risk of major depressive disorder or generalised anxiety disorder was significantly increased in women, those with severe clinical disease, psoriatic arthritis and previous depression/anxiety; risk of generalised anxiety disorder was significantly increased with Asian ethnicity and use of topical treatments only.

Topic expert feedback

Topic experts noted that there are tools for evaluation of physical, psychological and social wellbeing in psoriasis beyond the DLQI, which is recognised as not adequately capturing the impact of psoriasis. It was further noted that in [IMPACT](#) (Identification and Management of Psoriasis Associated Comorbidity) [studies](#), almost nobody reported having their mood addressed as part of the psoriasis consultation. Topic experts also noted that there are no psoriasis (or even skin) specific QOF (or CCG Outcomes Indicator Set) – anecdotally this translates to poor implementation.

Impact statement

The new evidence suggests that systematic screening for anxiety and depression can

identify clinically important levels of depression and anxiety that may be missed using DLQI alone. Women, those with severe disease, psoriatic arthritis and/or a prior history of psychiatric morbidity may be at particular risk. Topic experts noted that psychological issues may not always be addressed during consultations with patients, and that the DLQI may not fully capture all relevant information. CG153 currently recommends assessment of the impact of disease on physical, psychological and social wellbeing by asking patients about effect on daily living and mood, whether they are coping or distressed, and if they need further advice or support (and the Psoriasis quality standard includes a quality statement on assessment of disease impact). The guideline further recommends use of the DLQI in specialist settings (and non-specialist settings if practical) but does not note any subgroups of patients that may be at increased risk of mental health problems.

Although there appears to be new evidence that tools other than the DLQI could capture psychological comorbidities potentially missed by the DLQI, and subgroups at increased risk of these comorbidities, these issues are largely covered by CG91 'Depression in adults with a chronic physical health problem'. CG91 discusses recognition, assessment and management of depression, which includes depression with anxiety. CG153 already makes a link to CG91: 'Assess whether people with any type of psoriasis are depressed when assessing disease severity and impact, and when escalating therapy. If appropriate offer information, advice and support in line with Depression in adults with a chronic physical health problem (NICE clinical guideline 91) and Depression in children and young people (NICE clinical guideline 28)'. No impact on CG153 is therefore expected.

New evidence is unlikely to change guideline recommendations.

Simplified Psoriasis Index (SPI)

2-year Evidence Update

A study⁴ assessed the validity and reliability of the SPI assessment tool in randomly selected adult patients attending a tertiary referral psoriasis centre. The tool has separate

components for: current severity (SPI-s; weighted for functionally or psychosocially important sites), psychosocial impact (SPI-p), and past history and interventions (SPI-i). Unlike the PASI, it does not involve an estimation of body surface area affected –

which can be unreliable and does not take into account that some sites are more problematic for patients than others. Two versions of SPI are available, for professionals (proSPI) and for patient self-assessment (saSPI) – both versions include the psychosocial and past history assessments, but differ in that severity is assessed by either a healthcare professional or by the patient.

ProSPI-s, saSPI-s, and SPI-p were tested in 100 patients for: criterion validity (comparison with established tools – PASI and DLQI); construct validity (correlation with established tools – PASI and DLQI); and response distribution (whether the entire scale range is used):

- For professional assessment, proSPI-s was closely correlated with PASI.
- For psychosocial impact, SPI-p was closely correlated with DLQI.
- For response distribution, a wide range of scores were obtained for each component of the SPI (results presented graphically) suggesting minimal redundancy.

ProSPI-s, saSPI-s, SPI-p and SPI-i were then tested in 50 patients for test–retest reliability (consistency of scores across multiple uses of a tool):

- Strong test-retest reliability was seen for all components.

Finally, proSPI-s was tested in 12 patients by 12 assessors (144 assessments) for inter-rater reliability (consistency of scores between different observers):

- Strong inter-rater reliability was seen with proSPI-s among both experienced and inexperienced psoriasis assessors.

A second study⁵ assessed the SPI for responsiveness to change, and measured its equivalence to PASI. Changes from baseline in PASI and PSI scores at week 4 (n=100) and week 10 (n=65) were observed among patients starting a new psoriasis therapy at a tertiary referral psoriasis centre. The PASI scores were then used to derive:

- The ability of the professional (proSPI-s) and patient (saSPI-s) versions of the SPI to discriminate between responders and non-responders to therapy:
 - Responsiveness to change was detected well by proSPI-s, saSPI-s and PASI.

- Minimum clinically important difference values (namely, those corresponding to a change in psoriasis perceptible to the patient) for the proSPI-s and saSPI-s:
 - From ROC and PASI-based anchor analysis, the minimum clinically important difference for the proSPI-s was a mean absolute change in score of 5.25 (percentage change 63%). For the saSPI-s, the minimum clinically important difference was a mean absolute change in score of 7.25 (percentage change 71%).
- The proSPI-s and saSPI-s cut-off scores denoting mild, moderate and severe psoriasis:
 - Based on PASI cut-off scores for mild (PASI <10), moderate (PASI 10–20) and severe (PASI >20) psoriasis, equivalent scores were proposed for both the proSPI-s (mild <9, moderate 9–18, and severe >18) and the saSPI-s (mild <10, moderate 10–20, and severe >20).

4-year surveillance summary

No relevant evidence was identified.

Topic expert feedback

Topic experts noted that [IMPACT](#) (Identification and Management of Psoriasis Associated Comorbidity) results from qualitative [studies](#) have consistently shown patients want their skin to be examined when they visit the GP but this is not happening in many cases. In addition, they are not receiving a referral to a dermatologist in accord with the guideline, but this may not warrant a review of the guideline as it relates more to poor implementation. They went on to note that there are no psoriasis (or even skin) specific QOF (or CCG Outcomes Indicator Set) – anecdotally this translates to poor implementation. Finally, it was noted that with greater options for effective treatment, and awareness of that by patients and in primary care – the current guidelines for referral may be more strictly adhered to.

Impact statement

The 2-year Evidence Update found that in specialist settings, the SPI appears to be a valid and reliable psoriasis assessment tool that is comparable to other established tools such as the PASI and the DLQI, and appears to provide a simpler and more comprehensive means of psoriasis assessment. Although NICE CG153 does not recommend SPI for

assessment of psoriasis, its lack of validation outside of tertiary care settings meant that these results were deemed unlikely to have an impact on the guideline. However, the Evidence Update noted that the potential of the SPI to address some of the issues with current tools may warrant further research to validate it in a wider array of disease severities and settings including primary and secondary care. No further evidence on the SPI was identified by 4-year surveillance, therefore any impact on CG153 remains unlikely.

Topic experts noted concerns about GPs not always examining skin or referring people to a dermatologist. However CG153 makes specific recommendations about both these aspects of care, and the Psoriasis quality standard includes 2 quality statements on assessment of disease and 1 on referral to specialist services, therefore the issue is likely to relate to implementation therefore no impact on CG153 is anticipated.

New evidence is unlikely to change guideline recommendations.

Psoriasis Symptom Inventory

2-year Evidence Update

No relevant evidence was identified.

4-year surveillance summary

A multicentre crossover RCT⁶ (n=80 adults with mild to moderate plaque psoriasis) compared electronic and paper versions of the Psoriasis Symptom Inventory and also examined measurement properties of the electronic version. Patients randomly completed either the paper or electronic Psoriasis Symptom Inventory daily for 7 consecutive days, followed by the alternate version. Equivalence testing showed the 2 versions were highly concordant for both total and individual item scores. Response bias testing showed no differences based on completion order. All mean score differences, except for 1 item ('flaking'), were non-significant. Minimum values for reliability

and validity were exceeded for the electronic version.

Topic expert feedback

See comments in the section on SPI above.

Impact statement

The new evidence suggests that paper and electronic versions of the Psoriasis Symptom Inventory are equivalent, and the electronic format provides reliable data. CG145 does not make recommendations on the Psoriasis Symptom Inventory for self-assessment (instead it recommends the static Patient's Global Assessment) and the study did not examine efficacy versus other tools, therefore this evidence is unlikely to affect the guideline.

New evidence is unlikely to change guideline recommendations.

PASI: body regions and components

2-year Evidence Update

No relevant evidence was identified.

4-year surveillance summary

An RCT⁷ (n=not stated in the abstract) analysed body regions and components of PASI scores during adalimumab or methotrexate treatment in people with moderate-to-severe psoriasis. The authors noted that the PASI score is a non-linear scale that does not allow reliable assessment of subtle variations of its components (erythema, induration, and desquamation). The study aim was therefore to highlight treatment response

patterns potentially hidden by PASI's compounded weighted-average calculation. At week 16 a significantly greater percentage of adalimumab-treated patients, versus methotrexate- and placebo-treated patients, achieved PASI 75, PASI 90 and PASI 100 response in each body region and component. A greater percentage of adalimumab-treated patients reached PASI 100 response in the head and neck region than overall response (significance not stated in the abstract). Two key components of PASI (induration and desquamation) were affected by treatment more than erythema (the third component). Adalimumab was more effective in complete resolution of induration than methotrexate

(significance not stated in the abstract). For all PASI body regions and components, mean percent improvement in score at weeks 2, 4, 8, 12, and 16 was significantly greater for adalimumab than methotrexate or placebo. Twice as many patients treated with adalimumab had complete resolution of individual body regions versus methotrexate and placebo.

Topic expert feedback

See comments in the section on SPI above.

Impact statement

The new evidence suggests that assessing PASI improvement by body region and

component is a patient-relevant outcome that could reveal useful patterns in psoriasis treatment. CG153 currently recommends PASI in specialist settings to assess psoriasis severity, but not sub-assessment of body regions or PASI components. However the evidence is from a single trial of an unknown number of patients, and any impact on CG153 is unlikely until further studies validate these findings.

New evidence is unlikely to change guideline recommendations.

Nail Assessment in Psoriasis and Psoriatic Arthritis (NAPPA)

2-year Evidence Update

A multinational, multicentre study⁸ aimed to develop and validate a new tool for assessing patient-relevant nail psoriasis outcomes: the Nail Assessment in Psoriasis and Psoriatic Arthritis (NAPPA). The tool comprised 3 components: a questionnaire assessing quality of life (NAPPA-QoL); a questionnaire assessing patient-relevant treatment benefits (the Patient Benefit Index, NAPPA-PBI); and a psoriasis Clinical Assessment of Severity (NAPPA-CLIN). Development of the NAPPA-QoL and NAPPA-PBI questionnaires involved several steps:

- Surveying patients (n=120) from Germany and the USA, with acute or chronic nail psoriasis of any type or duration, to collect statements about nail psoriasis disease burden, needs and treatment goals.
- Conversion of the statements into questionnaires by an expert panel, including patients.
- Feasibility testing and longitudinal validation in patients (n=203) from 6 countries (Denmark, Germany, Italy, Japan, Spain, the USA) who were receiving treatment for nail psoriasis.

Based on Nail Psoriasis Severity Index (NAPSI) data collected as part of the validation study, the NAPPA-CLIN was then developed as a brief, less complex tool than those currently available for clinical assessment of nail psoriasis severity. Namely, the NAPPA-CLIN assesses a combination of only the 4 least and

most affected fingers and toes, rather than all 20 digits.

At baseline, the instructions and purpose of the NAPPA-QoL and NAPPA-PBI questionnaires were clear to most patients, with clarity increasing at 12–16 week follow-up. The mean completion time for both questionnaires was around 10 minutes. NAPPA-QoL and NAPPA-PBI showed good convergent validity with established measures of clinical status and quality of life. At baseline, there was moderate correlation of NAPPA-QoL global scores with clinical disease measures (such as the NAPSI hands and feet score) and with other measures of quality of life (such as the DLQI). At follow-up, there was low but significant correlations of NAPPA-PBI global scores with changes in clinical measures (for example the NAPSI hands and feet score) and in quality of life measures (for example the DLQI). NAPPA-QoL was responsive to the effects of treatment and was also sensitive to change: global score correlated significantly with changes in clinical measures (such as the NAPSI hands and feet score) and in quality of life measures (such as the DLQI). The internal consistency of all NAPPA-QoL scales met the typical standard for Cronbach's alpha. The NAPPA-CLIN correlated highly with total NAPSI score.

4-year surveillance summary

No relevant evidence was identified.

Topic expert feedback

No topic expert feedback was relevant to this evidence

Impact statement

The 2-year Evidence Update found that the NAPPA tool appears to be a valid, reliable and

practical alternative to the NAPS I in assessing patient-relevant nail psoriasis outcomes. Although NICE CG153 does not recommend NAPP A for assessment of nail psoriasis, limitations of the evidence (noted by the Evidence Update to include potential issues with applicability to the UK because developing the questionnaires and validation did not involve UK patients), meant that it was deemed unlikely to have an impact on the guideline. However, the Evidence Update noted that the potential of the NAPP A to address some of the

issues with current tools warranted further research to validate it, particularly in secondary care settings in the UK, and specifically in patients with nail disease as the primary problem. No further evidence on NAPP A was identified by 4-year surveillance, therefore impact on CG153 remains unlikely.

New evidence is unlikely to change guideline recommendations.

Skindex-29

2-year Evidence Update

An observational, prospective, multicentre study⁹ (n=380 patients ≥18 years with mild to severe psoriasis attending dermatology clinics) compared 4 self-administered quality of life instruments. Patients were randomised to 3 groups. All filled out Skindex-29, plus a second instrument chosen from: the DLQI, the Psoriasis Disability Index (PDI), or the Short-Form Health Survey 36 (SF-36). Psoriasis severity and affected body surface area were no different between the 3 groups. Skindex-29 was compared with the other 3 instruments on a group-by-group basis to avoid increased power of more patients completing Skindex-29. Floor and ceiling effects were also evaluated: a scale was deemed insensitive if more than 20% of patients reported the lowest or highest possible score. All subscales (symptoms, emotions, functioning) of Skindex-29 showed strong significant correlation with the global scores of all 3 of the other instruments. The symptoms subscale of Skindex-29 also showed a significant, albeit weaker, correlation with clinical severity on the PASI, with only PDI showing a similar correlation among the other 3 instruments. Skindex-29 exhibited a minimal floor and ceiling effect, whereas a substantial floor effect (suggesting reduced sensitivity in mild psoriasis) was seen with most subscales of the DLQI, SF-36 and PDI.

4-year surveillance summary

No relevant evidence was identified.

Topic expert feedback

No topic expert feedback was relevant to this evidence.

Impact statement

The 2-year Evidence Update found that in dermatology outpatients, the Skindex-29 quality of life instrument has good correlation with existing tools (the DLQI, the PDI, and the SF-36), and appears to have greater sensitivity to clinical severity than other instruments, particularly in mild psoriasis. Although NICE CG153 does not specifically recommend Skindex-29 for assessment of quality of life, limitations of the evidence (noted by the Evidence Update to include issues with applicability of results to the UK because the study was in Spain) meant that it was deemed unlikely to have an impact on the guideline. However, the Evidence Update noted that potential of the Skindex-29 to address some of the issues with current tools warranted further research to validate it, particularly in UK and primary care settings. No further evidence on Skindex-29 was identified by 4-year surveillance, therefore impact on CG153 remains unlikely.

New evidence is unlikely to change guideline recommendations.

Effect of treatment withdrawal on health-related quality of life and psoriasis

2-year Evidence Update

No relevant evidence was identified.

4-year surveillance summary

A post hoc sub-analysis¹⁰ of an RCT (REVEAL) examined the effects of withdrawing treatment on health-related quality of life (measured by DLQI) and objective disease activity (measured

by PASI). In the original RCT, adult patients with moderate-to-severe plaque psoriasis who received adalimumab from baseline and had 75% or greater improvement in the PASI score at weeks 16 and 33 were re-randomised to adalimumab 40 mg or placebo every other week from weeks 33 to 52. DLQI and PASI scores were compared at baseline (week 0), early in treatment (week 4), directly before randomised withdrawal (week 33), and up to 19 weeks after treatment discontinuation (week 52; last observations carried forward). In the patients (n=240) who underwent protocol-mandated discontinuation of psoriasis treatment after achieving PASI 75 response, mean PASI scores at week 52 were lower (i.e., better) compared with week 4, yet mean DLQI scores were higher (i.e., worse). An approximately twofold disproportionately greater degree of worsening of DLQI score compared with the degree of worsening of PASI was observed while patients underwent discontinuation of therapy (week 52) compared with early in treatment (week 4). There was a significant interaction between the PASI-DLQI correlation and study period (week 4 or 52).

Topic expert feedback

No topic expert feedback was relevant to this evidence.

Impact statement

The new evidence suggests that discontinuing therapy in patients who initially responded to treatment appears to disproportionately worsen patient-reported health-related quality of life relative to the worsening of PASI. CG153 recommends that reviewing response to systemic therapy should take into account the impact of the disease on the person's physical, psychological and social wellbeing, and the benefits versus the risks of continued treatment. The guideline does not specifically state that particular attention should be paid to psychological wellbeing after discontinuing systemic therapy, however the evidence is from a single post hoc analysis and results would need to be verified in other studies before any impact is considered.

New evidence is unlikely to change guideline recommendations.

153 – 03 In people with psoriasis (all types), which is the most accurate diagnostic tool compared with clinical diagnosis by a rheumatologist to help a non-specialist identify psoriatic arthritis?

153 – 04 In people with psoriasis (all types) and suspected psoriatic arthritis, how quickly should referral to a specialist be made in order to minimise the impact of disease on symptoms, joint damage and quality of life?

Recommendations derived from these review questions

1.2.2 Assessment and referral for psoriatic arthritis

- 1.2.2.1 Offer annual assessment for psoriatic arthritis to people with any type of psoriasis. Assessment is especially important within the first 10 years of onset of psoriasis.
- 1.2.2.2 Use a validated tool to assess adults for psoriatic arthritis in primary care and specialist settings, for example the Psoriasis Epidemiological Screening Tool (PEST)^a. Be aware that the PEST does not detect axial arthritis or inflammatory back pain.
- 1.2.2.3 As soon as psoriatic arthritis is suspected, refer the person to a rheumatologist for assessment and advice about planning their care.

a See: Ibrahim GH, Buch MH, Lawson C et al. (2009) Evaluation of an existing screening tool for psoriatic arthritis in people with psoriasis and the development of a new instrument: the Psoriasis Epidemiology Screening Tool (PEST) questionnaire. *Clinical and Experimental Rheumatology* 27: 469–74. The PEST questionnaire is reproduced in appendix T of the [full guideline](#).

Surveillance decision

These review questions should not be updated.

Comparing/amalgamating psoriatic arthritis assessment tools: Psoriatic Arthritis Screening Evaluation (PASE), Toronto Psoriatic Arthritis Screen (ToPAS), Psoriasis and Arthritis Screening Questionnaire (PASQ), and Psoriasis Epidemiology Screening Tool (PEST)

2-year Evidence Update

A study¹¹ aimed to develop a new psoriatic arthritis assessment tool by combining the most discriminatory questions from existing tools. The analysis used data from the previously reported CONTEST study¹² – a head-to-head comparison of 3 existing questionnaires: PASE, ToPAS and PEST. The questionnaires were compared using Classification Criteria for Psoriatic Arthritis (CASPAR) as the gold standard. In the CONTEST study, 657 patients (from 10 UK secondary care dermatology clinics) returned questionnaires, 318 returned positive questionnaires and were invited for examination, and 195 attended.

All questions from PASE, ToPAS and PEST were examined individually for sensitivity, specificity, and Youden's index (Youden's index=sensitivity + specificity – 1). Youden's index provided a simple summary measure of misclassification error for each questionnaire item. The maximal Youden's index for individual items was 0.19, and a pragmatic cut off point of 0.1 was used to identify candidate questions

The candidate questions were then combined using 4 alternative approaches:

- CONTEST: Inclusion of all questions with a Youden's index of 0.1 or more (for questions that asked about the same issue, the question with the highest discrimination was used).
 - Eight questions remained to give a score range of 0–8.
- CONTESTw: The same methodology as CONTEST, except weighting was given to questions that independently predicted arthritis.
 - One question from CONTEST was weighted as 5, one question was weighted as 2, and all others were

weighted as 1, giving a score range of 0–13.

- CONTESTjt: The same methodology as CONTEST, but with the addition of a mannequin diagram for patients to indicate any joints causing discomfort (a cut off was determined for the number of uncomfortable joints that could predict psoriatic arthritis).
 - An optimal cut-off of 6 joints or more was chosen and added to CONTEST as a dichotomised 0 or 1 score, giving a score range of 0–9.
- CONTESTtree: All individual questions were entered into a classification and regression tree analysis to identify psoriatic arthritis. Independent variables were selected that differentiated arthritis, but the classification system was flexible by allowing different combinations of predictor variables in different subgroups (for example, different questions could be asked of patients with and without enthesitis symptoms).
 - An additional 5 questions were added to CONTEST, giving a score range of 0–13.

Once developed, the 4 new questionnaires were assessed using ROC analysis against diagnosis of psoriatic arthritis by CASPAR criteria. ROC curves were then used to identify cut-off points for positivity to screen for psoriatic arthritis. The questionnaires were then assessed using ROC analysis in the UK cohort from the original CONTEST study to assess predictive ability for psoriatic arthritis. All questionnaires reached significance, except CONTESTtree (which was not pursued further): ROC analysis of the 3 remaining questionnaires was then performed in 2 validation cohorts of patients who had psoriasis but no previous diagnosis of inflammatory arthritis. The cohorts were from Ireland (n=100, of whom 29 were diagnosed with psoriatic arthritis on CASPAR) and the USA (n=145, of whom 80 were diagnosed with psoriatic arthritis). Questionnaire performance in these cohorts was similar to the UK, but CONTESTw performed less well.

ROC curves for the questionnaires were then examined to assess optimal cut-off points (a range of cut-off scores were analysed across the 3 cohorts and those with the best balance of sensitivity and specificity, in favour of higher sensitivity, were selected). The 2 strongest candidate questionnaires were CONTEST (cut-off score 4 out of 8) and CONTESTjt (cut-off score 5 out of 9). When these were tested in a UK cohort, they had greater sensitivities and specificities than the PEST tool currently recommended by NICE CG153.

4-year surveillance summary

A randomised study¹³ (n=949 patients with plaque psoriasis) compared 3 psoriatic arthritis screening tools: PASQ, PEST and ToPAS. Consecutive unselected patients were randomised to receive 1 of the 3 questionnaires. Patients were evaluated by rheumatologists to diagnose/exclude clinical psoriatic arthritis, which was used as the standard to analyse questionnaire accuracy. Of the 949 patients, 285 (30%) were diagnosed with psoriatic arthritis. Probable psoriatic arthritis was detected in 45%, 43%, and 43% of patients using PASQ, PEST, and ToPAS respectively. Sensitivity ranged from 0.67 to 0.84; specificity, 0.64 to 0.75; positive predictive value, 0.43 to 0.60; and negative predictive value, 0.83 to 0.91.

