Evaluation of guideline-endorsed red flags to screen for fracture in patients presenting with low back pain

Patricia C S Parreira,[1] Christopher G Maher,[1] Adrian C Traeger,[1] Mark J Hancock,[2] Aron Downie,[1] Bart W Koes,[3] Manuela L Ferreira[4]

ABSTRACT

Objectives (1) Describe the evolution of guideline-endorsed red flags for fracture in patients presenting with low back pain; (2) evaluate agreement between guidelines; and (3) evaluate the extent to which recommendations are accompanied by information on diagnostic accuracy of endorsed red flags.

Design Systematic review.

Data sources MEDLINE and PubMed, PEDro, CINAHL and EMBASE electronic databases. We also searched in guideline databases, including the *National Guideline Clearinghouse* and *Canadian Medical Association Infobase*.

Eligibility criteria for selecting studies Evidence-based clinical practice guidelines.

Data extraction Two review authors independently extracted the following data: health professional association or society producing guideline, year of publication, the precise wording of endorsed red flag for vertebral fracture, recommendations for diagnostic workup if fracture is suspected, if the guidelines substantiate the recommendation with citation to a primary diagnostic study or diagnostic review, if the guideline provides any diagnostic accuracy data.

Results 78 guidelines from 28 countries were included. A total of 12 discrete red flags were reported. The most commonly recommended red flags were older age, use of steroids, trauma and osteoporosis. Regarding the evolution of red flags, older age, trauma and osteoporosis were the first red flags endorsed (in 1994); and previous fracture was the last red flag endorsed (in 2003). Agreement between guidelines in endorsing red flags was only fair; kappa=0.32. Only 9 of the 78 guidelines substantiated their red flag recommendations by research and only nine provided information on diagnostic accuracy.

Summary/conclusion The number of red flags endorsed in guidelines to screen for fracture has risen over time; most guidelines do not endorse the same set of red flags and most recommendations are not supported by research or accompanied by diagnostic accuracy data.

BACKGROUND

Low back pain (LBP) is a leading cause of disability worldwide and is most commonly treated in primary healthcare settings.[1 2] While the majority of patients with this condition are diagnosed with non-specific LBP, in a small proportion of patients (<1% in primary care) the pain is the result of serious pathology.[3] The most common of these serious pathologies is vertebral fracture[4–6] followed by malignancy, infection and inflammatory disease.[4]

Identifying patients with an increased likelihood of vertebral fracture is a key objective of the clinical assessment for patients with LBP.[4]

Clinical guidelines endorse red flags as the ideal method to identify patients with a higher likelihood of vertebral fractures who then require further diagnostic workup.[7 8] Examples of red flags used to screen for vertebral fractures include a history of trauma and older age.[5] Inspection of clinical guidelines however reveals that guidelines usually do not endorse the same set of red flags and there is typically no information on diagnostic accuracy of the endorsed red flags.

The earliest report on red flags for vertebral fracture, which we identified, was published in 1872[9] and the first recognised clinical guideline for the management of acute LBP containing recommendations regarding vertebral fracture did not appear until 1994.[10] Since then, numerous guidelines have been published around the world endorsing a range of red flags for vertebral fracture. It is not known if these recommendations are consistent across guidelines or based on evidence. Therefore, the purpose of this study was: (1) describe the evolution of guideline-endorsed red flags for fracture in patients presenting with LBP; (2) evaluate consistency between guidelines; and (3) evaluate the extent to which recommendations are accompanied by information on diagnostic accuracy of endorsed red flags.

METHODS

Data sources

The review protocol was registered with the PROSPERO database prior to commencement (No CRD42017065614). To locate LBP guidelines which endorse red flags for vertebral fracture in patients presenting with LBP we searched MEDLINE and PubMed, PEDro, CINAHL and EMBASE electronic databases. We also searched in guideline databases, including the *National Guideline Clearinghouse* and *Canadian Medical Association Infobase*. Detailed search strategies used for each database are described in online supplementary appendix 1. The reference lists of relevant guidelines were screened and we used Web of Science citation index to identify guidelines citing other previous guidelines. There were no restrictions on date of publication. Guidelines in any language were considered, and included non-English language guidelines if a translation could be obtained.

