# Points to consider for reporting, screening for and preventing selected comorbidities in chronic inflammatory rheumatic diseases in daily practice: a EULAR initiative

Athan Baillet, <sup>1</sup> Laure Gossec, <sup>2</sup> Loreto Carmona, <sup>3</sup> Maarten de Wit, <sup>4</sup> Yvonne van Eijk-Hustings, <sup>5</sup> Heidi Bertheussen, <sup>4</sup> Kent Alison, <sup>6</sup> Mette Toft, <sup>4</sup> Marios Kouloumas, <sup>7</sup> Ricardo J O Ferreira, <sup>8</sup> Susan Oliver, <sup>9</sup> Andrea Rubbert-Roth, <sup>10</sup> Sander van Assen, <sup>11</sup> William G Dixon, <sup>12</sup> Axel Finckh, <sup>13</sup> Angela Zink, <sup>14</sup> Joel Kremer, <sup>15</sup> Tore K Kvien, <sup>16</sup> Michael Nurmohamed, <sup>17</sup> Desirée van der Heijde, <sup>18</sup> Maxime Dougados 19

Handling editor Hans WJ Bijlsma

► Additional material is published online only. To view please visit the journal online (http://dx.doi.org/10.1136/ annrheumdis-2016-209233).

For numbered affiliations see end of article.

#### Correspondence to

Dr Athan Baillet, Service de Rhumatologie CHU Grenoble, Av de Kimberley, Echirolles 38434, France; abaillet@chu-grenoble.fr

AB and LG contributed equally.

Received 20 January 2016 Revised 25 February 2016 Accepted 27 February 2016 Published Online First 16 March 2016

#### **ABSTRACT**

In chronic inflammatory rheumatic diseases, comorbidities such as cardiovascular diseases and infections are suboptimally prevented, screened for and managed. The objective of this European League Against Rheumatism (EULAR) initiative was to propose points to consider to collect comorbidities in patients with chronic inflammatory rheumatic diseases. We also aimed to develop a pragmatic reporting form to foster the implementation of the points to consider. In accordance with the EULAR Standardised Operating Procedures, the process comprised (1) a systematic literature review of existing recommendations on reporting, screening for or preventing six selected comorbidities: ischaemic cardiovascular diseases, malignancies, infections, gastrointestinal diseases, osteoporosis and depression and (2) a consensus process involving 21 experts (ie, rheumatologists, patients, health professionals). Recommendations on how to treat the comorbidities were not included in the document as they vary across countries. The literature review retrieved 42 articles, most of which were recommendations for reporting or screening for comorbidities in the general population. The consensus process led to three overarching principles and 15 points to consider, related to the six comorbidities, with three sections: (1) reporting (ie, occurrence of the comorbidity and current treatments); (2) screening for disease (eg, mammography) or for risk factors (eg, smoking) and (3) prevention (eg, vaccination). A reporting form (93 questions) corresponding to a practical application of the points to consider was developed. Using an evidence-based approach followed by expert consensus, this EULAR initiative aims to improve the reporting and prevention of comorbidities in chronic inflammatory rheumatic diseases. Next steps include dissemination and implementation.

#### **INTRODUCTION**

Chronic inflammatory rheumatic diseases (CIRDs) comprise different diseases such as rheumatoid arthritis (RA), spondyloarthritis (SpA), connective tissue disorders and crystal arthropathies. Although current management of CIRDs may result in

improvement/suppression of disease activity and improvement of function, comorbidities such as cardiovascular diseases, kidney diseases, lung diseases,<sup>3</sup> infections,<sup>4 5</sup> malignancies,<sup>6</sup> osteoporosis,<sup>7</sup> gastrointestinal diseases<sup>8</sup> and depression<sup>10</sup> remain an important issue.

These comorbidities are important to consider in patients with CIRDs for at least three reasons. The first is that some of these comorbidities are more frequently observed in patients with CIRDs in comparison to the general population. This is clearly the case for cardiovascular diseases in most of the CIRDs, 11 12 infections 4 and osteoporosis. 13 This higher prevalence is usually explained by either the activity of the disease itself, or by its treatment, in particular glucocorticoids. As an example, studies investigating 'traditional' risk factors for cardiovascular diseases (such as hypertension or hyperlipidaemia) have concluded that the prevalence of these risk factors is higher in patients with CIRDs. 14 15 Second, patients with CIRDs may receive suboptimal medical prevention services compared with the general population,<sup>5</sup> 16 17 possibly due to the focus on their rheumatic diseases or because no health professional is taking responsibility for the patient as a whole. For example, the screening for the detection of breast cancer (a cancer which is not more frequent in CIRDs than in the general population) by mammography may be less frequently performed in women with CIRDs. 14 18 The third reason is that some comorbidities might impact on outcomes. For example, it has been reported that in obese patients with RA, the disease activity is less well controlled regardless of the administered treatment. 19

The effective management of such comorbidities necessitates answers to the following questions: which information should be collected? Who should collect this information and how frequently? Who should be in charge of the management of any given comorbidity or risk factor, once detected? There is no definitive answer to the last questions, and it may well differ by comorbidity and/or countries/healthcare systems. However, most of the rheumatologists consider that it is their responsibility, at least, to assess comorbidities



To cite: Baillet A, Gossec L, Carmona L, et al. Ann Rheum Dis 2016;75: 965-973.

BMJ



and thereafter liaise with the appropriate health professional (eg, the general practitioner or the appropriate specialist)<sup>20</sup> for the treatment phase. 14 21 The person in charge of the data collection related to comorbidities is unclear. Patients themselves may play a role through the completion of a self-administered questionnaire. More frequently however, the rheumatology team (eg, rheumatologists and specialist nurses) will perform this, for example, using a predefined list of items to be checked by a nurse or a physician.<sup>22</sup> Although comorbidities are widely discussed in the recent literature, to date, the optimal role of the health professional in the assessment and follow-up care, as well as how and when data should be collected have not, as yet, been clearly defined. To this end, points to consider regarding comorbidities would be of interest. For clinical application, a pragmatic, easily understandable checklist corresponding to a minimum standardised core set of items to be collected regarding comorbidities in CIRDs in daily practice would also be of interest. Indeed, previous initiatives generated complex, 23 incomplete or irrelevant checklists for daily clinical practice.