Topic expert feedback

Topic experts noted that there are further screening tools that have been published for psoriatic arthritis, but thought they may have little impact on current recommendations. It was also noted that there is a new instrument to measure impact from psoriatic arthritis ([PsAID](#)) undergoing further validation in independent studies, and a new OMERACT (Outcome Measures in Rheumatology) approved core set of domains for psoriatic arthritis being submitted for publication.

It was further noted that from a patient perspective, the recommendation in CG153 to offer annual assessment for psoriatic arthritis to people with any type of psoriasis may not be being fully implemented in primary care. They went on to note that there are no psoriasis (or even skin) specific QOF (or CCG Outcomes Indicator Set) – anecdotally this translates to poor implementation. Finally, it was noted that with greater options for effective treatment, and

awareness of that by patients and in primary care – the current guidelines for referral may be more strictly adhered to.

Additionally, it was noted that although management of psoriatic arthritis is covered in the [NICE guideline on spondyloarthritis](#), it remains vital that the psoriasis guideline includes the impact of arthritis, early identification and appropriate referral.

Impact statement

The 2-year Evidence Update found that the CONTEST psoriatic arthritis assessment tool (which combines the most discriminatory questions from PASE, ToPAS, and PEST) appears to be an improvement over current instruments. Although CG153 currently only recommends PEST to assess adults for psoriatic arthritis, the Evidence Update concluded that lack of validation of CONTEST outside of secondary care settings meant that these results are unlikely to have an impact on the guideline. However, the Evidence Update noted that the potential of CONTEST to address some of the issues with current tools warranted further research to validate it in a wider array of disease severities and settings including primary and tertiary care. No further evidence on CONTEST was identified by 4-year surveillance, however a study was found on some of the tools that contributed to CONTEST. The study indicated that PASQ, PEST, and ToPAS have broadly similar efficacy in identifying psoriatic arthritis in patients with psoriasis. However no tool was stated to be more effective than any others therefore the evidence is unlikely to affect the recommendation to use PEST in CG153.

Issues raised by topic experts about patients not being annually assessed for psoriatic arthritis are likely to reflect problems with implementation, given that CG153 specifically states this should happen in all patients with psoriasis (and the Psoriasis quality standard includes a quality statement on annual assessment for psoriatic arthritis), therefore no impact on the guideline is anticipated.

A cross-referral from CG153 to the NICE guideline on spondyloarthritis will be considered.

New evidence is unlikely to change guideline recommendations.

Clinical indicators of psoriatic arthritis in people with psoriasis

2-year Evidence Update

A cross-sectional study¹⁴ (n=106) compared ultrasound with the modified NAPSI to investigate the nail plate, nail matrix and adjacent tendons in psoriatic nail disease, and to test links between nail involvement and extensor tendon enthesopathy. A total of 86 patients with psoriasis, with or without psoriatic arthritis (169 nails), and 20 healthy participants (40 nails) were assessed by rheumatologists using both the modified NAPSI and ultrasound. For the ultrasound assessment, 2 nails per patient were scanned – namely, the most severely affected nail (selected by the clinician who performed the modified NAPSI) and the corresponding nail on the other hand. The thickness of the extensor tendon at insertion was deemed normal or thickened by comparison with the proximal tendon. The ultrasonographer was unaware of nail or skin disease other than that involved in the scan. Nail abnormalities on ultrasound were significantly more frequent among patients with psoriasis than healthy participants, and there was significant agreement of 76% between abnormal findings on the modified NAPSI and ultrasound. Significantly more patients with clinical nail disease had enthesal extensor tendon thickening on ultrasound than patients without clinical nail disease in both psoriasis and psoriatic arthritis. Enteseal thickening of the extensor tendon was significantly more frequent in patients with an abnormality in the adjacent nail by physical examination. Nail thickness was significantly greater among patients with psoriasis than healthy participants, as was the thickness of the nail matrix and adjacent skin

4-year surveillance summary

A systematic review¹⁵ of 27 studies aimed to develop a minimal list of clinical signs and symptoms that dermatologists should look for (in addition to specific skin features and nail involvement) to improve detection of psoriatic arthritis in people with psoriasis. A list of clinical signs and symptoms observed in psoriatic arthritis were extracted from the included studies and submitted to a panel of dermatology experts through a DELPHI selection process. The 4 items that received a score higher than 90% in the DELPHI process were finally selected: peripheral inflammatory pain (100%), axial inflammatory pain (95%),

dactylitis (93%), buttock and sciatic pain (91%). The remaining items were not retained: distal interphalangeal joints involvement, talalgia, swollen Achille's tendon, costo-chondral involvement, uveitis, and mouth ulcerations.

A systematic review and meta-analysis¹⁶ of 25 studies examined whether some psoriatic skin features are associated with a higher risk of psoriatic arthritis. Mean age at psoriasis onset appeared to be similar in patients with skin disease alone and in those with psoriatic arthritis. There was no clinical type of psoriasis specifically associated with psoriatic arthritis, including pustular psoriasis of palms and soles. However, scalp lesions and intergluteal/perianal lesions were significantly associated with an increased risk of psoriatic arthritis in 1 cohort study and 2 cross-sectional studies. Nail involvement was significantly associated with psoriatic arthritis in the meta-analysis, particularly onycholysis. Moreover, nail psoriasis was also associated with distal interphalangeal joint arthritis. The extent of psoriasis (as measured by: >3 sites in 1 cohort study, and body surface area >75% in 1 case-control study and 3 cross-sectional studies) appeared to be significantly associated with psoriatic arthritis. The meta-analysis suggested a trend (though non-significant) for an association between high PASI and psoriatic arthritis risk.

A systematic review¹⁷ of 21 studies examined the link between psoriatic arthritis and nail changes. On average, 66% of people with psoriatic arthritis had nail changes. The type of nail changes and their associations varied widely between studies.

Topic expert feedback

Topic experts noted that although management of psoriatic arthritis is covered in the [NICE guideline on spondyloarthritis](#), it remains vital that the psoriasis guideline includes the impact of arthritis, early identification and appropriate referral

Impact statement

The 2-year Evidence Update found that ultrasound evaluation of nails in people with psoriasis appears to correlate well with NAPSI assessment. Additionally, extensor tendon enthesopathy can accompany both psoriasis and psoriatic arthritis, and enthesopathy of the tendon appears to be more frequent in patients with nail abnormalities as determined by physical examination. Although NICE CG153

does not currently note any link between nail disease and enthesopathy (which could indicate psoriatic arthritis risk), the Evidence Update deemed the findings as preliminary and unlikely to have an impact on the guideline. It was suggested that more research was needed to further investigate links between nail disease, tendon enthesopathy and psoriatic arthritis, and how this could translate into clinical practice – particularly in the early detection of arthritis.

Evidence from 4-year surveillance suggested the following may be indicators of psoriatic arthritis: peripheral inflammatory pain, axial inflammatory pain, dactylitis, buttock and sciatic pain (though these were aimed at dermatologists rather than primary care), scalp lesions, intergluteal/perianal lesions, nail involvement/changes (particularly onycholysis), and extent of psoriasis.

CG153 currently recommends assessing whether people with any type of psoriasis have psoriatic arthritis, and offering annual assessment for it using the PEST (which

records information on swollen joints, prior arthritis diagnosis, nail holes or pits, heel pain, and swollen and painful fingers or toes). Additionally, the guideline recommends that psoriasis severity assessment should record the body surface area affected by psoriasis and any involvement of nails, high-impact and difficult-to-treat sites (for example, the face, scalp, palms, soles, flexures and genitals). As soon as psoriatic arthritis is suspected, the person should be referred to a rheumatologist. These existing recommendations cater for most of the clinical indicators of psoriatic arthritis noted by the new evidence (particularly those not specifically aimed at specialists), therefore no impact on CG153 is anticipated. However the evidence reinforces the need for vigilance in all patients, particularly those with clinical features suggesting increased risk of psoriatic arthritis, to aid early identification and referral which topic experts noted as being vital.

New evidence is unlikely to change guideline recommendations.

Predictors of clinical outcome in psoriatic arthritis

2-year Evidence Update

A multicentre, prospective cohort study¹⁸ (n=197) examined predictors of clinical outcome in psoriatic arthritis. Patients from rheumatological outpatient clinics with early psoriatic arthritis (namely, having arthritis, enthesitis or dactylitis suggestive of psoriatic arthritis) were included on the Swedish Early Psoriatic Arthritis Register within 2 years of symptom onset. Patients were assessed on inclusion and after 2, 5 and 10 years. Of 223 patients who had received a 5-year assessment, 197 patients who fulfilled CASPAR criteria were included. At each visit, patients were clinically examined for joint problems, inflammation, deformities, axial disease, and nail psoriasis, and scored on several assessment tools and questionnaires. Laboratory measurement of biochemical markers and radiography were performed, and antirheumatic medication was reported. Mean Disease Activity Score including 28 joints (DAS28) and Mean Disease Activity Index for Psoriatic Arthritis (DAPSA) at baseline was significantly higher in women than men, and at

5-year follow-up had significantly decreased in both women and men, with the score in women remaining significantly higher. Significant predictors of minimal disease activity at 5-year follow-up in a multivariate age-adjusted analysis were: baseline Health Assessment Questionnaire score (a measure of functional status); and months of delay before specialist care. In univariate age-adjusted analysis male gender was the only predictor of remission at 5 years.

4-year surveillance summary

No relevant evidence was identified.

Topic expert feedback

Topic experts noted that although management of psoriatic arthritis is covered in the [NICE guideline on spondyloarthritis](#), it remains vital that the psoriasis guideline includes the impact of arthritis, early identification and appropriate referral.

Impact statement

The 2-year Evidence Update found that in early psoriatic arthritis, improved clinical outcomes at 5 years appear to be predicted by a short delay between onset of symptoms and diagnosis, higher baseline functional status, and male

gender. These data are consistent with recommendations in CG153 to offer annual assessment for psoriatic arthritis and to refer the patient to a rheumatologist as soon as psoriatic arthritis is suspected, and which topic experts also noted as being vital.

New evidence is unlikely to change guideline recommendations.

Multidisciplinary dermatology-rheumatology management

2-year Evidence Update

No relevant evidence was identified.

4-year surveillance summary

A systematic review¹⁹ of 3 studies (2 case series, 1 descriptive study; n=506) examined multidisciplinary dermatology-rheumatology management for patients with moderate-to-severe psoriasis and psoriatic arthritis. Studies were included that compared assessment in a multidisciplinary consultation with routine separate consultations. Patients were referred to the multidisciplinary consultation from dermatology and rheumatology consultations in all but 1 study, in which primary care was also involved. The reason for the referral was to confirm the diagnosis and/or treatment. Patients were evaluated on a weekly and monthly basis in 2 and 1 study, respectively. Multidisciplinary consultations led to improved skin and joint symptoms after changing treatment with higher scores for this type of consultation compared to usual care (significance not stated in the abstract) and a high level of satisfaction among patients (94% 'very satisfied'). However, waiting times were higher (significance not stated in the abstract).

Topic expert feedback

Topic experts noted that although management of psoriatic arthritis is covered in the [NICE guideline on spondyloarthritis](#), it remains vital that the psoriasis guideline includes the impact

of arthritis, early identification and appropriate referral.

Impact statement

The new evidence suggests that multidisciplinary management may be more effective and more satisfactory for patients than conventional consultations, though the authors stated that the evidence was scarce and limited therefore this was not conclusively demonstrated. CG153 recommends referral for dermatology specialist advice or to a rheumatologist in particular circumstances. Although multidisciplinary consultations are not specifically recommended, the guideline states that when offering systemic therapy (responsibility for which should be in specialist settings only), when choosing the systemic agent, and when reviewing response to therapy, consideration should be given to the presence and control of psoriatic arthritis (in consultation with a rheumatologist). Further recommendations state that multidisciplinary working and communication between specialties and, if needed, interdisciplinary team working (for example when both skin and joints are significantly affected) should be ensured. Limitations of the evidence mean it is unlikely to affect CG153, which already discusses collaboration between dermatologists and rheumatologists in care of people with psoriasis and psoriatic arthritis.

New evidence is unlikely to change guideline recommendations.

153 – 05 Are people with psoriasis at higher risk than people without psoriasis for significant comorbidities and are there subgroups within the psoriasis population at a further increased risk?

Recommendations derived from this review question

1.2.3 Identification of comorbidities

Surveillance proposal consultation document March 2017 – Psoriasis (2012) NICE guideline CG153

- 1.2.3.1 Offer adults with severe psoriasis^a of any type a cardiovascular risk assessment at presentation using a validated risk estimation tool. Offer further assessment of cardiovascular risk every 5 years, or more frequently if indicated following assessment. For further information see [Lipid modification](#) (NICE clinical guideline 67).
- 1.2.3.2 Discuss risk factors for cardiovascular comorbidities with people who have any type of psoriasis (and their families or carers where appropriate). Where appropriate offer preventative advice, healthy lifestyle information and support for behavioural change tailored to meet the needs of the individual in line with the following NICE guidance:
- [Lipid modification](#) (NICE clinical guideline 67)
 - [Obesity](#) (NICE clinical guideline 43)
 - [Preventing type 2 diabetes: population and community interventions](#) (NICE public health guidance 35)
 - [Prevention of cardiovascular disease](#) (NICE public health guidance 25)
 - [Alcohol-use disorders: preventing harmful drinking](#)(NICE public health guidance 24)
 - [Smoking cessation services](#) (NICE public health guidance 10)
 - [Four commonly used methods to increase physical activity](#) (NICE public health guidance 2)
 - [Promoting physical activity in the workplace](#) (NICE public health guidance 13)
 - [Promoting physical activity for children and young people](#) (NICE public health guidance 17).
- 1.2.3.3 For people with multiple comorbidities and/or multimorbidities and any type of psoriasis needing second- or third-line therapy, ensure multidisciplinary working and communication between specialties and, if needed, interdisciplinary team working (for example when both skin and joints are significantly affected).
- 1.2.3.4 Be aware that psoriasis of any type, especially if severe^b, is a risk factor for venous thromboembolism in adults, and:
- explain this risk to adults with any type of psoriasis
 - offer advice on how to minimise the risk (for example, during hospital admission, surgery, or periods of immobility)
 - manage the risk in line with [Venous thromboembolism: reducing the risk](#) (NICE clinical guideline 92).
- 1.2.3.5 Assess whether people with any type of psoriasis are depressed when assessing disease severity and impact, and when escalating therapy. If appropriate offer information, advice and support in line with [Depression in adults with a chronic physical health problem](#) (NICE clinical guideline 91) and [Depression in children and young people](#) (NICE clinical guideline 28).

a Severe psoriasis was defined as either requiring treatment with phototherapy or systemic agents or requiring hospital admission in the studies underpinning this recommendation.

b Severe psoriasis was identified by hospitalisations (including outpatient visits) for psoriasis (ICD-10 L40) or psoriatic arthritis.

Surveillance decision

This review question should not be updated.

Risk of cardiovascular disease

2-year Evidence Update

No relevant evidence was identified.

4-year surveillance summary

A systematic review and meta-analysis²⁰ of 16 case-control studies (898 cases, 1140 controls) examined cardiovascular risk markers in patients with psoriatic arthritis. Compared to

controls, patients with psoriatic arthritis showed a significantly higher common carotid artery intima-media thickness (CIMT), and a significantly higher frequency of carotid plaques. Moreover, a significantly lower flow-mediated dilatation (FMD) was found in people with psoriatic arthritis than controls, with no difference in nitrate-mediated dilation.

A systematic review and meta-analysis²¹ of 20 observational studies (n=not stated) examined the association between psoriasis and subclinical atherosclerosis. Patients with psoriasis had a significantly thicker CIMT and lower FMD than controls. In a subgroup analysis, people with psoriatic arthritis appeared to have less impaired FMD and thinner CIMT (significance not stated in the abstract). Patients with psoriasis with mean age >45 years had much thicker CIMT (significance not stated in the abstract). The impaired FMD seemed more pronounced in psoriatic patients with mean age <45 years (significance not stated in the abstract).

A systematic review and meta-analysis²² of 11 observational studies (n=32,973) examined risk of cardiovascular morbidity in patients with psoriatic arthritis. Risk of cardiovascular diseases, incident cardiovascular events, and morbidity risks for myocardial infarction, cerebrovascular diseases and heart failure were all significantly higher in patients with psoriatic arthritis compared with the general population. Significant heterogeneity was identified in all main analyses.

Topic experts identified a cohort study²³ (n=48,523 patients with psoriasis and 208,187 controls) examined the association between psoriasis and risk of major cardiovascular events (myocardial infarction, acute coronary syndrome, unstable angina, and stroke) During a median follow-up of 5.2 years, 1,257 patients with psoriasis (2.6%) had a major cardiovascular event, compared with 4,784 controls (2.30%). In the multivariable analysis, inflammatory arthritis, diabetes, chronic kidney disease, hypertension, transient ischemic attack, atrial fibrillation, valvular heart disease, thromboembolism, congestive heart failure, depression, current smoker, age (year), and male gender were statistically significant for the risk of major cardiovascular events. Age- and gender-adjusted risks of a major cardiovascular event for psoriasis were significant, whereas the fully adjusted risks were no longer significant. In conclusion,

neither psoriasis nor severe psoriasis were associated with the short-to-medium term (over 3-5 years) risk of major cardiovascular events after adjusting for known cardiovascular disease risk factors.

Topic expert feedback

Topic experts noted that in [IMPACT](#) (Identification and Management of Psoriasis Associated Comorbidity) [studies](#), almost nobody reported having their modifiable cardiovascular disease risk factors (smoking, obesity, inactivity) addressed as part of the psoriasis consultation. They went on to note that there are no psoriasis (or even skin) specific QOF (or CCG Outcomes Indicator Set) – anecdotally this translates to poor implementation.

Experts further noted that the IMPACT findings address the issue of whether psoriasis is an independent risk factor for cardiovascular disease. They thought that younger people with more severe psoriasis and psoriatic arthritis are a particularly vulnerable group. The experts queried whether this was clear enough in the guideline or whether there is a strong enough recommendation to refer this group early to cardiology and rheumatology services.

Impact statement

The new evidence suggests that psoriasis and psoriatic arthritis appear significantly associated with markers of subclinical atherosclerosis and cardiovascular risk (namely thicker CIMT and lower FMD), and cardiovascular and cerebrovascular morbidity is significantly higher in patients with psoriatic arthritis. Although CG153 does not specifically recommend assessing CIMT and FMD, it does recommend offering adults with severe psoriasis of any type a cardiovascular risk assessment at presentation and further assessment of cardiovascular risk every 5 years, or more frequently if indicated following assessment. It further recommends discussing risk factors for cardiovascular comorbidities with people who have any type of psoriasis, and offering preventative advice, healthy lifestyle information and support for behavioural change in line with NICE guidance. Introducing assessment of CIMT or FMD would need specific evidence of the efficacy of this approach, therefore the current evidence is unlikely to affect CG153.

Topic experts noted concerns about people not having their modifiable CVD risk factors

addressed as part of the psoriasis consultation, however CG153 makes specific recommendations about this therefore the issue is likely to relate to implementation therefore no impact on CG153 is anticipated.

Topic experts also noted that younger people with more severe psoriasis and psoriatic arthritis are particularly at risk of CVD, however the evidence did not appear to specifically show this. The evidence that neither psoriasis nor severe psoriasis were associated with the short-to-medium term risk of major

cardiovascular events after adjusting for known cardiovascular disease risk factors is likely indicative that psoriasis is associated with more cardiovascular ill health, representing a higher prevalence of other known risk factors. This is consistent with recommendations in CG153 to discuss risk factors for cardiovascular comorbidities and offer preventative advice, information and support.

New evidence is unlikely to change guideline recommendations.

Smoking prevalence

2-year Evidence Update

No relevant evidence was identified.

4-year surveillance summary

A systematic review and meta-analysis²⁴ of controlled studies examined the prevalence of smoking in patients with psoriasis and the relationship between smoking and psoriasis severity. A significant association was identified between smoking and psoriasis versus patients without psoriasis. Eight articles of 11 with data on smoking and psoriasis severity suggested that severity increased with smoking status.

Topic expert feedback

Topic experts noted that in [IMPACT](#) (Identification and Management of Psoriasis Associated Comorbidities) [studies](#), almost nobody reported having their modifiable CVD risk factors (smoking, obesity, inactivity) addressed as part of the psoriasis consultation.

Impact statement

The new evidence suggests an association between smoking and psoriasis as well as an association between smoking and severity of

psoriasis. Although CG153 does not specifically discuss the link between smoking and psoriasis outcomes, it does recommend discussing risk factors for cardiovascular comorbidities with people who have any type of psoriasis, and offering preventative advice, healthy lifestyle information and support for behavioural change in line with NICE guidance (including smoking cessation).

Stopping smoking is already recommended by CG153 in the context of reducing cardiovascular risk, therefore the evidence is unlikely to impact the guideline.

Topic experts noted concerns about people not having their modifiable CVD risk factors addressed as part of the psoriasis consultation, however CG153 makes specific recommendations about this therefore the issue is likely to relate to implementation therefore no impact on CG153 is anticipated.

New evidence is unlikely to change guideline recommendations.

Risk of chronic obstructive pulmonary disease (COPD)

2-year Evidence Update

No relevant evidence was identified.

4-year surveillance summary

A systematic review and meta-analysis²⁵ of 4 observational studies (n=13,418) examined the association between psoriasis and COPD. Patients with psoriasis were at a significantly greater risk of developing COPD than the

general population and the association between psoriasis and COPD was significantly stronger among patients with severe psoriasis.

Topic expert feedback

No topic expert feedback was relevant to this evidence.

Impact statement

The new evidence suggests an association between psoriasis (particularly severe psoriasis) and COPD. CG153 recommends

assessing the presence of comorbidities for people with any type of psoriasis, though does not specifically recommend assessing for COPD. However the guideline does note advice and support should be offered in line with NICE guidance (including smoking cessation). Given that stopping smoking would be key advice for people at risk of COPD,

which is already recommended as part of reducing cardiovascular risk, any impact on CG153 is unlikely.

New evidence is unlikely to change guideline recommendations.

Risk of non-alcoholic fatty liver disease (NAFLD)

2-year Evidence Update

No relevant evidence was identified.

4-year surveillance summary

A systematic review and meta-analysis²⁶ of 7 case-control studies (all low or moderate quality) examined risk of NAFLD in patients with psoriasis. People with psoriasis had a significantly increased risk of NAFLD compared to controls (6 studies; n=267,761). The association remained significant when only high/moderate quality studies were analysed (3 studies; n=3345 patients). The risk of NAFLD was significantly greater in patients with psoriatic arthritis (3 studies; n=505) and in patients with moderate to severe psoriasis compared to those with mild psoriasis (2 studies; n=51,930 patients).