Selection of guidelines

Two review authors (PCSP and ACT) independently screened titles and abstracts for possibly eligible
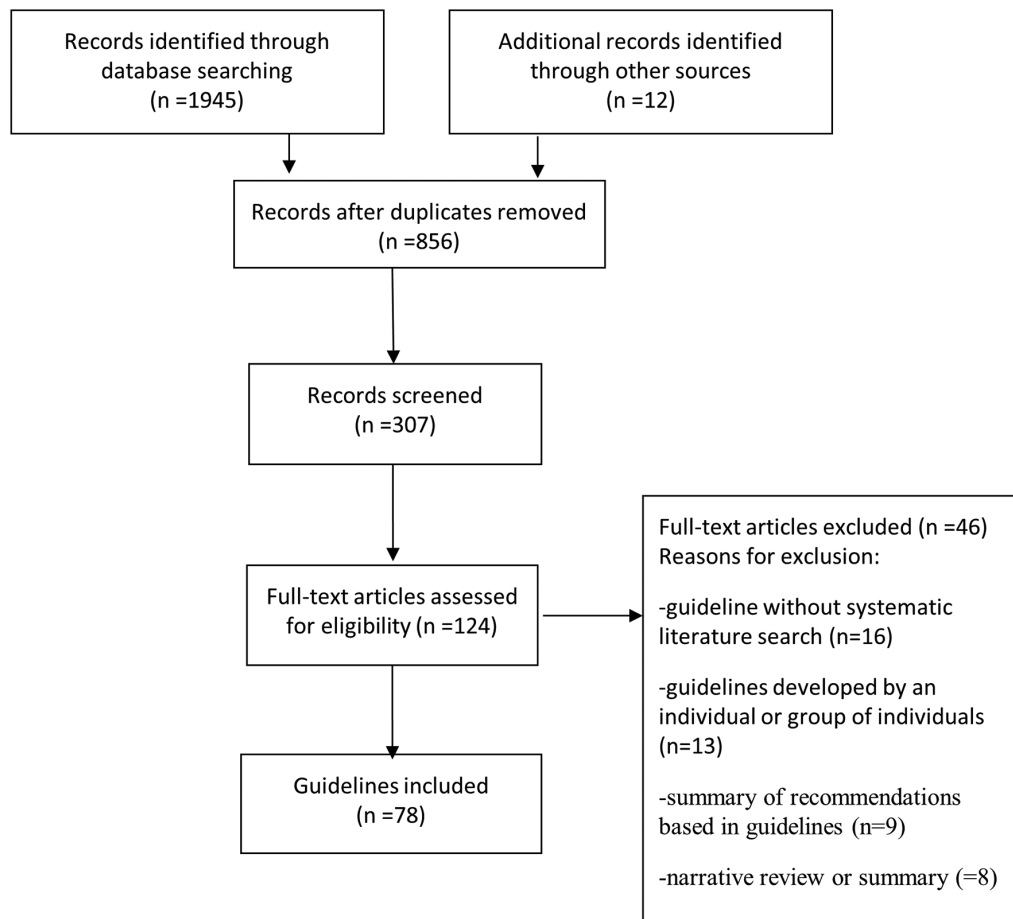
Figure 1 Selection of guidelines for inclusion in the systematic review.

studies and obviously ineligible records were excluded. Full-text papers were used to determine eligibility for inclusion in the review. The disagreements between review authors were resolved through discussion or by the arbitration of a third review author (CGM). Only one guideline was included per country per year. When one country had more than one guideline per year, the most recent multidisciplinary guideline was selected. Clinical practice guidelines were included if they (1) were produced by health professional association or society, public or private organisation, healthcare organisation or plan, or government agency; (2) were publicly available; (3) were based on a systematic literature search and review of existing scientific evidence published in peer-reviewed journals; and finally if (4) they contained systematically developed statements that included recommendations, strategies or information to guide decisions about appropriate healthcare. These criteria belong to the PEDro criteria for evidence-based clinical practice guidelines.

Data extraction and management

Two review authors (PCSP and ACT) independently extracted the data using standardised data extraction forms. The following data were extracted: (1) health professional association or society producing guideline, (2) year of publication, (3) the precise wording of endorsed red flag for vertebral fracture, (4) recommendations for diagnostic workup if fracture is suspected, (5) if the guidelines substantiate the recommendation with citation to a primary diagnostic study or diagnostic review, and (6) if the guideline provides any diagnostic accuracy data. The data from the guidelines were presented in a table. In the columns

were included each discrete red flag for vertebral fracture listed in a guideline. In the rows were listed all guidelines chronologically beginning with the earliest published guideline. For each cell in the table we noted yes or no to signify whether that specific red flag was endorsed by that guideline. The agreement among the guidelines in their endorsement of red flags was evaluated using Fleiss' kappa[11] (poor agreement <0.00; slight agreement 0.00–0.20; fair agreement 0.21–0.40; moderate agreement 0.41–0.60; substantial agreement 0.61–0.80; almost perfect agreement 0.81–1.00).