In the present initiative supported by the European League Against Rheumatism (EULAR), our objective was to develop points to consider regarding standardised items to be collected for comorbidities in CIRDs in daily practice, and to develop a practical reporting form to enhance applicability of these points to consider.

#### **METHODS**

The methodology used in this initiative was in accordance with the EULAR Standardised Operating Procedures.<sup>24</sup>

#### Task Force

Apart from the convenor, the clinical epidemiologist and the fellow in charge of the systematic literature review, 18 experts (4 patients, 4 nurse researchers, 5 epidemiologists in charge of registries and 5 clinicians) participated in this Task Force. SvA was the first author of the EULAR recommendations regarding vaccinations and MN was the convenor of the EULAR recommendations on cardiovascular comorbidities. The members of the Task Force came from 11 European countries and one member from the USA.

# Target population and target comorbidities

A first physical meeting of the Task Force in July 2014 allowed, via a consensual approach, to define the target population in terms of patients who should benefit from this initiative, but also to define the list of comorbidities to be targeted.

The selection of comorbidities was based on their frequency and severity (impact on mortality and disease outcomes).

# Hierarchical systematic literature review

A systematic literature review was performed using a hierarchical procedure to collect published recommendations or guidelines on reporting, screening for or prevention for each of the selected comorbidities. This systematic literature review was performed by one fellow (AB) in December 2014. Inclusion criteria were: (1) recommendations, (2) dealing with the reporting or the screening for and (3) the six selected comorbidities, that is, ischaemic heart diseases, infections, malignancies, gastrointestinal diseases, osteoporosis and depression. The first step consisted of checking whether there were specific recommendations available for patients with CIRDs. If none was available, the second step, retrieved recommendations in the general population proposed by international scientific societies. If these were

not available, the third step targeted recommendations to be applied at the general population level proposed by national scientific societies. As the search was hierarchical, when a recommendation was found for one of the six selected comorbidities, the next steps were not applied. We used a sensitive search of Medline via PubMed and Embase. The combination of keywords used for this search is summarised in online supplementary table S1. This search was completed by a hand search of references from relevant articles, or reviews.

From each selected manuscript, the following information was extracted: definition of the comorbidity, how to report its occurrence, proposed screening strategy and proposed screening time interval. All collected data were compiled in tables to help appraisal.

Furthermore, some additional articles reporting relevant trials (rather than recommendations) were also discussed when relevant to define levels of evidence of the points to consider.

# Consensus on points to consider and elaboration of a reporting form

During a second face-to-face meeting in January 2015, then by email exchanges, the Task Force developed overarching principles and points to consider, and a practical reporting form corresponding to the exact data to be collected. The points to consider deal with the six comorbidities, and the reporting form comprises for each comorbidity, three sections, related to (1) the reporting (ie, occurrence) of the comorbidity; (2) whether screening for disease (eg, mammography) or for risk factors (eg, hypertension as a risk factor of cardiovascular events) had been undertaken and (3) the uptake of any preventative measures (eg, vaccination).

Recommendations on treating the comorbidities were not included in the document as they vary across countries. 25 26

#### Votes for agreement

The Oxford Levels of Evidence were applied to rate the strength of the points to consider.<sup>27</sup> Members of the Task Force were asked to state their level of agreement with the points to consider, as well as with the reporting form, on a scale from 0 to 10 (10 being full agreement and 0 being total disagreement) by email in November 2015.

#### **RESULTS**

#### Target population

The EULAR Task Force considered that the points to consider would be applicable to all patients with CIRDs, including RA, SpA, connective tissue disorders and crystal arthropathies. Polyarticular osteoarthritis can also be considered a CIRD.<sup>28</sup> Thus, clinicians treating patients with polyarticular osteoarthritis might also rely on these points to monitor these patients.

# Choice of selected comorbidities

We restricted the scope of this Task Force to predetermined domains that is, clusters of diseases sharing the same disease mechanisms (ie, atherosclerosis) or involving a common organ/tissue (eg, gastrointestinal diseases). In each domain, we selected specific diseases of particular interest based on the selection of the Task Force members. The following conditions were selected: (1) cardiovascular diseases that is, myocardial infarction, angina, stroke, transient ischaemic attack, heart failure and lower limb peripheral arterial disease, (2) malignancies: lymphoma, skin, lung, colon, breast, prostate and cervical cancers, (3) infections: serious infections, chronic viral infections, tuberculosis (TB), non-TB opportunistic infections, (4) gastrointestinal

diseases: gastroduodenal ulcers and diverticulitis, (5) osteoporosis and (6) depression.

#### Systematic literature review

A total of 1162 abstracts were retrieved by the search. Of these, 42 were included in the final qualitative synthesis (see online supplementary figure S1). A total of 19 manuscripts provided recommendations on reporting or detecting a selected comorbidity, whereas 41 articles provided recommendations on screening for risk factors of selected comorbidities. Nine articles were national recommendations and 33 articles were international recommendations (table 1).

The recommendations for comorbidity screening specifically in CIRDs<sup>4</sup> <sup>11</sup> <sup>29</sup> <sup>30</sup> were generated by the EULAR Task Forces. Most of the available recommendations for reporting or screening for comorbidities were, nevertheless, recommendations for the general population.

# Overarching principles

Table 2 shows the overarching principles.

- A. The Task Force agreed that a role of the rheumatology team is to detect and collect the information related to the comorbidities. The Task Force members widely agreed on comorbidities of special interest, which need to be taken into account in the management of CIRDs.
- B. The assessment of comorbidities may involve the rheumatologists in charge and specialist nurses and patients themselves. The treatment of these comorbidities will most often not be performed by the rheumatology team, but the team should liaise with the appropriate health professionals (eg, general practitioners and/or specialist physicians) to ensure the comorbidity is appropriately managed.
- C. The Task Force agreed on the usefulness of standardised programmes to document comorbidities. The repetition of this standardised programme in a given patient has not been appropriately assessed. However (expert opinion), the Task Force considered such a repetition as useful and that such standardised programme should be performed at least every 5 years, as has been suggested specifically for cardiovascular diseases.<sup>31</sup>

# Specific EULAR points to consider for reporting, screening for and preventing comorbidities in CIRDs

Table 2 summarises the points to consider. Category of evidence ranged from 1a to 5 (table 2). Level of evidence was higher for

screening for risk factors, than for reporting the comorbidities or comorbidity treatments. There was high agreement within the Task Force regarding these points (table 2).