Topic expert feedback

Topic experts queried if there are better diagnostics/screening investigations for established incidence of metabolic syndrome and diabetes in people with psoriasis. (Note: metabolic syndrome can manifest as NAFLD in the liver).

Impact statement

The new evidence suggests an association between psoriasis and NAFLD, however the authors noted that data quality and heterogeneity may restrict the interpretation of the pooled data. CG153 recommends assessing the presence of comorbidities for people with any type of psoriasis, though does not specifically recommend assessing for NAFLD. However the guideline does note advice and support should be offered in line with NICE guidance (including preventing harmful drinking), and that methotrexate can cause a clinically significant rise in transaminases, that long-term methotrexate therapy may be associated with liver fibrosis, and to provide advice on modifiable risk factors for liver disease prior to and during methotrexate therapy. Limitations of the evidence noted by the authors mean that any impact on CG153 is currently unlikely.

New evidence is unlikely to change guideline recommendations.

Topical therapy

153 – 06 In people with chronic plaque psoriasis of the trunk and/or limbs, what are the clinical effectiveness, safety, tolerability, and cost effectiveness of topical vitamin D or vitamin D analogues, potent or very potent corticosteroids, tar, dithranol and retinoids compared with placebo or vitamin D or vitamin D analogues, and of combined or concurrent vitamin D analogues and potent corticosteroids compared with potent corticosteroid or vitamin D or vitamin D analogue alone?

Recommendations derived from this review question

The treatment pathway in this guideline begins with active topical therapies. The GDG acknowledged that the use of emollients in psoriasis was already widespread and hence the evidence review was limited to active topical therapies for psoriasis. Please refer to the BNF and cBNF for guidance on use of emollients.

1.3.1 General recommendations

1.3.1.1 Offer people with psoriasis topical therapy as first-line treatment.

1.3.1.2 Offer second- or third-line treatment options (phototherapy or systemic therapy) at the same time when topical therapy alone is unlikely to adequately control psoriasis, such as:

- extensive disease (for example more than 10% of body surface area affected) **or**
- at least 'moderate' on the static Physician's Global Assessment **or**
- where topical therapy is ineffective, such as nail disease.

See also recommendations 1.2.1.9; 1.4.1.1; 1.5.2.1; 1.5.3.4; 1.5.3.6; 1.5.3.8 and 1.5.3.10.

1.3.1.3 Offer practical support and advice about the use and application of topical treatments. Advice should be provided by healthcare professionals who are trained and competent in the use of topical therapies. Support people to adhere to treatment in line with [Medicines adherence](#) (NICE clinical guideline 76).

1.3.1.4 When offering topical agents:

- take into account patient preference, cosmetic acceptability, practical aspects of application and the site(s) and extent of psoriasis to be treated
- discuss the variety of formulations available and, depending on the person's preference, use:
 - cream, lotion or gel for widespread psoriasis
 - lotion, solution or gel for the scalp or hair-bearing areas
 - ointment to treat areas with thick adherent scale
- be aware that topical treatment alone may not provide satisfactory disease control, especially in people with psoriasis that is extensive (for example more than 10% of body surface area affected) or at least 'moderate' on the static Physician's Global Assessment.

1.3.1.5 If a person of any age with psoriasis requiring topical therapy has a physical disability, or cognitive or visual impairment offer advice and practical support that take into account the person's individual needs.

1.3.1.6 Arrange a review appointment 4 weeks after starting a new topical treatment in adults, and 2 weeks after starting a new topical treatment in children, to:

- evaluate tolerability, toxicity, and initial response to treatment (including measures of severity and impact described in recommendations 1.2.1.3, 1.2.1.6 and 1.2.1.7)
- reinforce the importance of adherence when appropriate

- reinforce the importance of a 4 week break between courses of potent/very potent corticosteroids (see recommendation 1.3.1.10).

If there is little or no improvement at this review, discuss the next treatment option with the person.

- 1.3.1.7 Discuss with people whose psoriasis is responding to topical treatment (and their families or carers where appropriate):
- the importance of continuing treatment until a satisfactory outcome is achieved (for example clear or nearly clear) or up to the recommended maximum treatment period for corticosteroids (see sections [1.3.2](#), [1.3.3](#) and [1.3.4](#))
 - that relapse occurs in most people after treatment is stopped
 - that after the initial treatment period topical treatments can be used when needed to maintain satisfactory disease control.
- 1.3.1.8 Offer people with psoriasis a supply of their topical treatment to keep at home for the self-management of their condition.
- 1.3.1.9 In people whose psoriasis has not responded satisfactorily to a topical treatment strategy, before changing to an alternative treatment:
- discuss with the person whether they have any difficulties with application, cosmetic acceptability or tolerability and where relevant offer an alternative formulation
 - consider other possible reasons for non-adherence in line with [Medicines adherence](#) (NICE clinical guideline 76).

How to use corticosteroids safely^a

- 1.3.1.10 Be aware that continuous use of potent or very potent corticosteroids may cause:
- irreversible skin atrophy and striae
 - psoriasis to become unstable
 - systemic side effects when applied continuously to extensive psoriasis (for example more than 10% of body surface area affected).

Explain the risks of these side effects to people undergoing treatment (and their families or carers where appropriate) and discuss how to avoid them.

- 1.3.1.11 Aim for a break of 4 weeks between courses of treatment with potent or very potent corticosteroids. Consider topical treatments that are not steroid-based (such as vitamin D or vitamin D analogues or coal tar) as needed to maintain psoriasis disease control during this period.
- 1.3.1.12 When offering a corticosteroid for topical treatment select the potency and formulation based on the person's need.
- 1.3.1.13 Do not use very potent corticosteroids continuously at any site for longer than 4 weeks.
- 1.3.1.14 Do not use potent corticosteroids continuously at any site for longer than 8 weeks.
- 1.3.1.15 Do not use very potent corticosteroids in children and young people.
- 1.3.1.16 Offer a review at least annually to adults with psoriasis who are using intermittent or short-term courses^b of a potent or very potent corticosteroid (either as monotherapy or in combined preparations) to assess for the presence of steroid atrophy and other adverse effects.
- 1.3.1.17 Offer a review at least annually to children and young people with psoriasis who are using corticosteroids of any potency (either as monotherapy or in combined preparations) to assess for the presence of steroid atrophy and other adverse effects.

1.3.2 Topical treatment of psoriasis affecting the trunk and limbs

- 1.3.2.1 Offer a potent corticosteroid applied once daily plus vitamin D or a vitamin D analogue applied once daily (applied separately, one in the morning and the other in the evening) for up to 4 weeks as initial treatment for adults with trunk or limb psoriasis.

- 1.3.2.2 If once-daily application of a potent corticosteroid plus once-daily application of vitamin D or a vitamin D analogue does not result in clearance, near clearance or satisfactory control of trunk or limb psoriasis in adults after a maximum of 8 weeks^c, offer vitamin D or a vitamin D analogue alone applied twice daily.
- 1.3.2.3 If twice-daily application of vitamin D or a vitamin D analogue does not result in clearance, near clearance or satisfactory control of trunk or limb psoriasis in adults after 8–12 weeks^c, offer either:
- a potent corticosteroid applied twice daily for up to 4 weeks **or**
 - a coal tar preparation applied once or twice daily.
- 1.3.2.4 If a twice-daily potent corticosteroid or coal tar preparation cannot be used or a once-daily preparation would improve adherence in adults offer a combined product containing calcipotriol monohydrate and betamethasone dipropionate applied once daily for up to 4 weeks.
- 1.3.2.5 Offer treatment with very potent corticosteroids in adults with trunk or limb psoriasis only:
- in specialist settings under careful supervision
 - when other topical treatment strategies have failed
 - for a maximum period of 4 weeks.
- 1.3.2.6 Consider short-contact dithranol for treatment-resistant psoriasis of the trunk or limbs and either:
- give educational support for self-use **or**
 - ensure treatment is given in a specialist setting.
- 1.3.2.7 For children and young people with trunk or limb psoriasis consider^d either:
- calcipotriol applied once daily (only for those over 6 years of age) **or**
 - a potent corticosteroid applied once daily (only for those over 1 year of age).

a See recommendations 1.3.4.2 and 1.3.4.4 for details on safe use of steroids at facial, flexural and genital sites.

b See recommendations 1.3.1.12 and 1.3.1.13 for details on safe duration of steroid use.

c See recommendation 1.3.1.8 for additional considerations before changing to the next treatment option.

d Please refer to the BNF for children for information on appropriate dosing and duration of treatment.

Surveillance decision

This review question should be updated.

The footnotes should be amended.

Miscellaneous topical treatments

2-year Evidence Update

A Cochrane review²⁷ of 177 RCTs (n=34,808) examined topical treatments for plaque psoriasis. The authors developed a 'combined' end point (to facilitate treatment comparisons) by taking Investigator's Assessment of Overall Global Improvement (or Investigator's Global Assessment of Disease Severity) data when available and failing that (in order of availability), data from: Total Severity Scores, PASI, Patient Assessment of overall Global Improvement (or Patient Global Assessment of

Disease Severity). Results given are based on the combined endpoint.

In psoriasis of the trunk and limbs, the following treatments were all significantly more effective than placebo:

- Vitamin D analogues (30 RCTs, n=4986).
- Potent corticosteroids (13 RCTs, n=2216).
- Very potent corticosteroids (10 RCTs, n=1264).
- Dithranol (3 RCTs, n=47).
- Vitamin D and corticosteroid combination products (namely, calcipotriol plus betamethasone dipropionate):
 - Once daily (4 RCTs, n=1416).

- Twice daily (2 RCTs, n=848).

For active treatment comparisons in psoriasis of the trunk and limbs:

- Vitamin D plus a corticosteroid was significantly more effective than corticosteroids alone (5 RCTs, n=2113), and vitamin D alone was significantly less effective than vitamin D plus a corticosteroid (17 RCTs, n=5856).
- Vitamin D analogues were no more effective than potent corticosteroids (14 RCTs, n=3542) or very potent corticosteroids (2 RCTs, n=82).
- Vitamin D alone was no more effective than dithranol (8 RCTs, n=1284) or than other vitamin D preparations (4 RCTs, n=513).

For psoriasis of the trunk, limbs and scalp, the rate of local adverse events (such as burning or irritation) was significantly higher with calcipotriol than betamethasone dipropionate (3 RCTs, n=1739).

The authors also identified studies of 26 other treatments versus placebo (n=1450). Around half of the treatments (including, for example, aloe vera cream, fish oil, herbal skin care products, and Mahonia aquifolium) performed significantly better than placebo. However, none of the studies assessed the same treatment therefore pooled analysis was not possible, and the authors stated that findings should be interpreted with caution. Treatments found not to be significantly better than placebo included topical caffeine, emollient lotion of Dead Sea salts, kukui nut oil, oleum horwathiensis, and tar.

4-year surveillance summary

See later sections for evidence on individual drugs.

Topic expert feedback

See later sections for evidence on individual drugs.

It was noted that the footnote on calcipotriol and potent corticosteroids in children and young people needed to be updated.

Impact statement

The 2-year Evidence Update found that in psoriasis of the trunk and limbs, corticosteroids perform at least as well as vitamin D analogues for treating chronic plaque psoriasis, and that vitamin D plus a corticosteroid is more effective than either corticosteroids alone or vitamin D alone. Evidence of the effect of complementary and alternative topical therapies in psoriasis is lacking. These data were deemed to be consistent with recommendations in NICE CG153 for topical therapy and unlikely to have an impact on the guideline.

We will add further footnotes to recommendation 1.3.2.7 'For children and young people with trunk or limb psoriasis consider either:

- calcipotriol applied once daily (only for those over 6 years of age) or
- a potent corticosteroid applied once daily (only for those over 1 year of age).'

There are currently different topical calcipotriol preparations available in the UK which vary in their licensing status for use in children and young people under 18. Additionally, potent topical corticosteroid preparations available in the UK vary in the age from which they are licensed for use in children.

New evidence is unlikely to change guideline recommendations.

Calcipotriol plus betamethasone dipropionate (aerosol foam)

2-year Evidence Update

See the Cochrane review²⁷ in 'Miscellaneous topical treatments' above. (Evidence summarised as calcipotriol/betamethasone dipropionate generally, not as specific formulation).

4-year surveillance summary

A multicentre, investigator-blind RCT²⁸ (n=376 adult patients with plaque psoriasis) compared calcipotriol/betamethasone

dipropionate aerosol foam, calcipotriol/betamethasone dipropionate ointment, aerosol foam vehicle and ointment vehicle (randomisation 3:3:1:1). At week 4, significantly more patients using calcipotriol/betamethasone dipropionate foam achieved the primary outcome of treatment success (clear or almost clear with at least a 2-step improvement according to the physician's global assessment of disease severity). Mean modified PASI score (excluding the head, which was not treated) was significantly improved with calcipotriol/betamethasone

dipropionate foam than the ointment formulation. Rapid, continuous itch relief occurred with both active treatments. One adverse drug reaction was reported with calcipotriol/betamethasone dipropionate foam (application site itch).

A double-blind, multicentre RCT²⁹ (n=302 patients aged >18 years with greater than mild severity plaque psoriasis) compared calcipotriol/betamethasone dipropionate aerosol foam, calcipotriol foam and betamethasone dipropionate foam once daily for 4 weeks. At Week 4, significantly more patients achieved treatment success (clear/almost clear from baseline in moderate/severe disease; clear from baseline in mild disease) with calcipotriol/betamethasone dipropionate foam than calcipotriol foam or betamethasone dipropionate foam. Mean modified PASI improved in all groups, with statistically significant differences in score at week 4 in favour of calcipotriol/betamethasone dipropionate foam versus calcipotriol foam and betamethasone dipropionate foam. Four (calcipotriol/betamethasone dipropionate), 10 (calcipotriol), and 8 (betamethasone dipropionate) adverse drug reactions were reported.

A multicentre double-blind RCT³⁰ (n=426 patients with greater than mild severity plaque psoriasis of the trunk and/or limbs) compared calcipotriol/betamethasone dipropionate aerosol foam with aerosol foam vehicle. Patients were randomised (3:1) to calcipotriol/betamethasone dipropionate aerosol foam or foam vehicle once-daily for 4 weeks. At week 4, significantly more patients using calcipotriol/betamethasone dipropionate aerosol foam achieved the primary outcome of treatment success (according to physician's global assessment) versus vehicle. For secondary outcomes, mean mPASI score was significantly lower for patients using calcipotriol/betamethasone dipropionate aerosol foam than vehicle. Significantly greater itch relief was observed for patients using calcipotriol/betamethasone dipropionate aerosol foam than vehicle from day 5 onwards. Adverse drug reactions were reported in 10 calcipotriol/betamethasone dipropionate aerosol foam patients (3.1%) and 2 vehicle patients (1.9%); events occurred in 1 patient each except application site pain (calcipotriol/betamethasone dipropionate

aerosol foam, 2 patients; vehicle, 1 patient). There were no clinically significant changes in calcium homeostasis.

Topic expert feedback

Topic experts noted that the current guideline recommends simultaneous therapies (steroids and vitamin D analogue) whereas in practice GPs will nearly always prescribe one OR the other as this is simpler. GPs are therefore tending to ignore section 1.3.2.1 of the guideline: 'Offer a potent corticosteroid applied once daily plus vitamin D or a vitamin D analogue applied once daily (applied separately, one in the morning and the other in the evening) for up to 4 weeks as initial treatment for adults with trunk or limb psoriasis'. The experts suggested it may be helpful to look again at the health economics of these approaches versus a combined preparation such as Dovobet (calcipotriol/betamethasone).

Topic experts further noted that there is a new formulation of the topical combination calcipotriol/betamethasone dipropionate as a foam application. Potential safety issues may need to be considered as efficacy has been reported to be greater than the current formulations. Some patients may find foam preferable to other formulations, which could improve adherence.

Experts also noted that consideration of plaque size was important (for example, combined calcipotriol/betamethasone foam formulation is suitable for large plaques 3-4 cm, whereas gel is better suited to small plaques).

Topic experts also queried whether a generic was available for Dovobet. The following information relevant to this query was identified:

Calcipotriol/betamethasone is category C in the drug tariff: 'Category C - Drugs which are not readily available as a generic, where the price is based on a particular proprietary product, manufacturer or as the case may be supplier'. The price set for the ointment (£19.84 for 30g) is based on Dovobet. The ointment is available as generic from a number of generics manufacturers, but whether it is prescribed generically or not the cost would be as per Dovobet because that is what is stated in the tariff. There is also a calcipotriol/betamethasone gel which is also category C in the tariff (the brand this is priced on is not stated), the cost of which is £37.21/60g and £69.11/120g – from MIMS this

is the cost of the Dovobet gel. If a generic gel was available, the NHS cost would still be the same as Dovobet because the tariff cost is set at the same as Dovobet. This is based on the October 2016 drug tariff. The tariff does get updated so while currently correct, it may change in future. The gel formulation is widely used, accounting for about 47% of all topical Dovobet prescribing (by items) versus approximately 12% in 2011. The foam (launched in June 2016) is only available as Enstilar, costing £39.68/60g.

Impact statement

The new evidence suggests that over 4 weeks, calcipotriol/betamethasone dipropionate aerosol foam is significantly more effective than calcipotriol/betamethasone dipropionate ointment, calcipotriol foam, betamethasone dipropionate foam, and foam vehicle. CG153 recommends that if a twice-daily potent corticosteroid or coal tar preparation cannot be used or a once-daily preparation would improve adherence in adults, a combined product containing calcipotriol monohydrate and

betamethasone dipropionate applied once daily for up to 4 weeks should be offered after the following sequence of treatments has been offered:

- potent corticosteroid applied once daily plus vitamin D or a vitamin D analogue applied once daily (applied separately, one in the morning and the other in the evening)
- vitamin D or a vitamin D analogue alone applied twice daily
- potent corticosteroid applied twice daily for up to 4 weeks or a coal tar preparation applied once or twice daily.

As the guideline does not specify the formulation of calcipotriol monohydrate and betamethasone dipropionate to use, treatment with the foam formulation is covered by current recommendations. No immediate need to update the guideline was identified.

New evidence is unlikely to change guideline recommendations.

Betamethasone valerate (adhesive plaster)

2-year Evidence Update

See the Cochrane review²⁷ in 'Miscellaneous topical treatments' above. (Evidence summarised as potent corticosteroid generally, not as specific formulation)

4-year surveillance summary

A multicentre, investigator-blinded, non-inferiority RCT³¹ (n=324 patients with mild-to-moderate chronic plaque psoriasis) compared a self-adhering medicated plaster containing betamethasone valerate (Betesil) with calcipotriol/betamethasone dipropionate ointment. Two to 4 plasters were applied to target plaques on the knees and elbows once a day and had to be worn for at least 20 consecutive hours. The control ointment was applied once a day on target plaques on the knees and elbows in adequate amounts. The maximum dose was 60 g/week. The mean adjusted 4-item psoriasis total severity score (TSS-4) significantly decreased through the study from baseline in both groups. The per-protocol primary analysis of week 4 data revealed a non-significant between-group difference in adjusted means, demonstrating non-inferiority of the betamethasone valerate

plaster with calcipotriol/betamethasone dipropionate ointment. Non-inferiority was also demonstrated in the intention-to-treat analysis. The psoriasis global assessment (PGA) and other secondary outcomes were significantly improved from baseline in both groups at week 4. The quality of life score was slightly better in the calcipotriol/betamethasone dipropionate group at week 4, but no difference was observed at follow-up. No safety or tolerability concerns were observed in either group.

Topic expert feedback

It was noted that betamethasone valerate plasters are licensed for chronic plaque psoriasis localised in difficult to treat areas (such as knees, elbows and anterior face of the tibia on an area not greater than 5% of the body surface). The cost of 4 plasters is £9.92.

Topic experts noted that there was some use of betamethasone valerate plasters in specialist settings (though there was uncertainty about use in primary care). They stated that the plasters were useful if lesions are itchy or for persistent plaques being perpetuated by continual scratching – treatment would usually start with an ointment, and then if psoriasis persists or is localised then the additional occlusion of the plasters can be useful.

Impact statement

The new evidence suggests that betamethasone valerate plaster appears to be non-inferior to calcipotriol/betamethasone dipropionate ointment in patients with mild to moderate chronic plaque psoriasis. CG153 does not make any recommendations specifically on betamethasone valerate in plaster form, but it does recommend offering a

potent corticosteroid (of which betamethasone valerate plasters are an example). Treatment with betamethasone valerate plasters is therefore covered by current recommendations, and no immediate need to update the guideline was identified.

New evidence is unlikely to change guideline recommendations.

Calcipotriol plus nicotinamide

2-year Evidence Update

See the Cochrane review²⁷ in 'Miscellaneous topical treatments' above. (Evidence summarised as Vitamin D generally, not as named drug)

4-year surveillance summary

An RCT³² compared topical calcipotriol/nicotinamide combination with calcipotriol alone in patients with mild to moderate psoriasis.

Topic expert feedback

It was noted that calcipotriol/nicotinamide combination is not available in the UK.

Impact statement

New evidence was found on calcipotriol/nicotinamide combination, however this formulation is not available in the UK therefore no impact on CG153 is expected.

New evidence is unlikely to change guideline recommendations.

Halobetasol and clobetasol

2-year Evidence Update

See the Cochrane review²⁷ in 'Miscellaneous topical treatments' above. (Evidence summarised as very potent corticosteroid generally, not as named drug).

4-year surveillance summary

A multicentre RCT³³ (n=202 patients with chronic, localised plaque psoriasis) compared halobetasol propionate ointment and clobetasol propionate ointment for 14 days. In both treatment groups, the local plaque severity index scores were significantly reduced at the end of treatment which was comparable in both treatment groups. At day 14, more patients on halobetasol than on clobetasol had a physician's global evaluation rating for almost total clearing of lesion (Grade 4) and marked improvement (Grade 3), whereas moderate improvement (Grade 2) and mild improvement were more frequently seen with clobetasol than halobetasol. The difference between the 2

groups for physicians' global evaluation was significant. Numerically, but not significantly, more patients on halobetasol showed >75% improvement in photographic assessment. There was a significant difference in the cosmetic acceptability and in the ease of application in favour of halobetasol. No significant difference was found in serum cortisol levels between the groups.

Topic expert feedback

It was noted that halobetasol is not available in the UK.

Impact statement

The new evidence suggests that halobetasol is more effective than clobetasol for chronic, localised plaque psoriasis. However halobetasol is not available in the UK therefore this evidence is unlikely to affect CG153.

New evidence is unlikely to change guideline recommendations.