RESULTS
Selection of guidelines

As shown in figure 1, the database search identified 1967 documents. After two reviewers (PCSP and ACT) independently screened titles, abstracts and full texts according to the inclusion and exclusion criteria, 78 guidelines were selected for inclusion. Clinical guidelines from 28 different countries were included in this review. The guidelines were published between 1987[12] and 2017,[13–17] with the publication date of one guideline not specified in the document (Malaysia).[18] The 78 guidelines included in the review were developed in South Africa,[19] Austria,[20 21] Australia,[22–24] Belgium,[13 25] Brazil,[26] Canada,[12 27–30] China,[31] Croatia,[32] Denmark,[14 33–36] Europe,[37] Finland,[16 38–40] France,[41] Germany,[17 42–47] Italy,[48] Israel,[49] Korea,[50] Malaysian,[18] Mexico,[51] Netherlands,[36 52–54] New Zealand,[55 56] Norway,[45 57 58] Philippines,[59] Scotland,[60] Spain,[61–64] Switzerland,[65] Sweden,[66] UK[67–71] and USA.[6 10 15 67 72–83] Only 32 of the 78 guidelines

explicitly nominated red flags to screen for fracture, with the remainder nominating red flags for serious pathology in general. In the latter case we considered the following red flags as alerting features for fracture (older age; a history of trauma; prolonged use of corticosteroids; and osteoporosis) and coded their presence as a yes in the matrix.

Guideline committee
The various committees responsible for the development and publication of guidelines appear to be different in size and in the professional disciplines involved. The number of members varied from 7 to 31.

Evolution and consistency of the guidelines
We noted a total of 12 discrete red flags reported in a total of 71 guidelines; eight guidelines did not provide any red flags for fracture. Older age, trauma and osteoporosis were the first red flags endorsed; being endorsed in the 1994 US guideline[10]; non-mechanical pain, thoracic pain,[82] deformity[31] and use of steroids[84] were endorsed in 1996; in 1997, night pain[56] was endorsed as a red flag. Some red flags emerged in the 2000s: female gender[65] and constant pain[37] in 2000; previous fracture[22] in 2003. The red flags most commonly referred to in the guidelines were: older age (the cut-off varied between 50 and over 70 years) (n=62/78, 78%), use of steroids (n=53/78, 67%), trauma (n=47/78, 59%) and osteoporosis (n=35/78, 44%). The red flags that were less frequently endorsed were night pain (n=3, 4%) and previous fracture (n=4, 5%). Only five of the included guidelines (6%) recommended combinations of red flags. Comparing the guidelines, there is only fair overall consistency among them (kappa Fleiss coefficient=0.317). Table 1 shows the evolution of guideline-endorsed red flags in patients presenting with LBP.

Table 1 also shows information on provision of diagnostic accuracy data by the guidelines to support endorsed red flags. Among the 78 guidelines included, only 9 (11%) substantiated recommended red flags by citation to a primary diagnostic accuracy study/diagnostic review and 9 (11%) provided diagnostic accuracy data (eg, sensitivity, specificity, likelihood ratio (LR)+, LR−).

Recommendations on diagnostic procedures in the guidelines
Table 2 describes recommendations from the 30 guidelines on further diagnostic workup with cases of suspected vertebral fracture. Of these, 28 guidelines were consistent with the recommendations that medical history and physical examination should focus on the identification of red flags. In total, 60% (n=18) of the clinical guidelines recommended plain radiographs; 33% (n=10) recommended MRI; 30% (n=9) recommended CT; and 13% (n=4) recommended bone scan.

DISCUSSION
Statement of principal findings
We located 78 guidelines endorsing a total of 12 red flags. The number of red flags endorsed in guidelines to screen for fracture has risen over time. In 1994 there were only three red flags endorsed and this rose to 11 by 2003. Beyond 2003, no additional red flags were suggested by guidelines. Only 30 clinical guidelines provided recommendations regarding further diagnostic workup in the presence of red flags, and of these, 60% recommended plain radiographs, 33% recommended MRI, 30% recommended CT and 13% recommended bone scan. Nevertheless, most guidelines do not endorse the same set of red flags (agreement between them was only fair; kappa Fleiss

coefficient=0.32) and most recommendations are not supported by research or accompanied by diagnostic accuracy data. Only 11% of the guidelines substantiated recommendations by citation to a primary diagnostic study or diagnostic review, and only 11% provided diagnostic accuracy data.