The following paragraphs deal specifically with each comorbidity.

# Reporting, screening for and prevention of ischaemic cardiovascular disease

#### Level of evidence

Two articles reported EULAR recommendations for reporting or screening for ischaemic cardiovascular diseases in patients with CIRDs<sup>11</sup> and systemic lupus erythematosus.<sup>29</sup> Two articles reported European and North American recommendations for ischaemic cardiovascular diseases in the general population.<sup>32</sup> <sup>33</sup> The systematic documentation of risk factors has been demonstrated to be useful for several comorbidities in RA, in a randomised controlled trial (level 1b<sup>14</sup>).

### **EULAR** points to consider

The Task Force addressed cardiovascular diseases related to atherosclerosis, including heart failure due to its impact on disease management (eg, non-steroidal anti-inflammatory drugs (NSAIDs)). As the cause of heart failure is difficult to ascertain, heart failure due to any cause should be collected (table 2).

#### Reporting, screening for and prevention of malignancies Level of evidence

Twenty-one articles reported European recommendations for reporting or screening for malignancies (breast, 34–38 colon, 39–42 prostate, 25–43–44 skin, 45–46 lung, 47–48 cervical cancers 49 and lymphoma 6–50–53) in the general population. A national recommendation was also considered for the screening for prostate cancer in the general population. 26 The literature demonstrated that screening for malignancies is useful in the general population (level 1b). 54–58

#### **EULAR** points to consider

The Task Force proposed that the reporting of malignancies should be as simple as possible, keeping in mind that other information might be of interest for the treatment decision of a particular patient. As there are discrepancies in prostatic-specific antigen testing across countries, the Task Force did not include prostate cancer in these EULAR points to consider (table 2 and see online supplementary table S2).

**Table 1** Publications found through a hierarchical literature review, corresponding to recommendations on reporting or detecting prevalent comorbidities, and/or on screening for comorbidity or for risk factors

Domain of comorbidities	Total number of publications of recommendations* (number of international recommendations)	Number of publications of recommendations for reporting or detecting prevalent comorbidities, n (%†)	Number of publications of recommendations for screening comorbidity risk factors n (%†)
Cardiovascular diseases	4 (4)	2 (50)	2 (50)
Malignancies	22 (21)	9 (39)	21 (91)
Infections	5 (3)	3 (60)	1 (20)
Gastrointestinal diseases	4 (2)	0 (0)	4 (100)
Osteoporosis	4 (4)	4 (100)	4 (100)
Depression	4 (0)	1 (25)	4 (100)

<sup>\*</sup>The number of publications is related to recommendation in both the general population and CIRDs.

<sup>†</sup>The percentages correspond to the number of publications of the column divided by the total number of publications regarding the comorbidity. CIRDs, Chronic inflammatory rheumatic diseases.

**Table 2** Overarching principles and points to consider for reporting or detecting prevalent comorbidities, screening for comorbidity or for risk factors and treatments/vaccination

Overarching principles		Mean (SD) level of agreement
A. Comorbidities such as cardiovascular diseases, malignancies, infections, osteoporosis, peptic ulcer and depression shou assessed and managed in patients with chronic inflammatory rheumatic diseases.	9.8 (0.5)	
B. All clinicians including health professionals such as nurses, treating general practitioners and rheumatologists and patiself-administered questionnaires and self-management programmes play a key role in the screening and detection of com	9.5 (0.9)	
C. Comorbidities should be subject to a systematic, standardised periodical review (eg, at least every 5 years) for those winflammatory rheumatic disease.	9.4 (0.8)	
Points to consider	Level of evidence	Mean (SD) level of agreement
Cardiovascular diseases		
1. History of myocardial infarction, pectoris angina, stent, stroke, transient ischaemic attack, heart failure and lower limb peripheral arterial disease should be documented.	5	9.7 (0.5)
<ol><li>Cardiovascular risk factors such as smoking status, body mass index, history of hypertension, hypercholesterolaemia, renal insufficiency and HEART-SCORE index should be documented.</li></ol>	1b	9.5 (0.9)
<ol><li>Current cardiovascular treatments such as antihypertensive therapy, antiplatelet therapy, diabetes insulin or non-insulin therapies, lipid-lowering agents and anticoagulants should be documented.</li></ol>	5	9.6 (0.7)
Malignancies		
4. History of malignancies should be documented.	5	9.6 (0.8)
5. Screening procedures for malignancy (including mammography, pap smear, visit to a dermatologist, faecal occult blood test, colonoscopy) and for malignancy risk factors (including family history of breast or colon cancer and personal history of inflammatory bowel disease) should be documented.	1b	8.9 (1.4)
Infections		
6. History of tuberculosis should be documented including prior results of chest X-ray, tuberculin skin test, interferon- $\gamma$ release assay and BCG vaccination.	2a	9.8 (0.5)
7. History of serious infections, opportunistic infections and chronic viral infections should be documented.	5	9.6 (0.5)
8. Vaccination status for infections including influenza, <i>Streptococcus pneumoniae</i> , herpes zoster, human papillomavirus, poliomyelitis, diphtheria, tetanus and hepatitis B should be documented.	1b	9.5 (0.7)
Peptic ulcer		
9. History of gastroscopy-proven peptic ulcer should be documented.	5	9.1 (0.9)
10. Risk factors for peptic ulcer such as age >65 years, proton pump inhibitor intake, personal history of complicated ulcer, <i>Helicobacter pylori</i> infection, current use of aspirin, non-steroidal anti-inflammatory drugs, corticosteroids and anticoagulants should be documented	5	9.1 (0.9)
Osteoporosis		
11. History of osteoporotic fracture should be documented.	5	9.5 (0.7)
12. Risk factors for osteoporosis including body mass index <19, physical inactivity, glucocorticoid exposure, alcohol intake, family history of femoral neck fracture, secondary osteoporosis, bone mineral density should be collected and the FRAX global risk should be calculated where applicable.	2b	9.0 (1.2)
13. Current or prior osteoporosis treatments including calcium/vitamin D supplementation, bisphosphonates, strontium ranelate, raloxifene, teriparatide and denosumab should be documented.	5	9.5 (0.7)
Depression		
14. History of depression, current depression and prior screening for depression should be documented.	5	9.0 (1.2)
15. Current treatments for depression should be collected.	5	9.2 (0.9)

BCG, Bacille Calmette Guérin; FRAX, Fracture Risk Assessment Tool.