Maxacalcitol

2-year Evidence Update

See the Cochrane review²⁷ in 'Miscellaneous topical treatments' above. (Evidence summarised as Vitamin D generally, not as named drug)

4-year surveillance summary

An RCT³⁴ compared maxacalcitol ointment with placebo applied twice daily for 8 weeks in patients with moderate or severe palmoplantar pustulosis.

Topic expert feedback

It was noted that maxacalcitol is not available in the UK.

Impact statement

New evidence was found on maxacalcitol, however this is not available in the UK therefore no impact on CG153 is expected.

New evidence is unlikely to change guideline recommendations.

Tropomyosin-receptor kinase A inhibitor 'CT327'

2-year Evidence Update

No relevant evidence identified.

4-year surveillance summary

An RCT³⁵ examined the topical tropomyosin-receptor kinase A inhibitor 'CT327' (drug name not specified in the abstract) for the treatment of pruritus due to psoriasis.

Topic expert feedback

It was noted that the drug is labelled with a manufacturer code; without knowing the

generic name its licensing status in the UK cannot be established.

Impact statement

New evidence was found on CT327, however its availability in the UK is unknown therefore no impact on CG153 is expected.

New evidence is unlikely to change guideline recommendations.

Fluorine-synthetic fibre socks

2-year Evidence Update

No relevant evidence identified.

4-year surveillance summary

A within-patient RCT³⁶ (n=17 patients with plantar pustulosis) compared fluorine-synthetic fibre socks with standard cotton socks (one sock worn on each foot) for 4 weeks.

The primary outcome of median percentage lesion reduction at week 4 was numerically but not significantly greater with fluorine-synthetic fibre socks than cotton socks. Among secondary outcomes, the overall reduction over time in the treated areas, and the perception of the disease by the patient, were significantly in favour of fluorine-synthetic fibre socks.

Topic expert feedback

No topic expert feedback was relevant to this evidence.

Impact statement

The new evidence found no significant difference in lesion reduction with fluorine-synthetic fibre socks versus cotton socks, though there appeared to be benefits for reduction in the extension of the treated areas and in the perception of the disease by the patient. CG153 does not make any recommendations on fluorine-synthetic fibre socks, however the evidence is from 1 small trial in which the primary outcome showed no significant benefit, therefore no impact on the guideline is expected.

New evidence is unlikely to change guideline recommendations.

Unlicensed dermatological preparations ('Specials')

2-year Evidence Update

No relevant evidence identified.

4-year surveillance summary

No relevant evidence identified.

Topic expert feedback

Topic experts noted updated guidance on '[Special' formulations](#)' from the British Association of Dermatologists. They stated it might be useful to update the guideline on these formulations, and where they fit.

Impact statement

Specials are unlicensed formulations, and this guidance on their use is based on expert opinion and consensus. As the formulations are not appraised or recommended on the basis of published evidence (the guidance notes that there is a lack of safety and efficacy data for specials), this information cannot be used to inform any potential changes to CG153.

New evidence is unlikely to change guideline recommendations.

153 – 07 In people with chronic plaque psoriasis at high impact or difficult-to-treat sites (scalp, flexures, face), what are the clinical effectiveness, safety, tolerability and cost effectiveness of vitamin D or vitamin D analogues, mild to very potent corticosteroids, combined or concurrent vitamin D or vitamin D analogue and potent corticosteroid, pimecrolimus, tacrolimus, tar, dithranol and retinoids compared with placebo, corticosteroids or vitamin D or vitamin D analogues?

Recommendations derived from this review question

1.3.3 Topical treatment of psoriasis affecting the scalp

- 1.3.3.1 Offer a potent corticosteroid^a applied once daily for up to 4 weeks^b as initial treatment for people with scalp psoriasis.
- 1.3.3.2 Show people with scalp psoriasis (and their families or carers where appropriate) how to safely apply corticosteroid topical treatment.
- 1.3.3.3 If treatment with a potent corticosteroid^a does not result in clearance, near clearance or satisfactory control of scalp psoriasis after 4 weeks^b consider:
- a different formulation of the potent corticosteroid (for example, a shampoo or mousse) **and/or**
 - topical agents to remove adherent scale (for example, agents containing salicylic acid, emollients and oils) before application of the potent corticosteroid.
- 1.3.3.4 If the response to treatment with a potent corticosteroid^a for scalp psoriasis remains unsatisfactory after a further 4 weeks^{b,c} of treatment offer:
- a combined product containing calcipotriol monohydrate and betamethasone dipropionate^d applied once daily for up to 4 weeks **or**
 - vitamin D or a vitamin D analogue^e applied once daily (only in those who cannot use steroids and with mild to moderate scalp psoriasis).
- 1.3.3.5 If continuous treatment with either a combined product containing calcipotriol monohydrate and betamethasone dipropionate^d applied once daily or vitamin D or a vitamin D analogue applied once daily for up to 8 weeks^b does not result in clearance, near clearance or satisfactory control of scalp psoriasis offer:
- a very potent corticosteroid applied up to twice daily for 2 weeks for adults only **or**
 - coal tar applied once or twice daily **or**

- referral to a specialist for additional support with topical applications and/or advice on other treatment options.
- 1.3.3.6 Consider topical vitamin D or a vitamin D analogue^{e,f} alone for the treatment of scalp psoriasis only in people who:
- are intolerant of or cannot use topical corticosteroids at this site **or**
 - have mild to moderate scalp psoriasis.
- 1.3.3.7 Do not offer coal tar-based shampoos alone for the treatment of severe scalp psoriasis.
- 1.3.4 Topical treatment of psoriasis affecting the face, flexures and genitals**
- 1.3.4.1 Offer a short-term mild or moderate potency corticosteroid^g applied once or twice daily (for a maximum of 2 weeks^b) to people with psoriasis of the face, flexures or genitals.
- 1.3.4.2 Be aware that the face, flexures and genitals are particularly vulnerable to steroid atrophy and that corticosteroids should only be used for short-term treatment of psoriasis (1–2 weeks per month). Explain the risks to people undergoing this treatment (and their families or carers where appropriate) and how to minimise them.
- 1.3.4.3 For adults with psoriasis of the face, flexures or genitals if the response to short-term moderate potency corticosteroids is unsatisfactory, or they require continuous treatment to maintain control and there is serious risk of local corticosteroid-induced side effects, offer a calcineurin inhibitor^h applied twice daily for up to 4 weeks. Calcineurin inhibitors should be initiated by healthcare professionals with expertise in treating psoriasis.
- 1.3.4.4 Do not use potent or very potent corticosteroids on the face, flexures or genitals.
- 1.3.4.5 When prescribing topical agents at facial, flexural and genital sites take into account that they may cause irritation and inform people undergoing treatment (and their families and carers where appropriate) of these risks and how to minimise them. See also recommendation 1.3.4.2.

a Only use potent corticosteroids according to UK marketing authorisation, which was limited to those over 1 year of age at the time of publication (October 2012).

b In children and young people the specified duration of therapy may not be appropriate. Please refer to the BNF for children for information on appropriate dosing and duration of treatment.

c See recommendation 1.3.1.8 for additional considerations before changing to the next treatment option.

d At the time of publication (October 2012), the combined product containing calcipotriol monohydrate and betamethasone dipropionate did not have UK marketing authorisation for this indication in children and young people. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. The patient (or their parent or carer) should provide informed consent, which should be documented. See the General Medical Council's [Good practice in prescribing medicines – guidance for doctors](#) for further information.

e In children, when offering an agent in the vitamin D or vitamin D analogue class choose calcipotriol, because at the time of publication (October 2012) calcitriol and tacalcitol did not have UK marketing authorisation for this group.

f Please refer to the BNF for children for information on appropriate dosing and duration of treatment.

g At the time of publication (October 2012), moderate potency corticosteroids did not have UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. The patient (or their parent or carer) should provide informed consent, which should be documented. See the General Medical Council's [Good practice in prescribing medicines – guidance for doctors](#) for further information.

h At the time of publication (October 2012), calcineurin inhibitors did not have UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. The patient (or their parent or carer) should provide informed consent, which should be documented. See the General Medical Council's [Good practice in prescribing medicines – guidance for doctors](#) for further information.

Surveillance decision

This review question should not be updated.

The footnotes should be amended.

Miscellaneous treatments for scalp psoriasis

2-year Evidence Update

A Cochrane review²⁷ (see section 145 – 07 'Miscellaneous topical treatments' for details) of topical treatments for chronic plaque psoriasis found evidence relevant to scalp psoriasis. The very potent corticosteroid clobetasol propionate was significantly more effective than placebo (4 RCTs, n=788). A combination of calcipotriol and betamethasone dipropionate was significantly more effective than betamethasone alone (3 RCTs, n=2444), and calcipotriol was significantly less effective than a combination of calcipotriol and betamethasone dipropionate (4 RCTs, n=2581). Vitamin D was less effective than potent corticosteroids: for example, calcipotriol was significantly less effective than either betamethasone dipropionate (2 RCTs, n=1676) or betamethasone valerate (2 RCTs, n=510). For psoriasis of the trunk, limbs and scalp, the rate of local adverse events (such as burning or irritation) was significantly higher with calcipotriol than betamethasone dipropionate (3 RCTs, n=1739).

4-year surveillance summary

A Cochrane review³⁷ of 59 RCTs (n=11,561) examined topical treatments for scalp psoriasis and focused on the following outcomes: 'clearance' or 'response' as assessed by the investigator global assessment (IGA), improvement in quality of life, adverse events requiring withdrawal of treatment and 'response' as assessed by the patient global assessment (PGA). In terms of clearance, as assessed by the IGA, steroids were significantly better than vitamin D (4 RCTs, n=2180). The 2-compound combination (i.e. corticosteroid plus vitamin D e.g. calcipotriol/betamethasone) was significantly superior to steroid monotherapy, however the additional benefit was small (4 RCTs, n=2474). The 2-compound combination was significantly more effective than vitamin D alone (4 RCTs, n=2008). In terms of treatment response, as assessed by the IGA, corticosteroids were significantly more effective than vitamin D (3 RCTs, n=1827). The 2-compound combination was significantly better than steroid monotherapy, but the additional benefit was small (3 RCTs, n=2444). It was also significantly more effective than vitamin D alone (4 RCTs, n=2222). Reporting of quality of life data was poor and data were insufficient to be

included for meta-analysis. Steroids caused significantly fewer withdrawals due to adverse events than vitamin D (4 RCTs, n=2291). The 2-compound combination and steroid monotherapy did not differ significantly in the number of adverse events leading to withdrawal (3 RCTs, n=2433 participants). The 2-compound combination led to significantly fewer withdrawals due to adverse events than vitamin D (3 RCTs, n=1970). No study reported the type of adverse event requiring withdrawal. In terms of treatment response, as assessed by the PGA, steroids were significantly more effective than vitamin D (3 RCTs, n=1827). The 2-compound combination was significantly better than steroid monotherapy, however the benefit was not clinically important (2 RCTs, n=2226). The 2-compound combination was significantly more effective than vitamin D (4 RCTs, n=2222). Common adverse events with these 3 interventions were local irritation, skin pain and folliculitis. Systemic adverse events were rare and probably not drug-related. In addition to the results of the major 3 comparisons, the 2-compound combination, steroids and vitamin D monotherapy were found to be more effective than the vehicle. Steroids of moderate, high and very high potency tended to be similarly effective and well tolerated. There were inherent limitations in the review concerning the evaluation of salicylic acid, tar, dithranol or other topical treatments.

Topic expert feedback

It was noted that the footnotes on potent corticosteroids for the scalp, and on calcipotriol for the scalp, needed to be updated.

Impact statement

The 2-year Evidence Update found that in scalp psoriasis, vitamin D is less effective than corticosteroids. These data were deemed consistent with recommendations in NICE CG153 for topical therapy and unlikely to have an impact on the guideline.

The authors of the Cochrane review identified by 4-year surveillance concluded that the 2-compound combination (i.e. corticosteroid plus vitamin D e.g. calcipotriol/betamethasone) as well as corticosteroid monotherapy were more effective and safer than vitamin D monotherapy. Given the similar safety profile and only slim benefit of the 2-compound combination over the steroid alone, the authors felt that monotherapy with generic topical steroids may be acceptable for short-term

therapy. This is consistent with CG153 that recommends initial treatment with a potent corticosteroid and only offering a combined product following an unsatisfactory response after 8 weeks of steroids.

Although evidence from the Cochrane review suggested that steroids of moderate, high and very high potency tended to be similarly effective and well tolerated (which could have implications for CG153 because potent corticosteroids are recommended first line for scalp psoriasis without first trying lower potency steroids), the authors stated that the following questions remain unanswered and should be investigated by future trials: 'Is there truly no difference in terms of effectiveness or safety between topical corticosteroids of different strength?' Therefore no impact is currently expected.

The Cochrane authors also noted that future RCTs should investigate how specific therapies improve the participants' quality of life and that long-term assessments are needed (i.e. 6 to 12 months).

We will amend guideline footnote 24 (which currently states 'Only use potent corticosteroids according to UK marketing authorisation, which was limited to those over 1 year of age at the time of publication [October 2012]'). The footnote relates to recommendation 1.3.3.1 'Offer a potent corticosteroid applied once daily for up to 4 weeks as initial treatment for people with scalp psoriasis'

There are currently several potent topical corticosteroid preparations available in the UK,

and the age from which they are licensed for use in children varies.

We will also amend guideline footnote 27 (which currently states 'In children, when offering an agent in the vitamin D or vitamin D analogue class choose calcipotriol, because at the time of publication [October 2012] calcitriol and tacalcitol did not have UK marketing authorisation for this group.'). The footnote relates to recommendation 1.3.3.4 'If the response to treatment with a potent corticosteroid for scalp psoriasis remains unsatisfactory after a further 4 weeks of treatment offer:

- a combined product containing calcipotriol monohydrate and betamethasone dipropionate applied once daily for up to 4 weeks or
- vitamin D or a vitamin D analogue applied once daily (only in those who cannot use steroids and with mild to moderate scalp psoriasis).'

Topical calcitriol and tacalcitol preparations are not licensed in children, so it is correct to say that they do not have a marketing authorisation for this age group. However, topical calcipotriol preparations available in the UK vary in their licensing status for use in children and young people under 18.

New evidence is unlikely to change guideline recommendations.

Calcipotriol plus betamethasone dipropionate (aerosol foam)

2-year Evidence Update

See the Cochrane review²⁷ in 'Miscellaneous treatments for scalp psoriasis' above. (Evidence summarised as calcipotriol/betamethasone dipropionate generally, not as specific formulation).

4-year surveillance summary

A double-blind, multicentre RCT²⁹ (n=302 patients aged >18 years with greater than mild severity plaque psoriasis) compared calcipotriol/betamethasone dipropionate aerosol foam, calcipotriol foam and betamethasone dipropionate foam once daily for 4 weeks. At week 4, significantly more

patients using calcipotriol/betamethasone dipropionate foam achieved treatment success of the scalp than those using calcipotriol foam, but not those using betamethasone dipropionate foam. Four (calcipotriol/betamethasone dipropionate), 10 (calcipotriol), and 8 (betamethasone dipropionate) adverse drug reactions were reported.

Topic expert feedback

See section 153 – 06 'Calcipotriol plus betamethasone dipropionate (aerosol foam)' for topic expert feedback on this intervention

Impact statement

The new evidence suggests that on the scalp, calcipotriol/betamethasone dipropionate

aerosol foam was significantly more effective than calcipotriol foam, but not betamethasone dipropionate foam. CG153 recommends that if the response to treatment with a potent corticosteroid for scalp psoriasis remains unsatisfactory after a further 4 weeks of treatment offer a combined product containing calcipotriol monohydrate and betamethasone dipropionate applied once daily for up to 4 weeks. However this is only recommended after the following sequence of treatments has been offered:

- potent corticosteroid applied once daily for up to 4 weeks
- a different formulation of the potent corticosteroid (for example, a shampoo or mousse)

- topical agents to remove adherent scale (for example, agents containing salicylic acid, emollients and oils) before application of the potent corticosteroid.

As calcipotriol/betamethasone dipropionate aerosol foam was not significantly more effective than betamethasone dipropionate foam (a potent steroid, which are recommended by CG153 as first line for scalp psoriasis) then the evidence is unlikely to affect the guideline.

New evidence is unlikely to change guideline recommendations.

Psoriasis of the face, flexures or genitals: calcineurin inhibitors

2-year Evidence Update

No relevant evidence identified.

4-year surveillance summary

No relevant evidence identified.

Topic expert feedback

It was noted that the footnote on calcineurin inhibitors needed to be updated.

Impact statement

We will amend guideline footnote [30](#) (which currently states 'At the time of publication [October 2012], calcineurin inhibitors did not have UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. The patient [or their parent or carer] should provide informed consent, which should be documented. See the General Medical Council's [Good practice in prescribing](#)

[medicines – guidance for doctors](#) for further information).’ The footnote relates to recommendation 1.3.4.3 ‘For adults with psoriasis of the face, flexures or genitals if the response to short-term moderate potency corticosteroids is unsatisfactory, or they require continuous treatment to maintain control and there is serious risk of local corticosteroid-induced side effects, offer a calcineurin inhibitor applied twice daily for up to 4 weeks. Calcineurin inhibitors should be initiated by healthcare professionals with expertise in treating psoriasis’.

It may be clearer to refer to topical calcineurin inhibitors in the footnote (there are oral calcineurin inhibitors such as ciclosporin that are licensed for psoriasis).

New evidence is unlikely to change guideline recommendations.

Phototherapy (broad- or narrow-band UVB light and (PUVA)

- 153 – 08** In people with psoriasis (all types), what are the clinical effectiveness, safety, tolerability and cost effectiveness of BBUVB, NBUVB and PUVA compared with each other or placebo/no treatment?
- 153 – 09** In people with psoriasis (all types), what are the clinical effectiveness, safety, tolerability and cost effectiveness of acitretin plus UVB (NBUVB and BBUVB) and acitretin plus PUVA compared with their monotherapies and compared with each other?
- 153 – 10** In people with psoriasis (all types), what are the clinical effectiveness, safety, tolerability and cost effectiveness of UVB (NBUVB or BBUVB) combined with dithranol, coal tar or vitamin D or vitamin D analogues compared with UVB alone or topical therapy alone?

Recommendations derived from these review questions

- 1.4.1.1 Offer narrowband ultraviolet B (UVB) phototherapy to people with plaque or guttate-pattern psoriasis that cannot be controlled with topical treatments alone. Treatment with narrowband UVB phototherapy can be given 3 or 2 times a week depending on patient preference. Tell people receiving narrowband UVB that a response may be achieved more quickly with treatment 3 times a week.
- 1.4.1.2 Offer alternative second- or third-line treatment when:
- narrowband UVB phototherapy results in an unsatisfactory response or is poorly tolerated **or**
 - there is a rapid relapse following completion of treatment (rapid relapse is defined as greater than 50% of baseline disease severity within 3 months) **or**
 - accessing treatment is difficult for logistical reasons (for example, travel, distance, time off work or immobility) **or**
 - the person is at especially high risk of skin cancer.
- 1.4.1.3 Consider psoralen^a (oral or topical) with local ultraviolet A (PUVA) irradiation to treat palmoplantar pustulosis.
- 1.4.1.4 When considering PUVA for psoriasis (plaque type or localised palmoplantar pustulosis) discuss with the person:
- other treatment options
 - that any exposure is associated with an increased risk of skin cancer (squamous cell carcinoma)
 - that subsequent use of ciclosporin may increase the risk of skin cancer, particularly if they have already received more than 150 PUVA treatments
 - that risk of skin cancer is related to the number of PUVA treatments.
- 1.4.1.5 Do not routinely offer co-therapy with acitretin when administering PUVA.
- 1.4.1.6 Consider topical adjunctive therapy in people receiving phototherapy with broadband or narrowband UVB who:
- have plaques at sites that are resistant or show an inadequate response (for example, the lower leg) to phototherapy alone, or at difficult-to-treat or high-need, covered sites (for example, flexures and the scalp), **and/or**
 - do not wish to take systemic drugs or in whom systemic drugs are contraindicated.

- 1.4.1.7 Do not routinely use phototherapy (narrowband UVB, broadband UVB or PUVA) as maintenance therapy.
- 1.4.1.8 Ensure that all phototherapy equipment is safety-checked and maintained in line with local and national policy^b.
- 1.4.1.9 Healthcare professionals who are giving phototherapy should be trained and competent in its use and should ensure an appropriate clinical governance framework is in place to promote adherence to the indications for and contraindications to treatment, dosimetry and national policy on safety standards for phototherapy^b.

a At the time of publication (October 2012), psoralen did not have UK marketing authorisation for this or any indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. The patient (or their parent or carer) should provide informed consent, which should be documented. See the GMC's [Good practice in prescribing medicines – guidance for doctors](#) for further information.

b See: [British Association Of Dermatologists: working party report on minimum standards for phototherapy services](#).

Surveillance decision

These review questions should not be updated.

The footnotes should be amended.

Methotrexate plus NBUVB

2-year Evidence Update

No relevant evidence identified.

4-year surveillance summary

An RCT³⁸ (n=120 patients with widespread plaque psoriasis) compared NBUVB plus methotrexate with NBUVB alone and methotrexate alone. End point of treatment (clearance) was 90% reduction in PASI score or treatment for up to 6 months, whichever was earlier; follow-up was 1 year. Achieving clearance took a significantly fewer number of weeks with NBUVB plus methotrexate than with either of the individual treatments. The number of phototherapy sessions was significantly less with NBUVB plus methotrexate than with NBUVB alone. The mean total cumulative dose of NBUVB for achieving clearance was significantly less with NBUVB plus methotrexate than with NBUVB alone, while the mean total cumulative dose of methotrexate was significantly less with NBUVB plus methotrexate than with methotrexate alone. Several limitations of the study were noted, including that the randomisation method was not specified, allocation to interventions was not specified, and blinding of

participants/personnel/ outcome assessment was not specified.

Topic expert feedback

Topic experts stated that an NBUVB/methotrexate combination was not usually used in practice – patients would normally start on methotrexate which would then possibly be supplemented with additional therapy (including UVB). However the experts were interested that studies had examined the combination treatment.

Impact statement

The new evidence suggests that the combination of NBUVB plus methotrexate can provide quicker improvement with less cumulative doses of both therapies compared with each one alone in the treatment of psoriasis. CG153 currently recommends both NBUVB and methotrexate as individual therapies but not in combination. However, this is a single trial with several limitations, therefore the evidence is currently unlikely to have an impact on the guideline.

New evidence is unlikely to change guideline recommendations.

PUVA, UVB, and photodynamic therapy (PDT)

2-year Evidence Update

No relevant evidence identified.