Strengths and weaknesses of the study
A strength of this review was that, to our knowledge, no previous studies have described the evolution of guideline-endorsed red flags for fracture in patients presenting with LBP and evaluated the consistency between them. Another strength of this review was that we searched seven electronic databases with a broad search strategy and without language restrictions. We ensured transparency of the methods by prospectively registering our study protocol on PROSPERO. A weakness of this review was that potential components such as type of sport and mode of injury have not been identified in guidelines for fracture in LBP. Another limitation of this review was that clinical guidelines are sometimes published in local databases and, as a consequence, some may have been missed in our searches.

Strengths and weaknesses in relation to other studies
Our results are in agreement with previous studies[4 5 85 86] which have concluded that the current evidence for the use of most red flags is inconsistent. The Cochrane review[4] of red flags for fracture only endorses 3 of the 12 red flags included in this review ('prolonged use of corticosteroids' (LR+ 3.97–48.50), 'significant trauma' (LR+ 3.42–12.85) and 'older age' (LR+ 3.69–9.39)), but also noted that estimates of LRs were imprecise. The only red flag that appeared informative in the Cochrane review ('presence of a contusion or abrasion' (LR+ 31.09)) was absent from all guidelines. In addition, most guidelines recommend further investigation when any red flag is present, a recommendation that has been criticised because of the high risk of false positive findings.[85 86] The high prevalence of false positives is well illustrated in a longitudinal study[87] of 482 patients attending a back pain triage clinic; a total of 213 out of 482 had night pain, but none were diagnosed with a serious pathology. Possibly, part of the problem is considering a single red flag in isolation.

Previous studies have shown that a more useful approach is to rely on a combination of red flags to identify individuals who require further diagnostic workup. Downie and colleagues[88] synthesised two Cochrane diagnostic systematic reviews and noted that the presence of multiple red flags increased the probability of fracture to between 42% and 90%. Another study[3] with 1172 patients presenting with LBP showed that the probability of fracture increased from 4% (pretest) to 90% (95% CI 34% to 99%) with the presence of three red flags. However, we found that only 7 of the 78 guidelines included in this review recommended a combination of red flags.

Interpretation of the study: possible explanations and implications for clinicians and policymakers
Our results found that several red flags endorsed by guidelines have poor or untested diagnostic accuracy. Based on that, we would advise clinicians to be cautious in using red flags as alerting features for those patients who require further diagnostic workup. There are important consequences if red flags are uncritically applied in clinical care. Adopting red flags that have high false positive rates (eg, night pain)[87] will encourage unnecessary imaging. The use of red flags that are uninformative (eg, female gender, age >50) may mean that patients with fractures could be missed.

Table 1 Evolution of guideline-endorsed red flags

| Country, year | Red flags | | | | Pain | | | | | | | |
	Older age	Trauma	Use of steroids	Osteoporosis	Thoracic	Night	Non-mechanical	Constant	Female gender	Deformity	Previous fracture	Combination of flags
Canada, 1987[12]*												
USA, 1994[10]	✓	✓		✓								✓
USA, 1995[72]	✓	✓		✓								✓
Netherlands, 1996[84]†	✓		✓									
USA, 1996[73]*												
UK, 1996[67]†	✓	✓	✓		✓		✓			✓		
Israel, 1996[49]‡												
New Zealand, 1997[56]†	✓	✓	✓			✓						
Germany, 1997[42]†		✓	✓									
Denmark, 1998[33]†	✓	✓		✓								
Switzerland, 1998[90]†	✓	✓	✓									
Australia, 1999[23]	✓	✓	✓									
Denmark, 1999[34]*												
Finland, 1999[38]	✓	✓	✓	✓						✓		
France, 2000[61]	✓	✓	✓									
UK, 2000[68]	✓	✓		✓				✓		✓		
Sweden, 2000[66]†	✓	✓		✓								
USA, 2001[74]*	✓											
Norway, 2002[57]†	✓	✓	✓	✓	✓			✓				
Netherlands, 2003[36]†	✓	✓	✓	✓								
Australia, 2003[32]	✓	✓	✓	✓							✓	✓
Denmark, 2003[35]†	✓	✓	✓	✓								
Germany, 2004[43]†	✓	✓	✓				✓					
New Zealand, 2004[55]†	✓	✓	✓			✓						
Netherlands, 2004[91]†	✓	✓	✓	✓								
Spain, 2005[62]†	✓	✓	✓	✓					✓			
Belgium, 2006[25]†	✓	✓	✓		✓		✓					
USA, 2006[75]	✓	✓	✓				✓	✓				
Europe, 2006[37]†	✓	✓	✓		✓			✓				
Italy, 2006[48]	✓	✓	✓	✓		✓			✓		✓	
Canada, 2007[27]†	✓	✓	✓	✓		✓						
USA, 2007[76]	✓		✓	✓								
Austria, 2007[20]†	✓	✓	✓	✓								
Spain, 2007[64]	✓	✓	✓	✓								
Norway, 2007[58]†	✓	✓	✓	✓	✓			✓	✓			
Canada, 2008[28]	✓		✓						✓		✓	
USA, 2008[76]§	✓		✓									✓
¶UK, 2008[69]												
USA, 2009[77]												
Korea, 2009[50]*												
USA, 2010[78]	✓	✓	✓	✓					✓	✓		
Netherlands, 2010[52]	✓	✓	✓						✓			