### Reporting, screening for and prevention of infections Level of evidence

Five articles reported recommendations for reporting or screening patients for infections. One article reported guidelines for the screening for *Mycobacterium tuberculosis* infection (TB) in adult patients with chronic kidney disease.<sup>59</sup> One article reported EULAR recommendations for TB screening in patients with systemic lupus erythematosus.<sup>29</sup> One article reported recommendation for TB screening in the general population in the USA.<sup>60</sup> EULAR recommendations reported screening for risk factors of non-TB opportunistic infections with a specific focus on vaccination in patients with CIRDs, and screening for non-TB opportunistic infections in patients with systemic lupus erythematosus.<sup>4</sup> <sup>29</sup> A national recommendation reported risk factors to be collected for serious lower respiratory tract

infection<sup>61</sup> in the context of an acute infection. Several articles led to level 2a evidence regarding screening for TB<sup>62</sup> <sup>63</sup>; and one trial demonstrated the efficacy of collecting vaccination status and recommending vaccination updates according to national recommendations by a nurse.<sup>14</sup>

## EULAR points to consider

The Task Force decided to focus on serious rather than severe infection as 'severe' implies a grading of the event (mild, moderate or severe), which is usually not formally defined contrary to a serious infection. A serious infection is defined as an infection that results in death, is life-threatening, requires hospitalisation or prolongation of existing hospitalisation or may result in persistent or significant disability/incapacity. The panel decided to report opportunistic infections on the basis of data from

biological registries in rheumatic diseases (see online supplementary table S2).<sup>65</sup>

# Reporting, screening for and prevention of gastrointestinal diseases

#### Level of evidence

Three articles reported European and the US recommendations for screening patients for gastroduodenal ulcers. <sup>9 30 66</sup> No recommendation for diverticulitis was found in CIRDs nor in the general population. No direct data were found within the scope of this hierarchical systematic literature review, on the interest of the screening for risk factors of peptic ulcers.

#### EULAR points to consider

In this area, it should be noticed that the colon/rectum cancer issue has been previously addressed in the 'Malignancies' section. Similarly, the presence of inflammatory bowel diseases was collected as a risk factor for colon cancer. Although the reporting of diverticulitis might impact disease management in CIRDs, we excluded this comorbidity from this minimal set of variables to collect as no recommendation was found in the literature. Therefore, in terms of reporting, the Task Force proposal is to focus on peptic ulcer, as this can have consequences on NSAIDs prescription (table 2 and see online supplementary table S2).

#### Reporting, screening for and preventing osteoporosis Level of evidence

Two articles reported EULAR recommendations for screening for osteoporosis in patients with systemic lupus erythematosus <sup>29</sup> and for patients taking medium-dose to high-dose glucocorticoid therapy in rheumatic diseases. <sup>30</sup> Two articles reported recommendations for screening for osteoporosis in the general population. <sup>13</sup> <sup>67</sup> Two articles allowed us to determine a 2b level of proof for screening for risk factors. <sup>14</sup> <sup>68</sup>

# EULAR points to consider

Apart from the report of the occurrence of osteoporotic fractures, the Task Force recommended a systematic review of predisposing factors of osteoporosis together with the calculation of a score for risk of osteoporotic fracture at 10 years (ie, FRAX).<sup>69</sup> Although risk of falls is important, the Task Force did not recommend collecting this information as no universal standardised tool was found (table 2 and see online supplementary table S2).

# Reporting, screening for and preventing depression Level of evidence

Four articles reported national recommendations for reporting or screening patients for depression in the general population or patients with chronic illness. To-73 Discrepancies were found among these national recommendations: an article recommended not to routinely screen for depression subgroups of the population who display average or high risk of depression, the population who display average or high risk of depression, the depression or chronic physical health problem with associated functional impairment for depression.

#### EULAR points to consider

With regards to the report/detection of depression, the Task Force proposed not to refer to any specific existing screening tool, but to use an open question to elicit the patient whether he/she has been formally diagnosed with depression. If the answer is yes, the patient should then be queried regarding the use of medications to treat depression. If the answer is no, the patient should be asked if he/she has ever been screened for depression (table 2 and see online supplementary table S2).

#### The comorbidities collection form

The Task Force elaborated a list of data to collect regarding comorbidities, in relation with the points to consider. The form comprises a total of 93 questions formulated in English. The data format allows a health professional (eg, either a nurse or a physician) to perform the data collection. The elaboration of the form was undertaken in collaboration with the participating patients, keeping in mind that a self-administered version of this form might be of great interest.

Table 3 provides an overview of the form and summarises the conclusions of the EULAR Task Force concerning the information to be regularly collected on the six selected comorbidities, and an example is presented in table 4. The full-text form is available with explanatory text online from the EULAR website and also presented as online supplementary table S2.

### **DISCUSSION**

This initiative focuses on reporting, screening for and preventing selected comorbidities of relevance in patients with CIRDs: points to consider formulated as three overarching principles and 15 points to consider have been developed. Furthermore, a simple though detailed form is made available, to be implemented in daily practice. The form is freely available for either

**Table 3** Overview of the practical form for reporting or detecting prevalent comorbidities, screening for comorbidity or for risk factors and treatments/vaccination

Comorbidity	Total number of questions in the form relating to this comorbidity (% of total)	Number of questions for reporting (% of total for the domain)	Number of questions for detecting (% of total for the domain)	Number of questions for risk factors (% of total for the domain)	Number of questions on treatments/vaccination (% of total for the domain)
Cardiovascular disease	26 (15)	8 (31)	0 (0)	13 (50)	5 (19)
Malignancies	38 (22)	30 (79)	5 (13)	3 (8)	0 (0)
Infections	54 (32)	36 (67)	0 (0)	0 (0)	18 (33)
Gastrointestinal diseases	11 (7)	2 (18)	0 (0)	9 (82)	0 (0)
Osteoporosis	34 (20)	16 (47)	4 (12)	7 (21)	7 (21)
Depression	6 (4)	2 (33)	2 (33)	0 (0)	2 (33)
Total form, all comorbidities	169 (100)	94 (56)	11 (7)	32 (19)	32 (19)

Percentages correspond to the number of the items of the form addressing the reporting of comorbidity or the detecting or the risk factors of a comorbidity divided by the number of question for this comorbidity.