4-year surveillance summary

A systematic review and meta-analysis³⁹ of 23 studies examined localised phototherapy and photodynamic therapy for psoriasis. A meta-analysis found no significant difference between PUVA and non-laser targeted UVB. For the primary outcome, the pooled effect estimate of the efficacy (75% reduction in severity score) were: 77% (topical PUVA), 61% (targeted UVB), and 22% (PDT).

A double-blind RCT⁴⁰ (n=21 patients with chronic plaque psoriasis) compared the Levia localised NBUVB phototherapy device with sham control (visible light). Each patient had 1 lesion randomised to receive the Levia treatment and one lesion treated with control. Treatment was administered 3 times a week for 12 weeks. The primary outcome was the percentage of lesions achieving clear or almost clear target lesion score (TLS; a rating of 0–4 each of erythema, scaling, and thickness, measured biweekly by a blinded assessor) after 12 weeks of treatment. Secondary endpoints included changes in target lesion pruritus visual analogue scale (recorded by patients), percentage improvement in TLS, and the percentage of subjects achieving 50% improvement in TLS (TLS-50). The primary endpoint, TLS of 3 or less, was not achieved, but the secondary endpoints of percentage improvement in TLS and TLS-50 were significantly superior in treated compared to

sham-treated lesions. Percentage improvement in pruritus VAS was not significant.

Topic expert feedback

Topic experts noted the following publication by [Moseley 2015](#) 'Guidelines on the measurement of ultraviolet radiation levels in ultraviolet phototherapy: report issued by the British Association of Dermatologists and British Photodermatology Group'

Topic experts also noted that new [BAD Standards for phototherapy](#) have been issued in October 2016.

Impact statement

The new evidence suggests that topical PUVA and targeted UVB (and specifically NBUVB) phototherapy are effective in the treatment of localised psoriasis, while PDT appears to have low efficacy. This evidence is consistent with CG153 which recommends both NBUVB and PUVA, but does not make recommendations on PDT.

A link to the British Association of Dermatologists guideline on the measurement of ultraviolet radiation levels in ultraviolet phototherapy should be made.

Footnote [32](#) to recommendations 1.4.1.8/9 contains a broken link to an old version of the British Association of Dermatologists: working party report on minimum standards for phototherapy services. This will be updated to link to [the latest version of the standards](#).

New evidence is unlikely to change guideline recommendations.

UV-free blue light

2-year Evidence Update

No relevant evidence identified.

4-year surveillance summary

An RCT⁴¹ (n=47 patients with mild plaque psoriasis) examined treatment at home with UV-free blue light. Patients were randomised to either high-intensity blue light treatment (453 nm LED, 200 mW/cm²) or low-intensity treatment (453 nm LED, 100 mW/cm²) of 1 psoriasis plaque for 12 weeks. A contralateral control plaque remained untreated. Patient compliance and satisfaction were high. The primary endpoint, change from baseline of the Local Psoriasis Severity Index, revealed a

significant improvement of the target compared to the control plaques for both the high and low-intensity groups.

Topic expert feedback

No topic expert feedback was relevant to this evidence.

Impact statement

The new evidence suggests that UV-free blue light home treatment can improve psoriasis plaques. CG153 does not include recommendations on the use of UV-free blue light, however the evidence is from a single small trial that did not compare the intervention to any other active treatment, therefore no impact on the guideline is currently anticipated.

New evidence is unlikely to change guideline recommendations.

153 – 11 In people with psoriasis (all types) who have been exposed to coal tar, phototherapy (BBUVB, NBUVB and PUVA) or systemic non-biological or biological therapy, what is the risk of skin cancer compared with people not exposed to these interventions and which individuals are at particular risk?

Recommendations derived from this review question

1.4.2 Risk of skin cancer and how to minimise risk

- 1.4.2.1 Do not use PUVA in people with psoriasis of any type and a genetic predisposition to skin cancer for example, xeroderma pigmentosum or familial melanoma.
- 1.4.2.2 Do not use PUVA when other appropriate treatments are available in:
- people with a personal history of skin cancer **or**
 - people who have already received 150 PUVA treatments **or**
 - children.
- 1.4.2.3 Use PUVA with caution or consider other treatment options in:
- people at risk of skin cancer (melanoma and non-melanoma type) (see 'Improving outcomes for people with skin tumours including melanoma' [NICE cancer service guidance])
 - people with lighter skin types, such as skin types I or II on the Fitzpatrick scale^[12]
 - people who are likely to require ciclosporin or long-term methotrexate
 - young people.
- 1.4.2.4 Offer lifetime skin cancer surveillance to people treated with PUVA who have:
- had more than 150 PUVA treatments **or**
 - developed skin cancer.
- 1.4.2.5 Ensure that a permanent record of the person's cumulative number of UV treatments is kept (for example, in a national record).

Surveillance decision

No new information was identified at any surveillance review.

This review question should not be updated.

Systemic therapy

153 – 12 In people with psoriasis (all types), what are the clinical effectiveness, safety, tolerability and cost effectiveness of systemic methotrexate, ciclosporin and acitretin compared with each other or with placebo?

Recommendations derived from this review question

1.5.1 General recommendations

- 1.5.1.1 Responsibility for use of systemic therapy should be in specialist settings only. Certain aspects of supervision and monitoring may be delegated to other healthcare professionals and completed in non-specialist settings, in which case, such arrangements should be formalised.
- 1.5.1.2 When offering systemic therapy, tailor the choice of agent and dosing schedule to the needs of the individual and include consideration of:
- the person's age
 - disease phenotype, pattern of activity and previous treatment history
 - disease severity and impact
 - the presence of psoriatic arthritis (in consultation with a rheumatologist)
 - conception plans
 - comorbidities
 - the person's views.
- 1.5.1.3 Be aware of the benefits of, contraindications to and adverse effects associated with systemic treatments. Explain the risks and benefits to people undergoing this treatment (and their families or carers where appropriate), using absolute risks and natural frequencies when possible^a. Support and advice should be provided by healthcare professionals who are trained and competent in the use of systemic therapies.
- 1.5.1.4 When reviewing response to systemic therapy, take into account:
- disease severity compared with baseline (for example, [PASI](#) baseline to endpoint score)
 - control of psoriatic arthritis disease activity (in consultation with a rheumatologist if necessary)
 - the impact of the disease on the person's physical, psychological and social wellbeing
 - the benefits versus the risks of continued treatment
 - the views of the person undergoing treatment (and their family or carers where appropriate).
- 1.5.1.5 Monitor people using systemic treatment for all types of psoriasis in accordance with national and local drug guidelines and policy. Take appropriate action in the event of laboratory abnormalities or adverse events.
- 1.5.1.6 Offer adjunctive topical therapy to people with psoriasis using systemic therapy to optimise treatment outcomes.
- 1.5.1.7 Offer people with psoriasis who are starting treatment with a systemic non-biological or biological drug the opportunity to participate in long-term safety registries (for example the British Association of Dermatologists Biologic Interventions Register).
- #### 1.5.2 Systemic non-biological therapy
- 1.5.2.1 Offer systemic non-biological therapy to people with any type of psoriasis if:
- it cannot be controlled with topical therapy **and**
 - it has a significant impact on physical, psychological or social wellbeing **and**

- one or more of the following apply:
 - psoriasis is extensive (for example, more than 10% of body surface area affected or a [PASI](#) score of more than 10) **or**
 - psoriasis is localised and associated with significant functional impairment and/or high levels of distress (for example severe nail disease or involvement at high-impact sites) **or**
 - phototherapy has been ineffective, cannot be used or has resulted in rapid relapse (rapid relapse is defined as greater than 50% of baseline disease severity within 3 months).

Choice of drugs

- 1.5.2.2 Offer methotrexate^b as the first choice of systemic agent for people with psoriasis who fulfil the criteria for systemic therapy (see previous recommendation 1.5.2.1) except in the circumstances described in recommendations 1.5.2.4 and 1.5.2.12.
- 1.5.2.3 In people with both active psoriatic arthritis and any type of psoriasis that fulfils the criteria for systemic therapy (see recommendation 1.5.2.1) consider the choice of systemic agent in consultation with a rheumatologist.
- 1.5.2.4 Offer ciclosporin^c as the first choice of systemic agent for people who fulfil the criteria for systemic therapy (see recommendation 1.5.2.1) and who:
- need rapid or short-term disease control (for example a psoriasis flare) **or**
 - have palmoplantar pustulosis **or**
 - are considering conception (both men and women) and systemic therapy cannot be avoided.
- 1.5.2.5 Consider changing from methotrexate to ciclosporin (or vice-versa) when response to the first-choice systemic treatment is inadequate.
- 1.5.2.6 Consider acitretin for adults, and in exceptional cases only for children and young people, in the following circumstances:
- if methotrexate and ciclosporin are not appropriate or have failed **or**
 - for people with pustular forms of psoriasis.

Drug regimens

- 1.5.2.7 Use incremental dosing of methotrexate (for example, starting with an initial dose of 5–10 mg once a week) and gradually increase up to an effective dose and a maximum of 25 mg a week. Assess the treatment response after 3 months at the target dose of methotrexate and stop treatment if the response is inadequate (for example, a decrease of less than 75% in [PASI](#) score or a decrease of less than 50% in [PASI](#) score and 5 points in [DLQI](#) score).
- 1.5.2.8 Use the lowest possible therapeutic dose of methotrexate to maintain remission.
- 1.5.2.9 Use 2.5–3 mg/kg a day of ciclosporin^c. Escalate to 5 mg/kg a day after 4 weeks only when there is no response to the lower dose or when rapid disease control is necessary (for example in severe unstable disease). Assess the treatment response after 3 months at the optimum dose of ciclosporin and stop treatment if the response is inadequate (for example, less than a 75% decrease in [PASI](#) score or less than a 50% decrease in [PASI](#) score and less than 5 points in [DLQI](#) score).
- 1.5.2.10 Use the lowest possible therapeutic dose of ciclosporin to maintain remission for up to 1 year. Consider other treatment options when disease relapses rapidly on stopping ciclosporin therapy (rapid relapse is defined as greater than 50% of baseline disease severity within 3 months of stopping treatment). Do not use ciclosporin continuously for more than 1 year unless disease is severe or unstable and other treatment options, including systemic biological therapy, cannot be used.
- 1.5.2.11 Use incremental dosing of acitretin to minimise mucocutaneous side effects and achieve a target dose of 25 mg daily in adults. Consider dose escalation to a maximum of 50 mg daily when no other treatment options are available. Assess the treatment response after 4 months

at the optimum dose of acitretin and stop treatment if the response is inadequate, for example:

- in plaque-type psoriasis, less than a 75% decrease in [PASI](#) score or less than a 50% decrease in [PASI](#) score and less than 5 points in [DLQI](#) score
- in pustular forms of psoriasis, not achieving clear or nearly clear on the static Physician's Global Assessment.

a See [appendix B](#) for details of the risk-benefit profiles of interventions recommended in this guideline.

b At the time of publication (October 2012), methotrexate did not have UK marketing authorisation for this indication in children and young people. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. The patient (or their parent or carer) should provide informed consent, which should be documented. See the General Medical Council's [Good practice in prescribing medicines – guidance for doctors](#) for further information.

c At the time of publication (October 2012), ciclosporin did not have UK marketing authorisation for this indication in children and young people under 16 years of age. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. The patient (or their parent or carer) should provide informed consent, which should be documented. See the General Medical Council's [Good practice in prescribing medicines – guidance for doctors](#) for further information.

Surveillance decision

This review question should not be updated.

Janus kinase inhibitors

2-year Evidence Update

No relevant evidence identified.

4-year surveillance summary

Tofacitinib

Five relevant RCTs⁴²⁻⁴⁶ were identified evaluating the use of tofacitinib in patients with moderate to severe plaque psoriasis. However, guidance on tofacitinib is covered by the in-development technology appraisal of [tofacitinib for the treatment of moderate to severe plaque psoriasis](#) (see link to 'Topic selection technology appraisal decisions: January 2015 – [current date]').

Baricitinib

An RCT⁴⁷ examined baricitinib in patients with moderate-to-severe psoriasis.

Itacitinib

An RCT⁴⁸ examined itacitinib in patients with stable, chronic plaque psoriasis.

Topic expert feedback

It was noted that baricitinib and itacitinib are not available in the UK. Baricitinib was [filed in March 2016](#) for a license in the EU for the treatment of rheumatoid arthritis, but has not been filed for a license for the treatment of psoriasis.

Impact statement

New evidence was found on tofacitinib however this is covered by an in-development technology appraisal therefore no impact on CG153 is expected.

New evidence was found on baricitinib and itacitinib however these are not available in the UK therefore no impact on CG153 is expected.

New evidence is unlikely to change guideline recommendations.

Fumaric acid esters

2-year Evidence Update

No relevant evidence identified.

4-year surveillance summary

A Cochrane review⁴⁹ and a systematic review⁵⁰ examined fumaric acid esters for psoriasis.

An RCT⁵¹ examined addition of the oral histamine antagonist cetirizine to reduce adverse events associated with fumaric acid ester treatment in psoriasis.

However, guidance on fumaric acid esters is covered by the in-development technology

appraisal [ID776] [dimethyl fumarate for treating moderate to severe plaque psoriasis](#).

Topic expert feedback

In October 2015, NICE was informed by the MHRA about some medicines safety issues that were under consideration at a European level. One of the medicines was Tecfidera (dimethyl fumarate) licensed for the treatment of multiple sclerosis (but there is unlicensed use in psoriasis). In March 2015 the MHRA [published a warning about a case of fatal PML](#) (progressive multifocal leukoencephalopathy) in a person with multiple sclerosis treated with dimethyl fumarate. There was ongoing review at PRAC (Pharmacovigilance Risk Assessment Committee) and CHMP (Committee for Medicinal Products for Human Use).

A drug safety update was issued in April 2016: [Dimethyl fumarate \(Tecfidera\): updated advice on risk of progressive multifocal leukoencephalopathy](#). This included a comment on unlicensed use of dimethyl

fumarate and other fumaric acid esters for psoriasis and being aware of the risks of severe, prolonged lymphopenia and serious opportunistic infections, including John Cunningham virus infection which can lead to progressive multifocal leukoencephalopathy.

Topic experts noted that dermatologists are using fumaric acid esters (unlicensed, off label).

Impact statement

At the time CG153 was developed, fumaric acid esters were not licensed for any indication within the UK and therefore were unable to be considered within the guideline. New evidence was found, and safety alerts have been issued, on fumaric acid esters however this is covered by an in-development technology appraisal therefore no impact on CG153 is expected.

New evidence is unlikely to change guideline recommendations.

Apremilast

2-year Evidence Update

No relevant evidence identified.

4-year surveillance summary

Plaque psoriasis

Two RCTs^{52,53} (ESTEEM 1 and ESTEEM 2) examined apremilast in moderate to severe plaque psoriasis, and an RCT⁵⁴ examined apremilast in patients with psoriatic arthritis and current skin involvement (≥ 1 plaque psoriasis skin lesion ≥ 2 cm in size).

However, guidance on apremilast for plaque psoriasis is covered by TA419 [Apremilast for treating moderate to severe plaque psoriasis](#).

Nail and scalp psoriasis

An article⁵⁵ reported the results of 2 double blind RCTs^{52,53} (ESTEEM 1 and ESTEEM 2; n=1255) of apremilast in patients with difficult-to-treat nail and scalp psoriasis. Patients were randomised (2:1) to apremilast 30 mg twice daily or placebo. At week 16, placebo patients switched to apremilast through week 32, followed by a randomised withdrawal phase to week 52. A priori efficacy analyses included patients with nail (target nail Nail Psoriasis Severity Index score >1) and moderate to very severe scalp (Scalp Physician Global Assessment score >3) psoriasis at baseline. At

baseline, across the 2 trials, 66% and 65% of patients had nail psoriasis; 67% and 66% had moderate to very severe scalp psoriasis. At week 16, apremilast produced significantly greater improvements in Nail Psoriasis Severity Index score versus placebo in both ESTEEM 1 and 2. At week 16, apremilast produced significantly greater response in both NAPSI-50 (50% reduction from baseline in target nail Nail Psoriasis Severity Index score) and ScPGA (Scalp Physician Global Assessment score 0 or 1) versus placebo in both studies. Improvements were generally maintained over 52 weeks in patients with PASI response at week 32.

Topic expert feedback

Topic experts drew attention to the publication of TA368 (now updated to TA419) since CG153 was published and noted that it is not mentioned in the NICE version of the guideline.

Impact statement

New evidence was found on apremilast in plaque psoriasis however this is covered by TA419, which is not mentioned in the guideline but is included in the [Psoriasis NICE pathway](#). Consideration will be given to covering TA419 in CG153.

The new evidence further suggested that apremilast can reduce the severity of nail and

scalp psoriasis. The scope of TA419 stated that outcomes examined included: 'other complications of psoriasis (including nail, scalp and joint outcomes)'. Additionally, the population in the scope of TA419 was 'Adults with moderate to severe plaque psoriasis' – nail and scalp were not excluded, therefore

apremilast in nail and scalp psoriasis is covered by TA419 and no impact on CG153 is expected.

New evidence is unlikely to change guideline recommendations.

Liraglutide/pioglitazone

2-year Evidence Update

No relevant evidence identified.

4-year surveillance summary

An RCT⁵⁶ (n=20 obese glucose-tolerant patients with PASI of at least 8) compared once-daily subcutaneous injections of the glucagon-like peptide-1 receptor agonist liraglutide with placebo for an 8-week period. No significant change in the primary end points of PASI or DLQI were found in the liraglutide group compared with the placebo group. For secondary end points, high sensitive C-reactive protein did not change in any of the groups. Liraglutide treatment resulted in a significantly greater bodyweight loss compared with placebo, accompanied by decreased cholesterol levels. No serious adverse events occurred during the 8-week observation period. The most common complaint was transient nausea, which occurred in 45% of the liraglutide-treated patients but in none from the placebo group.

A double blind RCT⁵⁷ (n=48 patients with moderate-to-severe plaque psoriasis) compared 30 mg daily oral pioglitazone (an insulin sensitising drug) with placebo for 10 weeks. There was no significant difference in the number of patients achieving the primary outcome of treatment success (PASI-75) between the pioglitazone group and placebo group. Compared to placebo, no significant difference was found in high-sensitive C reactive protein. Metabolic syndrome and insulin resistance were not affected.

A single-blind RCT⁵⁸ (n=44 adult patients with plaque-type psoriasis) compared methotrexate plus pioglitazone with methotrexate alone. For

the primary outcome, after 16 weeks of therapy, the percentage of reduction in the mean PASI score was greater with methotrexate plus pioglitazone than methotrexate alone (significance not stated in the abstract). PASI 75 was achieved in significantly more patients on methotrexate plus pioglitazone than in patients on methotrexate alone within 16 weeks. For the secondary outcome of DLQI at 16 weeks from baseline, there was no extra benefit by the addition of pioglitazone to methotrexate therapy.

Topic expert feedback

It was noted that liraglutide and pioglitazone are licensed in the UK for the treatment of type 2 diabetes. Any use in psoriasis would be off-label.

Impact statement

The new evidence suggests that liraglutide and pioglitazone are of no significant benefit in psoriasis. CG153 does not make recommendations on these off-label treatments, therefore no impact on the guideline is expected. Pioglitazone however appears to enhance the therapeutic effect of methotrexate. CG153 recommends methotrexate as the first choice of systemic agent for psoriasis, but does not make any recommendations about it being taken in conjunction with pioglitazone. The evidence for the benefit of this combination is from a single small trial therefore further evidence to confirm the result is needed. No impact on the guideline is currently anticipated

New evidence is unlikely to change guideline recommendations.

5-fluorouracil

2-year Evidence Update

No relevant evidence identified.

4-year surveillance summary

An RCT⁵⁹ (n=40 patients with resistant localised plaque psoriasis) evaluated 5-

fluorouracil (5-FU). Intralesional injection of 5% 5-FU was given in a dosage of 0.1 ml/cm² of each plaque using an insulin syringe. In all patients, a single plaque was kept as control and was given intralesional injection of distilled water. A total of 3 injections were given in each plaque at weekly intervals. After that, patients were followed-up regularly at the interval of 2 weeks up to 12 weeks. All the lesions (both treated and control) were assessed clinically as well as photographically at each visit and graded using psoriasis severity index scoring. At 12 weeks, out of 40 patients treated, 4 (10%) patients had clearance (>90% resolution), 19 (48%) had excellent (70%–90%) improvement, whereas 12 (30%) patients were moderately (30%–70%) improved, and only 5 (13%) patients had mild or no improvement. Results were significant with 5-FU versus control. Almost all patients had injection site pain which subsided within 1–2 hours. A total of 10 (25%) patients had necrosis after 1 or 2 injections

which healed during the follow-up period within 6–8 weeks.

Topic expert feedback

It was noted that injectable fluorouracil is licensed in the UK for treatment of cancers.

Impact statement

The new evidence suggests that intralesional 5-FU appears to be effective in resistant localised plaque psoriasis. CG153 does not make any recommendations on the use of 5-FU, however the evidence is from single small trial, and further evidence would be needed to confirm results. Additionally, intralesional injection of 5-FU for psoriasis would be off-label for both the indication and administration route, therefore no impact on CG153 is currently expected.

New evidence is unlikely to change guideline recommendations.

Methotrexate

2-year Evidence Update

No relevant evidence identified.

4-year surveillance summary

A systematic review and meta-analysis⁶⁰ examined methotrexate in psoriasis. Two meta-analyses, one for efficacy and one for safety outcomes, were conducted. For efficacy, significantly more patients achieved PASI75 at primary endpoint (12 or 16 weeks) with methotrexate than placebo (11 studies, n=705). For safety outcomes, the meta-analysis was extended to include studies employing the same dose range of methotrexate for other chronic inflammatory conditions, such as rheumatoid arthritis, to maximise capture of relevant safety data. Based on 2763 patient safety years, adverse events were found treatment limiting in a mean of 7% of patients

treated for 6 months, with an adverse effect profile largely in line with that encountered in clinical practice

Topic expert feedback

No topic expert feedback was relevant to this evidence.

Impact statement

The new evidence suggests that methotrexate is more effective than placebo in psoriasis, with adverse events in line with expectations from current clinical practice. This is consistent with CG153 that recommends offering methotrexate as the first choice of systemic agent for people with psoriasis who fulfil the criteria for systemic therapy.

New evidence is unlikely to change guideline recommendations.

Ponesimod

2-year Evidence Update

No relevant evidence identified.

4-year surveillance summary

An RCT⁶¹ examined oral ponesimod in chronic plaque psoriasis.

Topic expert feedback

It was noted that ponesimod is a new drug in development for multiple sclerosis but is not available in the UK.

Impact statement

New evidence was found on ponesimod however this is not available in the UK

therefore the evidence is unlikely to affect CG153.