 Table 4
 European League Against Rheumatism standardised reporting form for reporting ischaemic cardiovascular diseases, for risk factors and treatments

Cardiovascular comorbidity			
Report			.,
Has the patient ever had a diagnosis of	No	Yes	If yes, year of diagnosis
ischaemic cardiovascular disease including myocardial infarction, pectoris angina or a stent			
either stroke or transient ischaemic attack			
heart failure			
lower limb peripheral arterial disease			
Risk factors			
Smoking status	☐ Never ☐ Ever but cessation >1 year ago	☐ Ever but cessation <1 year ago ☐ Ongoing	
Height (m)	Weight (kg), body mass index (kg/m²)		
Diabetes	<ul><li>No</li><li>Yes and treated</li><li>Yes but not treated</li></ul>	Last year glycaemia was scree  ☐ Never done ☐ Don't know	ned:
Hypertension	☐ No ☐ Yes and treated ☐ Yes but not treated	Last year blood pressure was a  ☐ Never done ☐ Don't know	taken:
Hypercholesterolaemia	☐ No ☐ Yes and treated ☐ Yes but not treated	Last year lipids were screened  ☐ Never done ☐ Don't know	:
Renal insufficiency	☐ No (GFR >60) ☐ Yes, moderate (GFR 30–60) ☐ Yes, severe (GFR <30)	Last year GFR was estimated:  ☐ Never done ☐ Don't know	
Calculation of the global cardiovascular risk on the HEART-SCORE?		Year: □ Never done	Score (%)
Treatments	No	Yes	
Antihypertensive therapy			
Antiplatelet therapy			
Diabetes insulin or non-insulin therapies			
Lipid-lowering agents (statins or not)			
Anticoagulants (including heparin and non-heparin)			

GFR. glomerular filtration rate (mL/min).

integration in cohort data or use in daily practice by the rheumatology team. These recommendations were developed using the EULAR Standardised Operating Procedures for the elaboration, evaluation, dissemination and implementation of recommendations. <sup>24</sup> We have critically appraised the available recommendations. Thus, this was a data-driven and consensual approach.

Some limitations should be emphasised. First, the systematic literature review showed that specific CIRDs-dedicated recommendations for comorbidity screening are scarce.<sup>4</sup> 11 29 30 In most cases, recommendations for the management of comorbidities in CIRDs were extrapolated from those in the general population. Interestingly, recommendations are focused mainly on screening risk factors for comorbidities rather than on reporting a prevalent comorbidity or recording a still overlooked comorbidity as well as recoding treatment. Therefore, these points to consider were graded as level 5 evidence, except points to consider 2, 5-6, 8 and 12 (table 2). However, the documentation of risk factors is based on higher levels of proof. Second, the choice of the target population (ie, the list of rheumatic diseases comprised in CIRDs) is also open for criticism. We did not specifically include osteoarthritis, although some authors describe osteoarthritis as an inflammatory joint disorder with a substantially lower systemic inflammatory

burden compared with other CIRDs.<sup>28</sup> This dichotomy between inflammatory and non-inflammatory diseases is probably not clinically relevant since some comorbidities are prevalent in both osteoarthritis and the 'conventional' CIRDs; for this reason, patients with polyarticular osteoarthritis may also benefit from this form.

Some comorbidities such as fatigue, fibromyalgia or repetitive non-opportunistic non-serious infections would be important to collect, but are missing in this current proposal. However, the Task Force anticipated that the screening for a broad scope of comorbidities would make the final 'product' (eg, the proposed form) too complex or extensive to be implemented. Moreover, the Task Force excluded some diseases (eg, prostate cancer and diverticulitis) from these EULAR points to consider as concerns about the effectiveness of a systematic screening for certain comorbidities have recently been raised, mainly because of the anxiety induced by false-positive tests, the risk of overtreatment and the burden for medico-economic resources.<sup>74</sup> Finally, the cost-effectiveness of screening strategies was not often available in recommendations. The yield of routine screening for comorbidities and the cost of routine screening dramatically impact on the cost-effectiveness of screening strategies. Evidence from a Canadian modelling study suggests that routine screening for depression, resulting in increased rates of treatment, may

not reduce the burden of depression. Instead, focusing efforts on reducing episodes of relapse (eg, through long-term treatment in patients with known depression) may be a more efficient use of resources.<sup>75</sup>

Dissemination and implementation of recommendations is often an issue. In the present case, it is hoped that the proposed reporting form (available as online supplementary online data and on the EULAR website as a Word or PowerPoint document) will facilitate the dissemination and the implementation of the present initiative. This EULAR initiative provides recommendations and a reporting form to facilitate the screening for comorbidities rather than recommendations on the optimal management (eg, interval of time between mammographies) or optimal value of a specific risk factor (eg, blood pressure or cholesterol level). This choice was fostered by the intercountry variability of the existing recommendations. The hierarchical literature search was performed to retrieve recommendations, and the present points to consider are in accordance with other EULAR initiatives.<sup>4</sup> <sup>11</sup> Therefore, we expect that this form will be easily adapted at the national or local level. For instance, one could consider to systematically check for other comorbidities such as fibromyalgia: this could easily be added in the form once adapted to a given country. Finally, the EULAR reporting form is in English, which may present a challenge in some countries.

The points to consider are easy to understand and are limited in number. However, even intended as pragmatic, the reporting form turned out to be quite extensive. Indeed, a systematic screening for comorbidities may take up to an hour, <sup>14</sup> particularly when undertaken for the first time. However, for subsequent screenings (eg, 1 or 2 years later), the process should be quicker and will be more efficient if the initial screening is easily available (eg, if these data are available in the medical records or in electronic form). <sup>76</sup> We are aware that the reporting form is detailed and long, but this could be implemented as a hierarchical form (ie, with sections to be filled-in only if relevant). Furthermore, the assessment of comorbidities could be divided across several visits (eg, cardiovascular then cancers), if necessary.

Systematic screenings have been found to be useful for patients, as they draw attention to comorbidities that might otherwise be overlooked. The time necessary for this screening raises the question of where it should best be performed. Should it be the rheumatologist, perhaps as a dedicated outpatient visit, or a rheumatology nurse, for example, during a systematic yearly review? This initiative does not answer this question, but hopefully encourages a coherent and uniform approach for a review of comorbidities for people with CIRDs. We did not resolve the issue of who should then prescribe tests or treatments if needed; we believe the rheumatology team should collaborate with the patient's general practitioner in this regard.