New evidence is unlikely to change guideline recommendations.

Statins

2-year Evidence Update

No relevant evidence identified.

4-year surveillance summary

No relevant evidence identified.

Topic expert feedback

Topic experts highlighted some ongoing clinical trials, conference abstracts and published studies examining the efficacy of statins for psoriasis outcomes, along with safety and survival impact. However none of the evidence was eligible for inclusion in the surveillance review.

They noted that further studies are required to consider whether statins have a place in the treatment of psoriasis. For example, in patients with psoriasis who need a statin – should potential impact of statins on psoriasis outcomes be a consideration?

Impact statement

No new evidence was found on statins in psoriasis, therefore no impact on CG153 is currently anticipated.

New evidence is unlikely to change guideline recommendations.

Retinoids

2-year Evidence Update

No relevant evidence identified.

4-year surveillance summary

No relevant evidence identified.

Topic expert feedback

It was noted that a drug safety update was issued in July 2013: [Oral retinoids: pregnancy prevention—reminder of measures to minimise teratogenic risk](#). It stated that risk of fetal malformation with oral retinoids is extremely high. All oral retinoids have an associated Pregnancy Prevention Programme (PPP), which is supported by educational material for prescribers, pharmacists, and patients. Women of child-bearing potential should have pregnancy excluded before starting treatment. While taking these medicines, contraception must be consistently used. Acitretin is particularly highlighted in the safety alert as it has a longer half-life than the other retinoids and therefore the PPP and contraceptive measures must also be undertaken for

considerably longer after treatment has finished (before and during treatment and for at least 2 years after treatment has finished – though the [summary of product characteristics](#) for acitretin say contraceptive measures should be taken for 3 years after treatment has stopped).

Impact statement

CG153 recommends considering acitretin for adults, and in exceptional cases only for children and young people, if methotrexate and ciclosporin are not appropriate or have failed or for people with pustular forms of psoriasis.

The guideline makes general recommendations that offering systemic therapy should include several considerations, which include conception plans, though no specific safety issues with acitretin are noted in the guideline. Consideration will be given to including information from the safety update on oral retinoids in CG153.

New evidence is unlikely to change guideline recommendations.

153 – 13 In people with psoriasis (all types) who are being treated with methotrexate, are there specific groups who are at high risk of hepatotoxicity?

Recommendations derived from this review question

Methotrexate and risk of hepatotoxicity

1.5.1.12 When considering the risks and benefits of treating any type of psoriasis with methotrexate, be aware that methotrexate can cause a clinically significant rise in transaminases and that long-term therapy may be associated with liver fibrosis (see recommendations 1.5.2.13 to 1.5.2.16).

Surveillance decision

This review question should not be updated.

Methotrexate and liver disease

2-year Evidence Update

No relevant evidence identified.

4-year surveillance summary

A systematic review and meta-analysis⁶² of 32 double-blind RCTs (n=13,177) examined risk of liver injury in methotrexate use for rheumatoid arthritis, psoriasis, psoriatic arthritis or inflammatory bowel disease. Studies with less than 100 participants or of less than 24 weeks duration were excluded. The outcomes assessed were total liver adverse events, minor liver enzyme abnormalities (<3 upper limit of normal [ULN]), major liver enzyme abnormalities (>3 ULN or treatment withdrawal) and a composite outcome of liver failure, fibrosis, cirrhosis or death. Methotrexate was significantly associated with an increased risk of total adverse liver events, as well as minor and major liver enzyme abnormalities. Patients treated with methotrexate were not at increased risk of liver failure, cirrhosis or death.

A systematic review and meta-analysis⁶³ of 8 observational studies (n=429) assessed whether methotrexate use for psoriasis increases the risk of developing liver fibrosis. Studies were included if at least 2 liver biopsies were performed in patients. Risk of developing 'significant' (undefined in the abstract) liver fibrosis with methotrexate was not statistically significant, whereas there was a statistically significantly increased risk of developing 'any fibrosis' or cirrhosis. There was no clear association between cumulative dose of

methotrexate and fibrosis. Obesity, diabetes and alcohol use were under-reported.

Topic expert feedback

No topic expert feedback was relevant to this evidence.

Impact statement

The new evidence suggests that methotrexate appears to be associated with an increased risk of total adverse liver events, liver enzyme abnormalities, and 'any' (but not 'significant') liver fibrosis, but is not associated with liver failure, cirrhosis or death. The authors of the first review noted that long-term liver toxicity could not be assessed due to the short duration of included clinical trials, and the authors of the second review noted that the quality of the included studies was weak and the degree of selection bias meant the results were not generalisable to all patients with psoriasis taking methotrexate. CG153 already recommends that when considering the risks and benefits of treating any type of psoriasis with methotrexate, there should be awareness that methotrexate can cause a clinically significant rise in transaminases and that long-term therapy may be associated with liver fibrosis, which is consistent with the new evidence. The authors of the second review noted that high-quality, population-based studies that consider potential confounders common in the psoriasis population are justified for better prediction of the subset of patients at risk of liver fibrosis.

New evidence is unlikely to change guideline recommendations.

Methotrexate and lung disease

2-year Evidence Update

No relevant evidence identified.

4-year surveillance summary

A systematic review and meta-analysis⁶⁴ of 7 double-blind RCTs (6 with placebo comparator; n=504 respiratory adverse events in 1630 participants) evaluated the risk of pulmonary disease among patients with psoriasis, psoriatic arthritis, and inflammatory bowel disease treated with methotrexate. Studies with fewer than 50 participants or of less than 12 weeks' duration were excluded. Methotrexate was not associated with an increased risk of adverse respiratory events, respiratory infections, or non-infectious respiratory events. No pulmonary deaths occurred.

Topic expert feedback

No topic expert feedback was relevant to this evidence.

Impact statement

The evidence suggests that there was no increased risk of lung disease in methotrexate treated patients with non-malignant inflammatory diseases. CG153 does not make any recommendations related to the risk of lung disease in methotrexate use, therefore no impact of the new evidence on the guideline is expected.

New evidence is unlikely to change guideline recommendations.

153 – 14 In people with psoriasis (all types) who are being treated with methotrexate or who are about to begin treatment with methotrexate, what is the optimum non-invasive method of monitoring hepatotoxicity (fibrosis or cirrhosis) compared with liver biopsy?

Recommendations derived from this review question

Methotrexate and monitoring for hepatotoxicity

- 1.5.2.13 Before and during methotrexate treatment, offer the person with any type of psoriasis an evaluation for potential risk of hepatotoxicity. Use standard liver function tests and serial serum procollagen III levels to monitor for abnormalities during treatment with methotrexate, taking into account pre-existing risk factors (for example obesity, diabetes and alcohol use), baseline results and trends over time.
- 1.5.2.14 When using serum procollagen III levels to exclude liver fibrosis or cirrhosis, be aware that the:
- test cannot be used in children and young people
 - results may be unreliable in people with psoriatic arthritis
 - estimated positive predictive value is 23–95% and the estimated negative predictive value is 89–100%.
- 1.5.2.15 Provide advice on modifiable risk factors for liver disease prior to and during therapy, including alcohol intake and weight reduction if appropriate in line with [Alcohol-use disorders: preventing harmful drinking](#) (NICE public health guidance 24), and [Obesity](#) (NICE clinical guideline 43). For further advice on how to support attitude and behavioural change see [Behaviour change](#) (NICE public health guidance 6).

- 1.5.2.16 Seek timely specialist advice and consider referral to a clinician with expertise in liver disease if the results of liver tests are abnormal.

Surveillance decision

This review question should not be updated.

Diagnostic accuracy of noninvasive markers of liver fibrosis

2-year Evidence Update

No relevant evidence identified.

4-year surveillance summary

A systematic review and meta-analysis⁶⁵ of 17 diagnostic cohorts and case-control studies evaluated the diagnostic accuracy of noninvasive markers of liver fibrosis in patients with psoriasis taking methotrexate. Liver biopsy was the reference standard. Sensitivity and specificity were 38% and 83% for standard liver function tests (LFTs), 74% and 77% for procollagen-3 N-terminal peptide (P3NP), 60% and 80% for Fibroscan (a measure of fibroelastography), and 55% and 49% for ultrasound.

Topic expert feedback

No topic expert feedback was relevant to this evidence

Impact statement

The highest sensitivity observed across the tests was 74%, and the study authors concluded that the clinical utility of liver function tests, procollagen-3 N-terminal peptide and liver ultrasound is poor and if these tests are used in isolation, a significant proportion of patients with liver fibrosis may remain unidentified. This is consistent with the

approach used in developing CG153 where the Guideline Committee noted that the most important characteristics of a screening test included 'very good accuracy' (that is, high sensitivity). The sensitivity and specificity of the individual tests found by the new evidence broadly agree with the values quoted in the full version of CG153 for these tests. The study authors further stated that their confidence in these results was limited owing to low-quality data; old, small studies which displayed significant selection bias and significant variation in the prevalence of fibrosis. No studies were identified evaluating recently developed markers. They noted that larger prospective studies are required in this population to validate newer non-invasive methods. The latest evidence does not appear to have added to that available when CG153 was developed, and with the limitations of the evidence and that the study provided no alternatives to the current strategy recommended in CG153 (standard liver function tests and serial serum procollagen III levels to monitor for abnormalities during treatment with methotrexate), no impact on the guideline is expected.

New evidence is unlikely to change guideline recommendations.

153 – 15 In people with chronic plaque psoriasis eligible to receive biological therapy, if the first biological agent fails, which is the next effective, safe and cost effective strategy?

Recommendations derived from this review question

The GDG did not review evidence for any aspect of the use of a first biological agent because guidance on this is already available in the existing NICE technology appraisals^a. Recommendations 1.5.3.3 to 1.5.3.11 are replicated from the relevant TAs and are listed here in alphabetical order by drug.

- 1.5.3.1 Biological agents for psoriasis should be initiated and supervised only by specialist physicians experienced in the diagnosis and treatment of psoriasis.

- 1.5.3.2 If a person has both psoriasis and psoriatic arthritis, take into account both conditions before initiating or making changes to biological therapy and manage their treatment in consultation with a rheumatologist (see also [Etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis](#) [NICE technology appraisal guidance 199] and [Golimumab for the treatment of psoriatic arthritis](#) [NICE technology appraisal guidance 220]).
- 1.5.3.3 When using the [DLQI](#), healthcare professionals should take into account any physical, sensory or learning disabilities, or communication difficulties that could affect the responses to the [DLQI](#) and make any adjustments they consider appropriate.

Adalimumab

The recommendations in this section are from [Adalimumab for the treatment of adults with psoriasis](#) (NICE technology appraisal guidance 146).

- 1.5.3.4 Adalimumab is recommended as a treatment option for adults with plaque psoriasis for whom anti-tumour necrosis factor (TNF) treatment is being considered and when the following criteria are both met.
- The disease is severe as defined by a total [PASI](#) of 10 or more and a [DLQI](#) of more than 10.
 - The psoriasis has not responded to standard systemic therapies including ciclosporin, methotrexate and PUVA; or the person is intolerant of, or has a contraindication to, these treatments.
- 1.5.3.5 Adalimumab should be discontinued in people whose psoriasis has not responded adequately at 16 weeks. An adequate response is defined as either:
- a 75% reduction in the [PASI](#) score (PASI 75) from when treatment started **or**
 - a 50% reduction in the [PASI](#) score (PASI 50) and a 5-point reduction in [DLQI](#) from start of treatment.

Etanercept

The recommendations in this section are from [Etanercept and efalizumab for the treatment of adults with psoriasis](#) (NICE technology appraisal guidance 103).

- 1.5.3.6 Etanercept, within its licensed indications, administered at a dose not exceeding 25 mg twice weekly is recommended for the treatment of adults with plaque psoriasis only when the following criteria are met.
- The disease is severe as defined by a total [PASI](#) of 10 or more and a [DLQI](#) of more than 10.
 - The psoriasis has failed to respond to standard systemic therapies including ciclosporin, methotrexate and PUVA; or the person is intolerant to, or has a contraindication to, these treatments.
- 1.5.3.7 Etanercept treatment should be discontinued in patients whose psoriasis has not responded adequately at 12 weeks. Further treatment cycles are not recommended in these patients. An adequate response is defined as either:
- a 75% reduction in the [PASI](#) score from when treatment started (PASI 75) **or**
 - a 50% reduction in the [PASI](#) score (PASI 50) and a 5-point reduction in [DLQI](#) from when treatment started.

Infliximab

The recommendations in this section are from [Infliximab for the treatment of adults with psoriasis](#) (NICE technology appraisal guidance 134).

- 1.5.3.8 Infliximab, within its licensed indications, is recommended as a treatment option for adults with plaque psoriasis only when the following criteria are met.
- The disease is very severe as defined by a total [PASI](#) of 20 or more and a [DLQI](#) of more than 18.
 - The psoriasis has failed to respond to standard systemic therapies such as ciclosporin, methotrexate or PUVA, or the person is intolerant to or has a contraindication to these treatments.

1.5.3.9 Infliximab treatment should be continued beyond 10 weeks only in people whose psoriasis has shown an adequate response to treatment within 10 weeks. An adequate response is defined as either:

- a 75% reduction in the [PASI](#) score from when treatment started (PASI 75) or
- a 50% reduction in the [PASI](#) score (PASI 50) and a 5-point reduction in the [DLQI](#) from when treatment started.

Ustekinumab

The recommendations in this section are from [Ustekinumab for the treatment of adults with moderate to severe psoriasis](#) (NICE technology appraisal guidance 180).

1.5.3.10 Ustekinumab is recommended as a treatment option for adults with plaque psoriasis when the following criteria are met.

- The disease is severe, as defined by a total [PASI](#) score of 10 or more and a [DLQI](#) score of more than 10.
- The psoriasis has not responded to standard systemic therapies, including ciclosporin, methotrexate and PUVA, or the person is intolerant of or has a contraindication to these treatments.
- The manufacturer provides the 90 mg dose (two 45 mg vials) for people who weigh more than 100 kg at the same total cost as for a single 45 mg vial.

1.5.3.11 Ustekinumab treatment should be stopped in people whose psoriasis has not responded adequately by 16 weeks after starting treatment. An adequate response is defined as either:

- a 75% reduction in the [PASI](#) score (PASI 75) from when treatment started **or**
- a 50% reduction in the [PASI](#) score (PASI 50) and a 5-point reduction in the [DLQI](#) score from when treatment started.

Changing to an alternative biological drug

1.5.3.12 Consider changing to an alternative biological drug in adults if:

- the psoriasis does not respond adequately to a first biological drug as defined in NICE technology appraisals^a (at 10 weeks after starting treatment for infliximab, 12 weeks for etanercept, and 16 weeks for adalimumab and ustekinumab; primary failure) **or**
- the psoriasis initially responds adequately but subsequently loses this response, (secondary failure) **or**
- the first biological drug cannot be tolerated or becomes contraindicated.

1.5.3.13 For adults in whom there is an inadequate response to a second biological drug, seek supra-specialist advice from a clinician with expertise in biological therapy.

a NICE technology appraisal guidance [103](#), [134](#), [146](#) and [180](#).

Surveillance decision

This review question should not be updated.

First line use of biologics covered by published/in-development NICE technology appraisals: plaque psoriasis

2-year Evidence Update

No relevant evidence identified

4-year surveillance summary

Adults

Evidence was found on first line use of the following biologics for plaque psoriasis:

Surveillance proposal consultation document March 2017 – Psoriasis (2012) NICE guideline CG153

adalimumab, briakinumab, brodalumab, etanercept, ixekizumab, secukinumab, tildrakizumab and ustekinumab. However this evidence has not been formally incorporated into the surveillance review because the review question is concerned only with the next biologic to use after a first biologic fails. Additionally, this evidence is all covered by the following list of published or in-development NICE technology appraisals:

Published:

- [Adalimumab for the treatment of adults with \(plaque\) psoriasis](#) (June 2008) TA146
- [Etanercept and efalizumab for the treatment of adults \(plaque\) with psoriasis](#) (July 2006) TA103
- [Secukinumab for treating moderate to severe plaque psoriasis](#) (July 2015) TA350
- [Ustekinumab for the treatment of adults with moderate to severe \(plaque\) psoriasis](#) (September 2009) TA180
- [No new evidence was found for infliximab, which has the following technology appraisal: [Infliximab for the treatment of adults with psoriasis](#) (January 2008) TA134.]

In-development

- [Psoriasis – briakinumab \(plaque, moderate to severe\) \[ID65\]](#)
- [Psoriasis \(plaque, moderate, severe\) - ixekizumab \(after systemic therapy\) \[ID904\]](#)
- [Brodalumab for treating moderate to severe plaque psoriasis after systemic therapy \[ID878\]](#)
- [Tildrakizumab for chronic plaque psoriasis, moderate to severe](#) (see link to 'Topic selection technology appraisal decisions: January 2015 – [current date]')

Paediatric

Evidence was found on first line use of ustekinumab in people aged 12 to 17 years with moderate-to-severe plaque psoriasis, and on anti-TNF agents for paediatric psoriasis (a systematic review which included 1 study of etanercept). However this evidence has not been formally incorporated into the surveillance review because the review question is concerned only with the next biologic to use after a first biologic fails. Additionally, guidance on ustekinumab and etanercept is covered by the following in-development technology appraisal

- [Psoriasis \(plaque, chronic, severe, children, young people\) - adalimumab, etanercept and ustekinumab \[ID854\]](#)

Topic expert feedback

It was noted that the following drug safety updates have been issued: [Ustekinumab \(Stelara\): risk of exfoliative dermatitis](#) (January 2015) and [Tumour necrosis factor alpha inhibitors](#) – risk of tuberculosis (this includes

adalimumab, etanercept and infliximab; April 2014).

Topic experts noted the following:

- TA350 (secukinumab) has been issued since CG153 was published and is not mentioned in the NICE version of the guideline.
- Ixekizumab is now licensed by the EMA
- Biosimilars are available and licensed for infliximab and etanercept now they are off-patent (which are cheaper than the original drug, and will also push down costs of parent compounds). It would be useful to add information and details of these biosimilar drugs and where they fit into the pathway. Patients are being offered biosimilars in place of current branded versions of infliximab and etanercept, therefore efficacy and safety data might need to be considered, so that patients can make an informed choice.
- An adalimumab biosimilar may be available soon (patents will expire in the US in December 2016 and in Europe in April 2018)
- Adalimumab has had a license change so can be used weekly rather than fortnightly.
- Ustekinumab can be prescribed at a 90 mg dose if the patient is less than 100kg. Also flat pricing for ustekinumab (45 and 90 mg the same cost – dose escalation effective in partial responders). [Note: TA180 currently states ustekinumab is recommended when 'The manufacturer provides the 90 mg dose (two 45 mg vials) for people who weigh more than 100 kg at the same total cost as for a single 45 mg vial.']
- Paediatric use of some biologics (ustekinumab, adalimumab and etanercept) has now been licensed. Pharmacovigilance registry (BADBIR - British Association of Dermatologists Biologic Interventions Register) is now open for children and young people. This is a high need group (severe psoriasis in children/young people); use of biologics in this group presents specific risks and considerations; requires transition services. Specific recommendations are required.
- There have been newer targeted treatments (mainly directed at IL17 [such as secukinumab, ixekizumab, brodalumab] and IL12/23 [such as ustekinumab,

tildrakizumab, guselkumab]) approved and available for both psoriasis and psoriatic arthritis.

- New BAD guideline on biologic therapy for psoriasis is due for publication in early 2017 (current guideline is from 2009).
- Fear of reoccurrence seems to be an underlying concern once patients get on to systemic therapies/biologics and they are reluctant to reduce or come off therapy.
- Anecdotal reports of unequal access to biologic medicines.
- Ongoing safety surveillance of biologics required.

Impact statement

New evidence was found on adalimumab, briakinumab, brodalumab, etanercept, ixekizumab, secukinumab, tildrakizumab and ustekinumab. However this evidence is covered by several published or in-development NICE technology appraisals. No impacts on CG153 are therefore expected from evidence found for any biologics covered by published or in-development technology appraisals.

Secukinumab for treating moderate to severe plaque psoriasis (July 2015) TA350 was issued since CG153 was published and is not mentioned in the guideline, but is included in the Psoriasis NICE pathway. Consideration will

be given to covering TA350 in CG153, alongside the other incorporated technology appraisals of biologic treatments for psoriasis.

For biosimilars, the overview pages of both TA103 (etanercept) and TA134 (infliximab) note that 'The recommendations also apply to etanercept/infliximab biosimilar products that have a marketing authorisation allowing the use of the biosimilar for the same indication'. NICE has also issued a [position statement on biosimilars](#).

For paediatric use of biologics, new evidence was found on ustekinumab and etanercept. However this evidence is covered by an in-development NICE technology appraisal therefore no impact on CG153 is expected.

Consideration will be given to including information from the safety updates on ustekinumab and tumour necrosis factor alpha inhibitors in CG153.

Any impact of changes to licensing and prescribing of adalimumab and ustekinumab is within the remit of their respective technology appraisals, therefore no direct impact on CG153 is anticipated.

New evidence is unlikely to change guideline recommendations.

First line use of biologics covered by published/in-development NICE technology appraisals: psoriasis at specific sites and non-plaque psoriasis

2-year Evidence Update

No relevant evidence identified.

4-year surveillance summary

An RCT⁶⁶ (n=33) examined ustekinumab in palmo-plantar pustular psoriasis (PPPP) and palmo-plantar pustulosis (PPP). Patients were randomised to ustekinumab 45 mg or placebo at day 0 and week 4 with subsequent placebo cross-over to ustekinumab at week 16. There was no significant difference between ustekinumab and placebo in the proportion of patients achieving the primary outcome of a 50% improvement in the Palmo-Plantar Pustular Area and Severity Index at week 16 for patients with either PPPP or PPP.

A post hoc analysis⁶⁷ of an RCT (n=142 patients with moderate-to-severe plaque psoriasis; 58 had nail psoriasis and

105 had scalp psoriasis) examined ixekizumab for scalp and nail lesions. The study comprised a 20-week randomised, placebo-controlled period and a 48-week open-label extension. Patients were randomised to receive placebo, or 10, 25, 75 or 150 mg of ixekizumab injected subcutaneously at weeks 0, 2, 4, 8, 12 and 16. In the open-label extension, all patients received 120 mg ixekizumab every 4 weeks. At week 20 of the randomised phase, patients with scalp psoriasis in the 25-, 75- and 150-mg groups had significant mean change and percent improvement from baseline in Psoriasis Scalp Severity Index (PSSI) compared to placebo. Patients with nail psoriasis in the 75- and 150-mg groups had significant improvements from baseline in Nail Psoriasis Severity Index (NAPSI) compared to placebo. By week 48 of the open-label phase, 78% of patients with scalp psoriasis and 51% of patients with nail psoriasis experienced complete resolution of lesions.

A subanalysis⁶⁸ of a double-blind RCT examined secukinumab in patients with moderate-to-severe psoriasis and non-pustular involvement of the hands, feet and/or nails (n=131 with hand and/or foot psoriasis; n=304 with nail psoriasis). Patients were randomised (1:2:2:1) to 1 of 3 subcutaneous secukinumab 150 mg induction regimens ('single' [week 0], 'monthly' [Weeks 0, 4, 8], or 'early' [weeks 0, 1, 2, 4]) or placebo. At Week 12, a significantly higher percentage of subjects with hand and/or foot psoriasis achieved an Investigator's Global Assessment response (score of 0 [clear] or 1 [minimal]) and an improvement of >2 points on the 5-point hand/foot scale versus baseline) with the 'early' regimen versus placebo. The composite nail score significantly improved with the 'early' and 'monthly' regimens, but worsened with placebo. Secukinumab was well tolerated.

A post hoc analysis⁶⁹ of a multicentre RCT (BELIEVE, n=730 patients with moderate to severe psoriasis; 663 had scalp psoriasis, 457 nail, and 433 scalp and nail) examined adalimumab for scalp and/or nail psoriasis. Efficacy was assessed in the pooled treatment group (adalimumab with or without calcipotriol plus betamethasone dipropionate). At week 16, the proportion of patients achieving a PASI 75 response did not differ significantly between those with (68%) and without (64%) scalp involvement. PASI 75 response rates were lower in patients with nail psoriasis compared with patients without nail psoriasis at week 8 and week 16 (though the difference was only significant at week 8). At week 16, PASI 75 response rates did not differ significantly between patients with scalp and nail involvement (66%) and patients without both scalp and nail involvement (71%). Patients in all scalp and nail subgroups reported improvements in DLQI and pain scores throughout the study. Patients with scalp psoriasis exhibited large improvements in scalp symptoms, demonstrated by a median decrease from baseline PSSI at week 16 of 100%. Patients with nail psoriasis improved, demonstrated by a median decrease from baseline NAPSI at week 16 of 40%.

A systematic review⁷⁰ of 13 randomised and placebo-controlled studies examined the efficacy and safety of infliximab in plaque psoriasis (7 studies), psoriatic arthritis (5 studies), and palmoplantar psoriasis (1 study). The 1 trial of infliximab (5 mg/kg) in

palmoplantar psoriasis showed that 33% (4/12) of the infliximab group achieved a 75% improvement in the modified Palmoplantar Psoriasis Area and Severity Index versus 8% (1/12) with placebo. Overall, the most common drug-induced adverse events were pain, hepatic dysfunction, and infusion reaction

Topic expert feedback

See topic expert feedback in the previous section 'First line use of biologics covered by published/in-development NICE technology appraisals – plaque psoriasis'.

Additionally, topic experts noted that the scope for CG153 covered non-plaque psoriasis. Evidence for non-plaque psoriasis and also psoriasis at high-need sites was searched for during development of the original guideline, but generally there was little. However, these are a very important high-need group and therefore important to cover.

Impact statement

The new evidence suggests that:

- Ustekinumab appears to have limited efficacy in PPPP and PPP, but the authors noted that conclusions are limited by the small sample size of this study.
- Ixekizumab appears to improve nail and scalp psoriasis within 20 weeks, with maintenance of clinical response and complete resolution of plaques after a further year for the majority of patients with scalp psoriasis, and around half of patients with nail psoriasis.
- Secukinumab appears to have a beneficial effect on psoriasis of the hands/feet/nails over 12 weeks.
- Adalimumab appears to improve overall psoriasis and scalp and nail symptoms in patients with scalp psoriasis and/or nail involvement. Similar PASI 75 response rates are achieved in patients with and without scalp involvement, whereas patients with nail involvement demonstrate a moderate (possibly delayed) PASI 75 response rate.
- Infliximab appears to be moderately effective in palmoplantar psoriasis.

NICE has issued or is developing technology appraisals on all of the biologics examined by the new evidence for the indication plaque psoriasis. However psoriasis of the scalp, nails, hands and feet were not excluded from the scopes of the technology appraisals, therefore the use of these biologics for scalp, nails,

hands and feet is covered by their respective technology appraisals and no impact on CG153 is expected.

New evidence is unlikely to change guideline recommendations.

First line use of biologics not covered by published/in-development NICE technology appraisals

2-year Evidence Update

No relevant evidence identified.

4-year surveillance summary

An RCT⁷¹ examined the anti-IL-23A monoclonal antibody 'BI655066' (generic name: risankizumab) for treatment of moderate-to-severe psoriasis.

An RCT⁷² examined the anti-CD6 monoclonal antibody itolizumab in moderate to severe chronic plaque psoriasis.

An RCT⁷³ examined intradermal injection of the anti-TNF-alpha antibody 'DLX105' (generic name not stated in the abstract) in patients with chronic plaque psoriasis.

Topic expert feedback

It was noted that risankizumab, itolizumab and DLX105 are not available in the UK.

Impact statement

New evidence was found on risankizumab, itolizumab and DLX105, which are not currently the subject of a published or in-development NICE technology appraisal. A surveillance review can consider evidence on unappraised drugs to fill gaps between technology appraisals, however these drugs are not available in the UK therefore the evidence is unlikely to affect CG153.

New evidence is unlikely to change guideline recommendations.

Clinical efficacy ranking of biological agents

2-year Evidence Update

No relevant evidence identified.

4-year surveillance summary

A systematic review and network meta-analysis⁷⁴ of 27 RCTs (n=10,629) examined efficacy and safety of new biologic agents targeting the interleukin-23/T helper 17 cell pathway for moderate to severe plaque psoriasis. Efficacy and safety outcomes at weeks 10-16 were compared using a random-effects network meta-analysis of direct and indirect comparisons among the therapeutic options. There were 6 direct drug-to-drug comparisons in the network, with a high degree of consistency between the direct and the indirect evidence. From the available evidence, infliximab 5mg/kg every 8 weeks and secukinumab 300mg every 4 weeks were among the most effective short-term treatment, but ranked as the biologic most likely to produce any adverse event or an infectious adverse event, respectively. Ustekinumab 90mg every 12 weeks, the third most efficacious, was the only agent that did not

show increased risk of adverse events when compared with placebo.

A systematic review and meta-analysis⁷⁵ of 16 RCTs with different time points aimed to estimate the efficacy of biologics in the treatment of moderate-to-severe plaque psoriasis in the currently approved conditions of use in the European Union at relevant time points for evaluation of response in clinical practice (failure assessment as recommended in the SmPCs and/or at the end of the induction phase). From the meta-analysis at the primary endpoint times, infliximab (at week 10) had the greatest probability of response with respect to placebo for all PASI-based efficacy measures (PASI 50, PASI 75 and PASI 90). At the end of the induction phase (week 24), ustekinumab 45 mg had the greatest probability of achieving PASI 75 response, followed by ustekinumab 90 mg, infliximab, adalimumab and etanercept. At the time points recommended for primary failure assessment according to the approved SmPCs, ustekinumab 45 mg (at week 28) also had the greatest probability of achieving PASI 50 response, followed by ustekinumab 90 mg, infliximab, adalimumab and etanercept.

Topic expert feedback

Topic experts noted that a new BAD guideline on biologic therapy for psoriasis is due for publication in early 2017 (the [current guideline](#) is from 2009).

Impact statement

The first review ordered the biologic treatments from most to least effective as infliximab, secukinumab and ustekinumab (though ustekinumab had fewer adverse effects). However the authors noted that treatment recommendations should also consider long term outcomes and costs.

In the second review, in terms of the most relevant efficacy measures (PASI 50 and PASI 75) and time points (end of induction phase [week 24] and time to assess primary failure as per the SmPCs), in the currently approved conditions of use, ustekinumab was the most effective, followed by infliximab, adalimumab and etanercept.

CG153 did not review evidence for any aspect of the use of a first biological agent because guidance on this is already available in the existing NICE technology appraisals, and

therefore makes no recommendations on the first biologic to use. Though it does recommend that if a person has psoriasis and psoriatic arthritis, both conditions should be taken into account before initiating or making changes to biological therapy. In terms of changing to an alternative biologic, CG153 recommends considering this if: the psoriasis does not respond adequately to a first biological drug, or the psoriasis initially responds adequately but subsequently loses this response, or the first biological drug cannot be tolerated or becomes contraindicated. GG153 does not specify a sequence or provide any guidance on the sequence with which to prescribe drugs. The current [BAD guideline \(2009\) on biologic therapy for psoriasis](#) contains a section 'How to determine the optimal choice and sequence of therapy', but this is now several years old and a new version is due for publication in early 2017. This guidance is awaited therefore no impact on CG153 is currently expected.

New evidence is unlikely to change guideline recommendations.

Cost effectiveness of sequential biologic therapies in patients exposed to previous biologic therapy

2-year Evidence Update

No relevant evidence identified.

4-year surveillance summary

A cost-effectiveness analysis⁷⁶ assessed sequential biologic therapies in patients with severe psoriasis who have been exposed to previous biologics. A 2-part model with a 10-year time horizon was built to model an initial 13.5-week 'trial' phase and a longer-term 'treatment' period with annual Markov cycles. PASI response rates from subgroup analyses of 3 randomised placebo-controlled trials evaluating biologic agents were considered. A meta-analysis of these data provided probabilities of achieving PASI response (50/75/90) in the short term, and published evidence and assumptions were used to predict outcomes over the longer term. Benefits were measured in quality-adjusted life years (QALYs), and costs (2013-14) to the UK NHS included drugs, administration, monitoring, and hospitalisation. Costs and benefits were discounted 3.5% per annum. Cost

effectiveness of sequential biologic therapy was measured using an incremental cost-effectiveness ratio (ICER) compared to best supportive care (BSC). Extensive sensitivity analyses were performed to assess the impact of alternative assumptions on the results. The results indicated that over 10 years, switching to a second biologic following intolerance to or failure of a first is likely to generate more QALYs than BSC, but at a higher cost. Base case results suggest the ICER of the second biologic compared to BSC is 17,681 per QALY; however, sensitivity analyses indicate that changes in the efficacy of BSC, drug costs, dropout rates, and rates of hospitalisation have a significant impact, causing the ICER to range from less than 10,000 to over 50,000 per QALY.

Topic expert feedback

No topic expert feedback was relevant to this evidence.

Impact statement

The new evidence suggests that further biologic therapy for patients with psoriasis who have previously been treated with biologic therapy may be cost effective, although the

authors noted that there is considerable uncertainty in the results. This evidence is consistent with CG153 which recommends changing to an alternative biological drug in adults if: the psoriasis does not respond adequately to a first biological drug, or the psoriasis initially responds adequately but subsequently loses this response, or the first biological drug cannot be tolerated or becomes contraindicated. The guideline further recommends that for adults in whom there is an inadequate response to a second biological drug, supra-specialist advice should be sought

from a clinician with expertise in biological therapy. As the new evidence is consistent with CG153 no impact is expected. The authors of the cost effectiveness analysis noted that future studies should be designed to evaluate the clinical efficacy of biologic therapies in patients exposed to a previous biologic, with particular attention given to short-term and longer-term responses.

New evidence is unlikely to change guideline recommendations.

Combined systemic therapies

2-year Evidence Update

No relevant evidence identified.

4-year surveillance summary

A systematic review and meta-analysis⁷⁷ of 17 RCTs examined combined use of systemic agents for plaque psoriasis. Most studies favoured combination therapy, albeit with low significance and low quality of evidence. Etanercept plus methotrexate was the only combination therapy investigated with an adequate sample size (n=478). In the short term, this combination had significantly superior efficacy (PASI 75) with a moderate quality of evidence compared with etanercept monotherapy. There was however a significant increase in adverse events, though the authors stated the overall safety profile remained acceptable.

Topic expert feedback

Topic experts noted that combined therapy with etanercept plus methotrexate is used in clinical

practice – usually in high need patients where other treatments haven't worked (including biologics).

Impact statement

The new evidence suggests that combined therapy with etanercept plus methotrexate may be beneficial but adverse effects are increased. The authors stated that for most other combinations, combination therapy was favoured but with low significance and low quality of evidence. CG153 recommends offering adjunctive topical therapy to people with psoriasis using systemic therapy to optimise treatment outcomes, but makes no recommendations on combining systemic therapies. Limitations of the new evidence noted by the authors mean that it is unlikely to affect the guideline.

New evidence is unlikely to change guideline recommendations.

Etanercept maintenance after achieving control with ciclosporin

2-year Evidence Update

No relevant evidence identified.

4-year surveillance summary

An RCT⁷⁸ (n=120 patients with moderate-to-severe plaque psoriasis) examined the efficacy of etanercept as replacement therapy for ciclosporin. Patients with plaque psoriasis were given ciclosporin 5 mg/kg/day until achievement of PASI50 at which point ciclosporin was tapered to 0 over 6 weeks. At week 6, patients were randomised to receive

etanercept (50 mg/week) or placebo for an additional 24 weeks. Patients in the etanercept group experienced a reduction in mean PASI score (non-significant versus ciclosporin) at week 30; patients in the placebo group had a mean PASI increase (significant versus ciclosporin). Patient-reported adverse events were not significantly different between groups

Topic expert feedback

No topic expert feedback was relevant to this evidence.

Impact statement

The new evidence suggests that etanercept appears to be effective and tolerable as replacement therapy for ciclosporin in plaque psoriasis. The full version of CG153 notes that once satisfactory control is achieved with ciclosporin, unlike other systemic treatments (where the same treatment is continued at the minimal effective dose in order to maintain disease control and quality of life), ciclosporin has predictable nephrotoxic effects and is not generally considered suitable for long-term disease management. CG153 recommends that ciclosporin at the lowest possible therapeutic dose can be used to maintain

remission for up to 1 year, and it should not be used continuously for more than 1 year unless disease is severe or unstable and other treatment options, including systemic biological therapy, cannot be used. The new evidence suggests that etanercept could be an option for maintenance once control has been achieved with ciclosporin, but the evidence is from a single trial and etanercept may not be a suitable option for all patients therefore it is unlikely to affect the current guideline.

New evidence is unlikely to change guideline recommendations.

Biologics for psoriatic arthritis

2-year Evidence Update

No relevant evidence identified (management of psoriatic arthritis out of scope of CG153).

4-year surveillance summary

No relevant evidence identified (management of psoriatic arthritis out of scope of CG153).

Topic expert feedback

It was noted that [Ustekinumab for treating active psoriatic arthritis \(June 2015\) TA340](#) was issued since CG153 published and is not mentioned in the NICE version of the guideline.

Impact statement

TA340 Ustekinumab for treating active psoriatic arthritis was issued since CG153 published, which is not mentioned in the guideline but is included in the [Psoriasis NICE pathway](#) (via a link to the [NICE pathway on spondyloarthritis](#)). Consideration will be given to covering TA340 in CG153, alongside the other cross-referrals to technology appraisals of biologic treatments for psoriatic arthritis in recommendation 1.5.3.2.

New evidence is unlikely to change guideline recommendations.

Cognitive behavioural therapy

153 – 16 In people with psoriasis (all types), how effective are cognitive behavioural therapy (group and individual) interventions alone or as an adjunct to standard care compared with standard care alone for managing psychological aspects of the disease in reducing distress and improving quality of life?

Recommendations derived from this review question

No recommendations were derived.

Surveillance decision

This review question should not be updated.

Cognitive behavioural therapy

2-year Evidence Update

An RCT⁸¹ (n=135 patients with mild to moderate plaque psoriasis) examined whether tailored computerised cognitive behavioural therapy (CCBT) can reduce distress, and improve quality of life and clinical severity. Participants were randomised to a 6-week CCBT programme ('eTIPs'; 6 modules of CBT plus education tailored to psoriasis), or to a control of usual care. Primary outcomes were anxiety and depression measured on the Hospital Anxiety and Depression Scale. For complete cases (patients who provided usable post-intervention data), the reduction in the CCBT group in mean anxiety score from baseline to follow-up after the 6-week intervention was significantly greater than that seen in the control group. However, this difference was not significant when all cases (every patient, including those with incomplete data) were analysed. Depression scores at follow-up did not differ significantly between groups in either the complete-case or all-case analysis. Of the secondary outcomes, in the complete-case analysis, a significantly greater improvement was seen in quality of life score (measured by the DLQI) in the CCBT group from baseline to follow-up than in the control group. This difference was also significant in the all-case analysis. Psoriasis severity (measured by self-administered PASI) was no different between groups at follow-up in either of the analyses.

4-year surveillance summary

A pilot RCT⁸² (n=29 people with psoriasis) examined an 8-week mindfulness-based cognitive therapy treatment as an adjunct to usual psoriasis therapy versus usual psoriasis therapy alone. All patients completed self-reported measurements of psoriasis severity, perceived stress, distress and quality of life, at baseline and again post-intervention. The mindfulness group reported significantly lower psoriasis severity (Self-Assessed PASI) and quality of life impairment scores (DLQI) than the control group. There was no significant difference between groups on perceived stress (Perceived Stress Scale) or distress scores (Hospital Anxiety Depression Scale).

A single-blind RCT⁸³ (n=40 patients with psoriasis) compared an 8-week CBT/biofeedback course plus narrow-band UVB phototherapy with an 8-week course of

narrow-band UVB phototherapy only. Outcomes were evaluated at baseline and the end of the study. Significantly more patients in the CBT group achieved PASI75 compared with the UVB-only group. General Health Questionnaire-12 cases were reduced significantly more in the CBT group than in the UVB-only group. The Skindex-29 emotional domain showed a significant improvement in the CBT group compared with UVB-only.

Topic expert feedback

Topic experts noted that there is very poor access to specialist psychology support. See [BAD Psychodermatology Working party 2012](#) and [APPGS \(All Party Parliamentary Group on Skin\) report 2013 'The psychological and social impact of skin diseases on people's lives'](#).

One topic expert noted that a wellbeing service was used in their area but was dependent on patients to access. They noted direct access to psychological support was a local issue not well funded – but were not sure if anything could strengthen the guideline for CCGs to act on.

Impact statement

Evidence from the 2-year Evidence Update found that tailored CCBT for people with mild to moderate psoriasis appears to reduce anxiety and increase quality of life. The Evidence Update concluded that although CG153 does not include recommendations specifically about the treatment of anxiety, or the use of psychological therapies tailored to psoriasis, limitations of the evidence (noted to include high attrition rate in the CCBT group, low baseline clinical depression, DLQI does not measure distress which is known to influence medicines adherence, and self-administered PASI may be less objective than clinician rating) meant any impact on the guideline was unlikely. The Evidence Update stated that further research was needed, particularly among a population with higher rates of anxiety and depression, on the use of CCBT in treating comorbid psychological problems such as anxiety.

New evidence from 4-year surveillance suggested that mindfulness as an adjunct to usual therapy could improve psoriasis and quality of life, though this was a small pilot study. Further new evidence found that CBT plus biofeedback may increase the beneficial effect of UVB therapy by reducing the severity of psoriasis, improving quality of life and reducing minor psychiatric disorders.

Overall, although CBT appeared to be of benefit, the 3 studies examined different CBT-based interventions (computerised, mindfulness, and in combination with biofeedback) and used differing adjunctive therapies, and 2 had a small number of participants (with 1 study being a pilot), therefore it is difficult to make conclusions about the efficacy of CBT in general for psoriasis. CG153 does make general recommendations about offering people with any type of psoriasis support and information on strategies to deal with the impact on their physical, psychological and social wellbeing, to assess impact of disease on physical, psychological and social wellbeing by asking specific questions including if they need further advice or support, and to refer people for dermatology specialist advice if any type of psoriasis is having a major impact on a person's physical, psychological or social

wellbeing. Additionally, some of these issues are covered by CG91 'Depression in adults with a chronic physical health problem' that discusses recognition, assessment and management, which includes depression with anxiety. CG153 already makes a link to CG91: 'Assess whether people with any type of psoriasis are depressed when assessing disease severity and impact, and when escalating therapy. If appropriate offer information, advice and support in line with Depression in adults with a chronic physical health problem (NICE clinical guideline 91) and Depression in children and young people (NICE clinical guideline 28)'. Therefore no impact on the guideline is currently anticipated.

New evidence is unlikely to change guideline recommendations.

Areas not currently covered in the guideline

NQ – 01 Does weight loss through diet and/or exercise improve psoriasis and treatment response, and are there particular demographic, phenotypic or other biomarkers (for example age or disease severity) that identify those most likely to benefit?

This review question was not addressed by the guideline.

Surveillance decision

This review question should be added.

Effect of calorie-restriction/weight loss/exercise on psoriasis in overweight patients

2-year Evidence Update

An RCT⁸⁴ (n=60 overweight and obese patients >18 years with plaque psoriasis) examined the effect of a calorie-restricted diet on psoriasis severity. Patients were randomised to a low-energy diet (800–1000 kcal/day of formula-based food) for 8 weeks, followed by an 8-week re-introduction of normal food intake (up to 1200 kcal/day), or to a control group (ordinary healthy foods). All participants also attended 8 group sessions held fortnightly with a dietitian who provided dietary advice and

encouragement. Participants were asked not to change their antipsoriatic treatment, tobacco use, or physical exercise levels during the study. Drugs for other medical conditions could be changed as needed. At 16 weeks, the primary outcome of mean PASI score had decreased more in the diet group than in controls, although the between-group difference was non-significant. However, significant between-group differences in mean change from baseline in favour of the low-energy diet were seen for the secondary outcomes of DLQI score, weight and BMI.

A multicentre RCT⁸⁵ (n=303 overweight or obese patients aged 18–80 years with chronic

plaque psoriasis that had not cleared after 4 weeks of continuous systemic treatment) also looked at the impact of a dietary intervention, but with the addition of a physical exercise component. Topical agents could be used as needed on limited areas (scalp, palms, soles). Patients were randomised to either a 20-week dietary plan (energy intake 0.8 times resting metabolic rate for 12 weeks and 1.0 times resting metabolic rate for 8 weeks) plus physical exercise (40 minutes of continuous aerobic physical exercise 3 times a week), or to a control group receiving a single 15-minute session at baseline about weight loss to control psoriasis. At 20 weeks, the primary outcome of median PASI score had decreased significantly more in the diet group than in the control group. Among secondary outcomes, significant differences in median change from baseline were seen between the diet group and control group for weight and BMI.