It will be interesting to evaluate the impact of this initiative in terms of implementation in daily practice. It will also be critical to take the opportunity to propose a lay version of the reporting form in order to encourage a patient-centred approach to care, as the involvement of patients is mandatory to achieve an optimal decision-making process. 77

### **Author affiliations**

<sup>1</sup>Department of Rheumatology, Université Joseph Fourier, GREPI—CNRS, Grenoble Hospital, France

<sup>2</sup>Department of Rheumatology, Sorbonne Universités, UPMC Univ Paris 06, Institut Pierre Louis d'Epidémiologie et de Santé Publique, GRC-UPMC 08 (EEMOIS); AP-HP, Pitié Salpêtrière Hospital, Paris, France

<sup>3</sup>Instituto de Salud Musculoesquelética, Madrid, Spain

<sup>4</sup>EULAR Standing Committee of People with Arthritis/Rheumatism in Europe (PARE), Zurich, Switzerland

<sup>5</sup>Integrated Care, Maastricht University Medical Centre, Maastricht, The Netherlands <sup>6</sup>Salisbury NHS Foundation Trust Hospital, Salisbury, UK

<sup>7</sup>Cyprus League Against Rheumatism, Cyprus, Nikosia, Cyprus

<sup>8</sup>Départment of Rheumatology, Centro Hospitalar e Universitário de Coimbra; Health Sciences Research Unit: Nursing (UlCiSA:E), Coimbra, Portugal

<sup>9</sup>Independent Nurse Consultant, North Devon, UK

<sup>10</sup>Department of Internal Medicine, University of Cologne, Cologne, Germany
 <sup>11</sup>Department of Internal Medicine, Division of Infectious Diseases, University
 Medical Centre Groningen, University of Groningen, Groningen, The Netherlands
 <sup>12</sup>Arthritis Research UK Centre for Epidemiology, Manchester Academic Health
 Science Centre, The University of Manchester, Manchester, UK

<sup>13</sup>Division of Rheumatology, Geneva University Hospital, Geneva, Switzerland <sup>14</sup>Epidemiology Unit, German Rheumatism Research Centre, and Rheumatology, Charité, University Medicine, Berlin, Germany

<sup>15</sup>Albany Medical College and The Center for Rheumatology, Albany, USA <sup>16</sup>Department of Rheumatology, Diakonhjemmet Hospital, Oslo, Norway

 $^{17}\!\mbox{\mbox{Amsterdam}}$  Rheumatology immunology Center | VUmc and Reade, The Netherlands

<sup>18</sup>Department of Rheumatology, Leiden University Medical Center, The Netherlands <sup>19</sup>Department of Rheumatology, Paris Descartes University—Hôpital Cochin. Assistance Publique—Hôpitaux de Paris. INSERM (U1153): Clinical epidemiology and biostatistics, PRES Sorbonne Paris-Cité, Paris, France

Twitter Follow William Dixon at @WGDixon

**Acknowledgements** The authors thank Mr Xavier Romand, Mr Jason Hubac and Dr Dounia Bettache for their help in the literature review. The authors thank Pr. Thierry Thomas for his critical review of the manuscript.

Funding EULAR.

**Competing interests** None declared.

Provenance and peer review Not commissioned; externally peer reviewed.

#### REFERENCES

- Maradit-Kremers H, Crowson CS, Nicola PJ, et al. Increased unrecognized coronary heart disease and sudden deaths in rheumatoid arthritis: a population-based cohort study. Arthritis Rheum 2005;52:402–11.
- 2 Hickson LJ, Crowson CS, Gabriel SE, et al. Development of reduced kidney function in rheumatoid arthritis. Am J Kidney Dis 2014;63:206–13.
- 3 Giles JT, Danoff SK, Sokolove J, et al. Association of fine specificity and repertoire expansion of anticitrullinated peptide antibodies with rheumatoid arthritis associated interstitial lung disease. Ann Rheum Dis 2014;73:1487–94.
- 4 van Assen S, Agmon-Levin N, Elkayam O, et al. EULAR recommendations for vaccination in adult patients with autoimmune inflammatory rheumatic diseases. Ann Rheum Dis 2011;70:414–22.
- 5 Dougados M, Soubrier M, Antunez A, et al. Prevalence of comorbidities in rheumatoid arthritis and evaluation of their monitoring: results of an international, cross-sectional study (COMORA). Ann Rheum Dis 2014;73:62–8.
- 6 Eichenauer DA, Engert A, Dreyling M, et al. Hodgkin's lymphoma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol 2011;22 (Suppl 6):vi55–8.
- 7 Baillet A, Payraud E, Niderprim V-A, et al. A dynamic exercise programme to improve patients' disability in rheumatoid arthritis: a prospective randomized controlled trial. Rheumatology (Oxford) 2009;48:410–15.
- 8 Bremander A, Petersson IF, Bergman S, et al. Population-based estimates of common comorbidities and cardiovascular disease in ankylosing spondylitis. Arthritis Care Res (Hoboken) 2011;63:550–6.
- 9 Lanza FL, Chan FK, Quigley EM, et al. Guidelines for prevention of NSAID-related ulcer complications. Am J Gastroenterol 2009;104:728–38.
- 10 Matcham F, Rayner L, Steer S, et al. The prevalence of depression in rheumatoid arthritis: a systematic review and meta-analysis. Rheumatology (Oxford) 2013:52:2136–48.
- Peters MJ, Symmons DP, McCarey D, et al. EULAR evidence-based recommendations for cardiovascular risk management in patients with rheumatoid arthritis and other forms of inflammatory arthritis. Ann Rheum Dis 2010;69:325–31.
- Nurmohamed MT, Heslinga M, Kitas GD. Cardiovascular comorbidity in rheumatic diseases. Nat Rev Rheumatol 2015;11:693–704.
- 13 Kanis JA, Burlet N, Cooper C, et al. European guidance for the diagnosis and management of osteoporosis in postmenopausal women. Osteoporos Int 2008:10:200-428
- Dougados M, Soubrier M, Perrodeau E, et al. Impact of a nurse-led programme on comorbidity management and impact of a patient self-assessment of disease activity on the management of rheumatoid arthritis: results of a prospective, multicentre, randomised, controlled trial (COMEDRA). Ann Rheum Dis 2015;74:1725–33.

- 15 Solomon DH, Curhan GC, Rimm EB, et al. Cardiovascular risk factors in women with and without rheumatoid arthritis. Arthritis Rheum 2004;50:3444–9.
- 16 MacLean CH, Louie R, Leake B, et al. Quality of care for patients with rheumatoid arthritis. JAMA 2000;284:984–92.
- 17 Curtis JR, Arora T, Narongroeknawin P, et al. The delivery of evidence-based preventive care for older Americans with arthritis. Arthritis Res Ther 2010; 12:R144
- 18 Kremers HM, Bidaut-Russell M, Scott CG, et al. Preventive medical services among patients with rheumatoid arthritis. J Rheumatol 2003;30:1940–7.
- Stavropoulos-Kalinoglou A, Metsios GS, Panoulas VF, et al. Underweight and obese states both associate with worse disease activity and physical function in patients with established rheumatoid arthritis. Clin Rheumatol 2009;28:439–44.
- 20 Gossec L, Salejan F, Nataf H, et al. Challenges of cardiovascular risk assessment in the routine rheumatology outpatient setting: an observational study of 110 rheumatoid arthritis patients. Arthritis Care Res (Hoboken) 2013;65:712–17.
- 21 Dougados M, Nataf H, Steinberg G, et al. Relative importance of doctor-reported outcomes vs patient-reported outcomes in DMARD intensification for rheumatoid arthritis: the DUO study. Rheumatology (Oxford) 2013;52:391–9.
- van Eijk-Hustings Y, van Tubergen A, Boström C, et al. EULAR recommendations for the role of the nurse in the management of chronic inflammatory arthritis. Ann Rheum Dis 2012;71:13–19.
- 23 Loza E, Lajas C, Andreu JL, et al. Consensus statement on a framework for the management of comorbidity and extra-articular manifestations in rheumatoid arthritis. Rheumatol Int 2015;35:445–58.
- 24 van der Heijde D, Aletaha D, Carmona L, et al. 2014 Update of the EULAR standardised operating procedures for EULAR-endorsed recommendations. Ann Rheum Dis 2015;74:8–13.
- 25 Horwich A, Parker C, de Reijke T, et al. Prostate cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol 2013;24(Suppl 6): vi106–14
- 26 Braillon A, Dubois G. [PSA (prostate specific antigen): Haute Autorite de Santé, American Cancer Society and National Health Service. Discrepancy between concepts for assessment]. Presse Med 2011;40:112–14.
- 27 Howick J, Chalmers I, Glasziou P, et al. Explanation of the 2011 Oxford Centre for Evidence-Based Medicine (OCEBM) Levels of Evidence. Oxford Centre for Evidence-Based Medicine. http://www.cebm.net/index.aspx?o=5653
- 28 Sellam J, Berenbaum F. The role of synovitis in pathophysiology and clinical symptoms of osteoarthritis. *Nat Rev Rheumatol* 2010;6:625–35.
- 29 Mosca M, Tani C, Aringer M, et al. European League Against Rheumatism recommendations for monitoring patients with systemic lupus erythematosus in clinical practice and in observational studies. Ann Rheum Dis 2010:69:1269–74.
- 30 Duru N, van der Goes MC, Jacobs JW, et al. EULAR evidence-based and consensus-based recommendations on the management of medium to high-dose glucocorticoid therapy in rheumatic diseases. Ann Rheum Dis 2013;72:1905–13.
- 31 Nurmohamed MT. EÜLAR Recommendations update on cardiovascular disease in RA[abstract]. Ann Rheum Dis 2015;74(Suppl 9).
- 32 Conroy RM, Pyorala K, Fitzgerald AP, et al. Estimation of ten-year risk of fatal cardiovascular disease in Europe: the SCORE project. Eur Heart J 2003;24:987–1003.
- 33 Wood D. European and American recommendations for coronary heart disease prevention. Eur Heart J 1998;19 Suppl A(Suppl A):A12–19.
- 34 Aebi S, Davidson T, Gruber G, et al. Primary breast cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol* 2011;22(Suppl 6): vi12–24
- 35 Aebi S, Davidson T, Gruber G, et al. Primary breast cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol 2010;21(Suppl 5): v9–14.
- 36 Kataja V, Castiglione M, Group EGW. Primary breast cancer: ESMO clinical recommendations for diagnosis, treatment and follow-up. *Ann Oncol* 2009;20(Suppl 4):10–14.
- 37 Pestalozzi B, Castiglione M, Group EGW. Primary breast cancer: ESMO clinical recommendations for diagnosis, treatment and follow-up. *Ann Oncol* 2008;19(Suppl 2):i7–10
- 38 Senkus E, Kyriakides S, Penault-Llorca F, et al. Primary breast cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol 2013;24 (Suppl 6):vi7–23.
- 39 Labianca R, Nordlinger B, Beretta GD, et al. Primary colon cancer: ESMO Clinical Practice Guidelines for diagnosis, adjuvant treatment and follow-up. Ann Oncol 2010;21(Suppl 5):v70–7.
- 40 Labianca R, Nordlinger B, Beretta GD, et al. Early colon cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol 2013;24 (Suppl 6):vi64–72.
- 41 Schmoll HJ, Van Cutsem E, Stein A, et al. ESMO Consensus Guidelines for management of patients with colon and rectal cancer. a personalized approach to clinical decision making. Ann Oncol 2012;23:2479–516.
- 42 Van Cutsem E, Oliveira J, Group EGW. Primary colon cancer: ESMO clinical recommendations for diagnosis, adjuvant treatment and follow-up. *Ann Oncol* 2009;20(Suppl 4):49–50.