4-year surveillance summary

An RCT⁸⁶ (n=262 obese patients with moderate to severe plaque psoriasis on infliximab, etanercept, ustekinumab or adalimumab) examined the effect of weight reduction on treatment outcomes with biologics. Patients were randomised to a low-calorie (<1000 kcal/day for 8 weeks) or a normal diet. At week 24, the diet group had lost weight whereas the control group had gained weight (significance not stated in the abstract). Average improvement in mean PASI score was greater in the diet than the control group (significance not stated in the abstract). PASI 75 was achieved by significantly more patients in the diet than in the control group. The mean body surface area values at week 24 were lower in the diet than the control group (significance not stated in the abstract).

An RCT⁸⁷ (n=44 obese patients with mild-to-severe plaque psoriasis treated with immunosuppressive drugs) examined the effect of an energy-restricted diet enriched in n-3 polyunsaturated fatty acids (PUFAs) and poor in n-6 PUFAs, on response to immunomodulating drugs. Patients were randomised to an energy-restricted diet (20 kcal/kg/ideal body weight/day) enriched with n-3 PUFAs (average 2.6 g/day) or their usual diet for 6 months. All patients continued immunomodulating therapy throughout the study. At 3 and 6 months, a significant clinical improvement from baseline in PASI, itch scores and DLQI was observed in patients on the low-calorie high n-3 PUFAs diet

versus controls. Patients on the intervention diet, but not controls, also saw a significant decrease in body weight, waist circumference, serum triglycerides, serum total cholesterol and n-6/n-3 ratio intake

A prospective observational follow-up study⁸⁸ in a cohort (n=56 eligible, n=32 completed) derived from an RCT examined long-term effects of weight reduction on severity of psoriasis. Patients underwent a 64-week weight-loss program consisting of an initial 16-week randomised phase with a low-energy diet for 8 weeks and 8 weeks of normal food intake combined with 2 low energy diet products/day, followed by a 48-week period of weight maintenance with the latter diet. After the randomisation phase, the control group received the same 8 + 8-week low energy diet intervention, and all patients were then followed for 48 weeks while on the weight-loss maintenance diet. After the 16-week low energy diet period, significant reductions in weight, PASI and DLQI were seen. At week 64, the significant reductions in weight, PASI and DLQI were maintained.

A systematic review and meta-analysis⁸⁹ of 7 RCTs (n=878) examined the effect of a dietary and lifestyle weight loss intervention on psoriasis severity in overweight and obese patients. Five RCTs were included in the meta-analysis. There was a significantly greater reduction in PASI score in patients receiving a weight loss intervention than in controls. Significantly more participants in the intervention group than in the control group achieved a 75% reduction in the PASI score.

Topic expert feedback

Topic experts drew attention to lifestyle interventions for psoriasis and that management of obesity can reduce disease severity/improve outcomes. They stated that this was an important area particularly given that many patients with psoriasis are overweight or obese. It was further noted that in [studies](#) conducted by [IMPACT](#) (Identification and Management of Psoriasis Associated Comorbidity), almost nobody reported having modifiable cardiovascular disease risk factors (including obesity and inactivity) addressed as part of the psoriasis consultation. It was also noted that research in this area was promoted by the NICE research recommendation 'Does reduction of relevant, modifiable cardiovascular risk factors (for example weight loss, exercise or statins) improve psoriasis and are there

particular demographic, phenotypic or other biomarkers (for example age or disease severity) that identify those most likely to benefit?’

Experts further noted that ideally, examining this area would encompass impact of weight loss on treatment response (as well as disease severity). They stated that the two are related, but obesity contributes to poor response to biologic therapy (and probably to other interventions). If a review of this area highlighted an evidence gap, that in itself would be important, but it was noted that there is some evidence in this area.

Impact statement

The 2-year Evidence Update found that an energy-restricted diet, with or without the addition of physical exercise, can reduce psoriasis severity and improve health-related quality of life in overweight or obese patients with psoriasis. However, some limitations of the studies were noted, particularly the short duration (16-20 weeks) therefore long-term maintenance of weight loss and improvement in psoriasis could not be ascertained. The Evidence Update concluded that further, longer-term research was needed to more

firmly establish the place of diet and exercise in treating psoriasis.

Evidence from 4-year surveillance appeared to support the positive impact of an energy restricted diet on psoriasis in overweight patients, with 2 studies examining longer term effects over periods of 6 months and 64 weeks, suggesting that benefits can be sustained.

CG153 does not currently make recommendations specifically linking weight loss to psoriasis outcomes. However it does recommend that patients are given information about relevant lifestyle risk factors, that the presence of comorbidities should be assessed, and that risk factors for cardiovascular comorbidities should be discussed with advice and support offered in line with the relevant NICE guidance (including guidance on obesity and increasing physical activity). Offering advice on weight loss is already covered by current recommendations, and no immediate need to update the guideline was identified.

New evidence is unlikely to change guideline recommendations.

NQ – 02 In people with psoriasis (all types), what is the most appropriate position for PUVA in the treatment pathway, taking into account its risks and benefits compared with systemic non-biological and biological therapies?

This review question was not addressed by the guideline.

Surveillance decision

This review question should not be added.

Place of PUVA in the treatment pathway

2-year Evidence Update

No relevant evidence identified.

4-year surveillance summary

No relevant evidence identified.

Topic expert feedback

Topic experts stated that the requirement (as stated in all NICE technology appraisals of biologics for psoriasis) to have tried and not

responded to PUVA (which is associated with increased risk of skin cancer) before commencing biologic therapy may not be appropriate. Experts noted that the need to re-examine this area was heightened by changes to the indication specified in the latest licenses for 2 biologics (adalimumab and secukinumab), which now reads ‘moderate to severe chronic plaque psoriasis in adults who are candidates for systemic therapy.’ Namely, these licenses

do not now specify which other treatments should already have been tried.

Topic experts did go on to note that there are some patients for whom PUVA may still be appropriate – older people, patients who do not want or cannot take systemic treatments, or those with severe psoriasis that is not responding to other treatments. They stated that PUVA is consistently, predictably effective and so remains a useful modality to have available in an important, but small, subset of patients.

Impact statement

Topic experts suggested that recommendations in NICE technology appraisals of biologics for

psoriasis, which stipulate prior treatment with PUVA as a pre-requisite for biologic therapy, may be inappropriate. Examining the place of PUVA in the treatment pathway could not meaningfully be addressed while PUVA is a pre-requisite for biologic therapy. However, review of NICE technology appraisals is outside the remit of the surveillance process. Information has been passed to the NICE technology appraisals team for consideration.

New evidence is unlikely to change guideline recommendations.

NQ – 03 In people with chronic plaque psoriasis, how effective are biological agents used earlier in the treatment pathway?

This review question was not addressed by the guideline.

Surveillance decision

This review question should not be added.

Effect of biologics on depressive symptoms and quality of life

2-year Evidence Update

No relevant evidence identified.

4-year surveillance summary

A systematic review⁷⁹ examined the effect of biologics on depressive symptoms in patients with psoriasis.

Topic experts identified a study⁸⁰ (n=119 patients with plaque psoriasis) examining the relationship between mental health, psoriasis severity and patient's quality of life following treatment with biologics, other systemic agents and topical agents.

However, CG153 is concerned only with the next biologic to use after a first biologic fails as guidance on the use of first-line biological therapy for psoriasis is covered by several NICE technology appraisals.

Topic expert feedback

Topic experts stated that the potentially beneficial effect of biologics on psychological problems may be one reason to re-examine

when they are most appropriately prescribed, and that the place of biologics in the treatment pathway may need to be reviewed.

Experts further noted that there are people for whom earlier treatment with biologics may be appropriate, which includes people with depression or psychological distress. However they explained that DLQI defines the level of impact of the disease, but does not measure depression or anxiety. So in order to evaluate whether, for example, earlier treatment for those in distress is beneficial, a tool to capture this distress would need to be included in the eligibility criteria (a suggested example was PHQ9 for depression).

They additionally highlighted that the indication specified in the latest licenses for 2 biologics (adalimumab and secukinumab) now reads 'moderate to severe chronic plaque psoriasis in adults who are candidates for systemic therapy.' Namely, these licenses do not specify which other treatments should already have been tried. Nor is it a requirement to have a PASI score of 10. Therefore prior standard systemic therapy in these biologics is largely

driven by health economic modelling. So it would be appropriate to consider the benefit of biologics earlier in the treatment pathway for people with psychological issues.

Topic experts also stated that people with severe disease of the nails, hands or feet are likely to benefit from biologics, but may have a PASI less than 10. The use of biologics in this population would also benefit from re-examination

Impact statement

New evidence was found on the effect of biologics on depressive symptoms and quality of life in patients with psoriasis, and topic

experts noted the potentially beneficial effect of biologics on psychological problems may be a reason to re-examine when they are most appropriately prescribed. However, recommendations in CG153 on the first-line use of biological agents are incorporated from several NICE technology appraisals. Review of NICE technology appraisals is outside the remit of the surveillance process. Information has been passed to the NICE technology appraisals team for consideration.

New evidence is unlikely to change guideline recommendations.

NQ – 04 Does treating psoriasis modify the risk of cardiovascular disease and are there any clinical (for example, demographic or phenotypic) or laboratory (for example genetic or immune) markers that identify those most likely to benefit?

This review question was not addressed by the guideline.

Surveillance decision

This review question should not be added.

Effect of psoriasis treatments on cardiovascular events

2-year Evidence Update

No relevant evidence was identified.

4-year surveillance summary

A systematic review and meta-analysis⁹⁰ of 34 controlled studies and RCTs (6 in psoriasis/psoriatic arthritis) examined the effects of tumour necrosis factor inhibitors, methotrexate, non-steroidal anti-inflammatory drugs and corticosteroids on cardiovascular events in rheumatoid arthritis, psoriasis and psoriatic arthritis. In psoriasis/psoriatic arthritis, systemic therapy (unspecified in the abstract) significantly decreased the risk of all cardiovascular events.

A systematic review and meta-analysis⁹¹ of 5 clinical trials (n=49,795) examined the effect of TNF inhibitors on cardiovascular events in psoriasis and psoriatic arthritis. Overall, compared with topical/phototherapy treatment, TNF inhibitors were associated with a

significantly lower risk of cardiovascular events. Additionally, compared with methotrexate, risk of cardiovascular events was also significantly decreased in the TNF inhibitor group. Meanwhile, TNF inhibitors were linked to a significantly reduced incidence of myocardial infarction compared with topical/phototherapy or methotrexate treatment. Mortality rate did not differ significantly between the TNF inhibitor group and other therapy.

Topic expert feedback

No topic expert feedback was relevant to this evidence.

Impact statement

The new evidence suggests that systemic therapies for psoriasis and psoriatic arthritis appear to be associated with a decrease in risk of cardiovascular events. Analysis specifically of TNF inhibitors indicates that as a treatment group they appear to benefit cardiovascular risk. The authors of the first study stated that the evidence was limited, and the authors of

the second study stated that rigorous RCTs would be needed to evaluate whether TNF inhibitors truly result in reduction of cardiovascular diseases. As psoriasis is known to be associated with increased cardiovascular risk, any side effects of systemic therapies on reducing cardiovascular events is of potential benefit to patients. The full version of CG153 notes that 'There was insufficient data for any of the outcomes regarding the impact of different treatments for psoriasis on the incidence of comorbidities' therefore no recommendations are made in the guideline about choosing systemic therapies on the basis of effect on cardiovascular disease as well as on psoriasis outcomes. However, limitations and uncertainties of the new evidence noted by the authors mean that any impact on CG153 is currently unlikely.

New evidence is unlikely to change guideline recommendations.

treatment planning and measurement of outcomes
- measure burden and cumulative effect of disease activity, severity and impact for people with both psoriasis and psoriatic arthritis?

[New evidence](#) relevant to the research recommendation was found but an update of the related review question is not planned because the new evidence is insufficient to trigger an update.

Surveillance decision

The research recommendation will be retained because there is evidence of research activity in this area.

RR – 02 What is the impact of methotrexate compared with other approaches to care (for example other systemic non-biological or biological treatments) on risk of significant liver disease in people with psoriasis and do risk factors such as obesity, alcohol use or diabetes alter this risk?

[New evidence](#) relevant to the research recommendation was found but an update of the related review question is not planned because the new evidence is insufficient to trigger an update.

Surveillance decision

The research recommendation will be retained because there is evidence of research activity in this area.

RR – 03 In people with psoriasis, does early intervention with systemic treatments improve the long-term prognosis of psoriasis severity, comorbidities (including psoriatic arthritis), or treatment-related adverse effects, and are there any clinical (for example demographic or phenotypic) or laboratory (for example genetic or immune) biomarkers that can be used to identify those most likely to benefit from this treatment approach?

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

Surveillance decision

The research recommendation would normally be proposed to be removed from the NICE version of guideline and the NICE research recommendations database because there is no evidence of research activity in this area. However topic experts noted that earlier use of systemic therapies in the treatment pathway (for example biologics in severe psoriasis) was an area of interest therefore the research recommendation will be retained.

RR – 04 Do structured psoriasis-focussed self-management programmes improve patient confidence, wellbeing and disease control compared with standard care?

[New evidence](#) relevant to the research recommendation was found but an update of the related review question is not planned because the new evidence is insufficient to trigger an update.

Surveillance decision

The research recommendation will be retained because there is evidence of research activity in this area.

- RR – 05** **In people of all ages with psoriasis:**
- 1. How should topical therapies be used to maintain disease control i) safely; ii) effectively and iii) what are the health economic implications?**
 - 2. What are the risks of ‘real life’ long term corticosteroid use, are there particular people at risk and what strategies can be used to modify or avoid risks?**

[New evidence](#) relevant to the research recommendation was found but an update of the related review question is not planned because the new evidence is insufficient to trigger an update.

Surveillance decision

The research recommendation will be retained because there is evidence of research activity in this area.

Other research recommendations

The following research recommendations were not deemed as priority areas for research by the guideline committee. No decisions will be taken the status of these research recommendations.

- RR – 06** **What is the validity and accuracy of existing and future screening instruments for PsA in dermatology and primary care settings?**

[New evidence](#) relevant to the research recommendation was found but an update of the related review question is not planned because the new evidence is insufficient to trigger an update.

Surveillance decision

This research recommendation will be considered again at the next surveillance point.

- RR – 07** **What is the efficacy of the ASAS criteria for identifying inflammatory back pain in a psoriasis population?**

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

Surveillance decision

This research recommendation will be considered again at the next surveillance point.

- RR – 08** **Does treating psoriasis modify the risk of cardiovascular disease and are there any clinical (for example, demographic or phenotypic) or laboratory (for example genetic or immune) markers that identify those most likely to benefit?**

[New evidence](#) relevant to the research recommendation was found but an update of the related review question is not planned because the new evidence is insufficient to trigger an update.

Surveillance decision

This research recommendation will be considered again at the next surveillance point.

RR – 09 What is the natural history of psoriatic arthritis and are there any adverse prognostic markers that identify individuals at risk of severe/aggressive/destructive disease?

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

Surveillance decision

This research recommendation will be considered again at the next surveillance point.

RR – 10 Does reduction of relevant, modifiable cardiovascular risk factors (for example weight loss, exercise or statins) improve psoriasis and are there particular demographic, phenotypic or other biomarkers (for example age or disease severity) that identify those most likely to benefit?

[New evidence](#) relevant to the research recommendation was found and an update of the related review question is planned.

Surveillance decision

This research recommendation will be considered again at the next surveillance point.

RR – 11 What is the natural history of psoriasis and are there any adverse prognostic markers that identify individuals at risk of severe recalcitrant disease who might benefit from early intervention?

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

Surveillance decision

This research recommendation will be considered again at the next surveillance point.

RR – 12 How does the documented increased risk of CVD/CVD risk factors among people with psoriasis compare to that observed with other chronic diseases?

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

Surveillance decision

This research recommendation will be considered again at the next surveillance point.

RR – 13 What are the risks and benefits of proactively 'screening' the psoriasis population for comorbidities?

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

Surveillance decision

This research recommendation will be considered again at the next surveillance point.

RR – 14 What are the efficacy, safety and cost effectiveness of NBUVB compared to oral/topical PUVA in the treatment of palmoplantar pustulosis?

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

Surveillance decision

This research recommendation will be considered again at the next surveillance point.

RR – 15 What are the long term risks (for example skin cancer and ageing) of NBUVB, are there any individuals at particular risk and what strategies can be used to modify or avoid these risks?

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

Surveillance decision

This research recommendation will be considered again at the next surveillance point.

RR – 16 In people with psoriasis, what is the clinical effectiveness, safety, tolerability and cost effectiveness of NBUVB phototherapy and acitretin versus acitretin and placebo?

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

Surveillance decision

This research recommendation will be considered again at the next surveillance point.

RR – 17 In people with psoriasis, when inducing remission, what are the clinical effectiveness (including duration of remission and psychological benefit), cost effectiveness, safety, tolerability and patient acceptability of complex topical therapies with or without NBUVB compared to a short course of systemic therapy (for example, ciclosporin)?

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

Surveillance decision

This research recommendation will be considered again at the next surveillance point.

- RR – 18** **What is the risk of skin cancer in people with psoriasis exposed to phototherapy, systemic (including biological) therapies and are there any strategies that can modify or avoid this risk?**

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

Surveillance decision

This research recommendation will be considered again at the next surveillance point.

- RR – 19** **In people with psoriasis, are there any clinical (for example, demographic or phenotypic) or laboratory (for example genetic or immune) markers that identify people who will respond to treatment with, or who will remain in remission following, treatment with methotrexate or ciclosporin?**

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

Surveillance decision

This research recommendation will be considered again at the next surveillance point.

- RR – 20** **In people with psoriasis, including pustular forms, what is the efficacy, optimal dosing, safety and cost-effectiveness of systemic non-biological agents for maintenance therapy (moderate to long term outcomes are important)?**

[New evidence](#) relevant to the research recommendation was found but an update of the related review question is not planned because the new evidence is insufficient to trigger an update.

Surveillance decision

This research recommendation will be considered again at the next surveillance point.

- RR – 21** **What is the most effective, safe and cost effective methotrexate dosing regimen to treat psoriasis and what is the role of folic acid in reducing efficacy or improving safety of methotrexate?**

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

Surveillance decision

This research recommendation will be considered again at the next surveillance point.

- RR – 22** **In children with psoriasis, what are the clinical effectiveness, safety, tolerability and cost effectiveness of methotrexate, ciclosporin and acitretin?**

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

Surveillance decision

This research recommendation will be considered again at the next surveillance point.

RR – 23 In people with palmoplantar pustulosis, what are the clinical effectiveness, safety, tolerability and cost effectiveness of acitretin and methotrexate?

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

Surveillance decision

This research recommendation will be considered again at the next surveillance point.

RR – 24 What is the clinical utility and validity of non-invasive markers of liver fibrosis (for example, FibroScan, FibroTest and ultrasound) in people with psoriasis receiving methotrexate or other treatment interventions?

[New evidence](#) relevant to the research recommendation was found but an update of the related review question is not planned because the new evidence is insufficient to trigger an update.

Surveillance decision

This research recommendation will be considered again at the next surveillance point.

RR – 25 In people with psoriasis being treated with systemic non-biological or biological therapies what clinical or other markers predict optimal treatment outcomes?

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

Surveillance decision

This research recommendation will be considered again at the next surveillance point.

RR – 26 Does a psoriasis-specific cognitive behavioural therapy intervention improve distress, quality of life and psoriasis severity compared with standard care?

[New evidence](#) relevant to the research recommendation was found but an update of the related review question is not planned because the new evidence is insufficient to trigger an update.

Surveillance decision

This research recommendation will be considered again at the next surveillance point.

Editorial and factual amendments identified during surveillance

During surveillance editorial or factual amendments were identified:

- We will update the hyperlink in footnote 32 to recommendations 1.4.1.8/9, to link to the [latest BAD Standards for phototherapy](#) which have now been issued (Oct 2016).
- We will link to a 2015 [guideline](#) from the British Association of Dermatologists and British Photodermatology Group on the measurement of ultraviolet radiation levels in ultraviolet phototherapy.
- We will update the cross-referral in recommendation 1.2.3.2 to CG67 Lipid modification – which has been updated and replaced by CG181 [Cardiovascular disease](#).
- We will add a cross-referral to NG5 [Medicines optimisation](#) alongside existing cross-referrals to CG76 [Medicines adherence](#).
- We will add a cross-referral from recommendation 1.1.1.3 to NG43 [Transition from children's to adults' services for young people using health or social care services](#).
- We will correct the titles of the guidelines cross-referred to by recommendation 1.2.3.2, some of which have changed slightly since CG153 was published.
- We will correct broken hyperlinks on the word 'PASI' in several recommendations
- We will add information about the following MHRA Drug Safety Updates to footnotes:
 - [Oral retinoids: pregnancy prevention—reminder of measures to minimise teratogenic risk](#) (July 2013) [Relevant to recommendations on acitretin]
 - [Ustekinumab \(Stelara\): risk of exfoliative dermatitis](#) (January 2015) [relevant to recommendations on ustekinumab]
 - [Tumour necrosis factor alpha inhibitors](#) – risk of tuberculosis (April 2014) [relevant to recommendations on adalimumab, etanercept and infliximab]
- We will update the following footnotes relating to drug licensing:
 - Additional footnotes are needed to recommendation 1.3.2.7. There are currently different topical calcipotriol preparations available in the UK which vary in their licensing status for use in children and young people under 18. Additionally, potent topical corticosteroid preparations available in the UK vary in the age from which they are licensed for use in children.
 - Footnote 24 to recommendation 1.3.3.1. There are currently several potent topical corticosteroid preparations available in the UK, and the age from which they are licensed for use in children varies.
 - Footnote 27 to recommendation 1.3.3.4. Topical calcitriol and tacalcitol preparations are not licensed in children, so it is correct to say that they do not have a marketing authorisation for this age group. However, topical calcipotriol preparations available in the UK vary in their licensing status for use in children and young people under 18.
 - Footnote 30 to recommendation 1.3.4.3. It may be clearer to refer to topical calcineurin inhibitors (there are oral calcineurin inhibitors such as ciclosporin that are licensed for psoriasis).
- We will cross-refer to or incorporate the following technology appraisals issued since CG153 was published: [Ustekinumab for treating active psoriatic arthritis](#) (2015) TA340; [Secukinumab for treating moderate to severe plaque psoriasis](#) (2015) TA350; [Apremilast for treating active psoriatic arthritis](#) (2015) TA372; and [Apremilast for treating moderate to severe plaque psoriasis](#) (2016) TA419.
- We will cross-refer to NG65 [Spondyloarthritis in over 16s](#).

- We will add other relevant guidelines that have published since CG153 was issued to the current list of 9 guidelines cross-referred to by recommendation 1.2.3.2 related to risk factors for cardiovascular comorbidities.
- We will cross-refer to PH49 [Behaviour change: individual approaches](#) and PH6 [Behaviour change: general approaches](#) in the 'Principles of care section' given that some aspects of psoriasis management will involve changing behaviours.

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