- 43 Horwich A, Hugosson J, de Reijke T, et al. Prostate cancer: ESMO Consensus Conference Guidelines 2012. Ann Oncol 2013;24:1141–62.
- 44 Horwich A, Parker C, Bangma C, et al. Prostate cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol 2010;21(Suppl 5): v129–33.
- 45 Dummer R, Hauschild A, Guggenheim M, et al. Cutaneous melanoma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol 2012;23(Suppl 7):vii86–91.
- 46 Willemze R, Dreyling M, Group EGW. Primary cutaneous lymphoma: ESMO clinical recommendations for diagnosis, treatment and follow-up. *Ann Oncol* 2009;20(Suppl 4):115–18.
- 47 D'Addario G, Fruh M, Reck M, et al. Metastatic non-small-cell lung cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol 2010;21(Suppl 5):v116–19.
- 48 Fruh M, De Ruysscher D, Popat S, et al. Small-cell lung cancer (SCLC): ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol 2013;24(Suppl 6):vi99–105.
- 49 Colombo N, Carinelli S, Colombo A, et al. Cervical cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol 2012;23(Suppl 7): vii27–32.
- 50 Dreyling M, Geisler C, Hermine O, et al. Newly diagnosed and relapsed mantle cell lymphoma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up dagger. Ann Oncol 2014;25(Suppl 3):iii83–92.
- 51 Dreyling M, Thieblemont C, Gallamini A, et al. ESMO Consensus conferences: guidelines on malignant lymphoma. part 2: marginal zone lymphoma, mantle cell lymphoma, peripheral T-cell lymphoma. Ann Oncol 2013;24:857–77.
- 52 Eichenauer DA, Engert A, Andre M, et al. Hodgkin's lymphoma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol 2014;25 (Suppl 3):iii70–5.
- 53 Ghielmini M, Vitolo U, Kimby E, et al. ESMO Guidelines consensus conference on malignant lymphoma 2011 part 1: diffuse large B-cell lymphoma (DLBCL), follicular lymphoma (FL) and chronic lymphocytic leukemia (CLL). Ann Oncol 2013;24:561–76.
- Kerlikowske K, Grady D, Rubin SM, et al. Efficacy of screening mammography. A meta-analysis. JAMA 1995;273:149–54.
- Martin-Hirsch P, Lilford R, Jarvis G, et al. Efficacy of cervical-smear collection devices: a systematic review and meta-analysis. *Lancet* 1999;354:1763–70.
- 56 Jellema P, van der Windt DA, Bruinvels DJ, et al. Value of symptoms and additional diagnostic tests for colorectal cancer in primary care: systematic review and meta-analysis RMJ 2010:340:c1269
- 57 Bafounta ML, Beauchet A, Aegerter P, et al. Is dermoscopy (epiluminescence microscopy) useful for the diagnosis of melanoma? Results of a meta-analysis using techniques adapted to the evaluation of diagnostic tests. Arch Dermatol 2001;137:1343–50.
- 58 Brenner H, Stock C, Hoffmeister M. Effect of screening sigmoidoscopy and screening colonoscopy on colorectal cancer incidence and mortality: systematic review and meta-analysis of randomised controlled trials and observational studies. *BMJ* 2014;348:q2467.
- 59 Abubakar I, Griffiths C, Ormerod P, et al. Diagnosis of active and latent tuberculosis: summary of NICE guidance. BMJ 2012;345:e6828.
- Diagnostic Standards and Classification of Tuberculosis in Adults and Children. This official statement of the American Thoracic Society and the Centers for Disease Control and Prevention was adopted by the ATS Board of Directors, July 1999. This statement was endorsed by the Council of the Infectious Disease Society of America, September 1999. Am J Respir Crit Care Med 2000;161:1376–95.
- 61 Woodhead M, Blasi F, Ewig S, et al. Guidelines for the management of adult lower respiratory tract infections—full version. Clin Microbiol Infect 2011;17(Suppl 6): E1–59.
- 62 Menzies D, Pai M, Comstock G. Meta-analysis: new tests for the diagnosis of latent tuberculosis infection: areas of uncertainty and recommendations for research. *Ann Intern Med* 2007;146:340–54.
- 63 Roy A, Eisenhut M, Harris RJ, et al. Effect of BCG vaccination against Mycobacterium tuberculosis infection in children: systematic review and meta-analysis. BMJ 2014;349:q4643.
- 64 US Food and Drug Administration website: http://www.fda.gov/Safety/MedWatch/ HowToReport/ucm053087.htm
- 65 Mariette X, Gottenberg JE, Ravaud P, et al. Registries in rheumatoid arthritis and autoimmune diseases: data from the French registries. Rheumatology (Oxford) 2011;50:222–9.
- 66 Rubin G, Meineche-Schmidt V, Roberts A, et al. The use of consensus to develop guidelines for the management of Helicobacter pylori infection in primary care. European Society for Primary Care Gastroenterology. Fam Pract 2000;17(Suppl 2): S21–6.
- 67 Kanis JA, McCloskey EV, Johansson H, et al. European guidance for the diagnosis and management of osteoporosis in postmenopausal women. Osteoporos Int 2013;24:23–57.

- 68 Hippisley-Cox J, Coupland C. Predicting risk of osteoporotic fracture in men and women in England and Wales: prospective derivation and validation of QFractureScores. BMJ 2009;339:b4229.
- 69 Kanis JA, Johnell O, Oden A, et al. FRAX and the assessment of fracture probability in men and women from the UK. Osteoporos Int 2008;19:385–97.
- 70 NCCfMHLUNIfHaCE. Depression in adults with a chronic physical health problem. Treatment and management[NICE Clinical Guidelines, no. 91]. 2009.
- 71 Joffres M, Jaramillo A, Dickinson J, et al, Canadian Task Force on Preventive Health C. Recommendations on screening for depression in adults. CMAJ 2013;185:775–82.
- 72 Force USPST. Screening for depression: recommendations and rationale. Ann Intern Med 2002;136:760–4.
- 73 Force USPST. Screening for depression in adults: U.S. preventive services task force recommendation statement. Ann Intern Med 2009;151:784–92.
- 74 Ashford NA, Bauman P, Brown HS, et al. Cancer risk: role of environment. Science 2015;347:727.
- 75 Steineck G, Helgesen F, Adolfsson J, et al. Quality of life after radical prostatectomy or watchful waiting. N Engl J Med 2002;347:790–6.
- 76 Bender Ignacio RA, Chu J, Power MC, et al. Influence of providers and nurses on completion of non-targeted HIV screening in an urgent care setting. AIDS Res Ther 2014:11:24.
- 77 Zangi HA, Ndosi M, Adams J, *et al.* EULAR recommendations for patient education for people with inflammatory arthritis. *Ann Rheum Dis* 2015;74:954–62.