Continued

Table 1 Continued

Country, year	Red flags				Pain				Female gender	Deformity	Previous fracture	Combination of flags
	Older age	Trauma	Use of steroids	Osteoporosis	Thoracic	Night	Non-mechanical	Constant				
Norway, 2010[45]†	✓		✓	✓	✓			✓				
Germany, 2010[44]	✓	✓	✓	✓								
Mexico, 2011[51]†	✓	✓	✓		✓					✓		
Austria, 2011[21]†	✓	✓	✓	✓								
Canada, 2011[35]§	✓	✓	✓							✓		
USA, 2011[79]	✓		✓	✓								
Philippines, 2008[59]†	✓	✓	✓		✓		✓					
Germany, 2011[46]	✓	✓	✓	✓								
USA, 2012[80]§	✓	✓	✓						✓			
Spain, 2012[63]†	✓	✓	✓	✓	✓					✓		
China, 2013[31]	✓	✓	✓	✓		✓						✓
Brazil, 2013[26]*	✓	✓										
USA, 2013[81]†	✓	✓	✓	✓								
Netherlands, 2013[53]	✓	✓	✓				✓				✓	
UK, 2013[70]*	✓									✓		
Germany, 2013[92]	✓	✓	✓	✓								
Scotland, 2013[60]			✓									
USA, 2014[47]		✓							✓			
Finland, 2008[39]†	✓	✓	✓	✓								
Germany, 2014[93]	✓	✓		✓								
Croatia, 2013[32]‡		✓										
USA, 2015[83]	✓	✓		✓					✓			
South Africa, 2015[19]	✓	✓		✓								
Canada, 2015[30]§	✓	✓		✓								
Finland, 2015[40]†	✓	✓		✓					✓	✓		
Netherlands, 2015[54]*												✓
Spain, 2015[61]*									✓			
Australia, 2016[24]†	✓	✓		✓					✓			✓
USA, 2016[82]	✓	✓		✓					✓			
Malaysia, accessed in 2017[18]†	✓	✓										
UK, 2016[71]*												✓
Germany, 2017[17]†	✓	✓		✓								
Denmark, 2017[14]*									✓			
USA, 2017[15]*				✓								
Belgium, 2017[13]	✓	✓		✓	✓				✓			
Finland, 2017[16]†	✓			✓					✓			

Cells shaded in grey correspond to red flag endorsed by citation to a primary diagnostic accuracy study or diagnostic review.
*There is no recommendation for red flags for fracture.
†Covers all serious pathologies, not fracture in isolation.
‡Translation was not possible.
§Guidelines that provided diagnostic accuracy data, for example, sensitivity/specificity, likelihood ratios.
¶UK 2009 did not endorse red flags for fracture but offer 'Osteoporotic fractures typically affect older people (women more than men) and those with other chronic illnesses; particularly if they have used long term oral steroids.'

Table 2 Guideline recommendations on diagnostic workup to confirm vertebral fracture

Country, year	Medical history/ physical examination	Recommended investigation in presence of red flags				
		Plain X-ray	Bone scan	CT	MRI	Other recommendation
USA, 1994[10]*	✓	✓	✓	✓	✓	
USA, 1995[72]*	✓	✓	✓	✓	✓	
Australia, 1999[23]	✓	✓	✓			
France, 2000[41]	✓					
Australia, 2003[22]	✓					✓†
USA, 2006[75]	✓					
Italy, 2006[48]		✓				
USA, 2007[6]	✓	✓				
Spain, 2007[64]	✓	✓				
Canada, 2008[28]	✓	✓			✓	
USA, 2008[76]	✓				✓	
UK, 2008	✓				✓	
USA, 2010[78]	✓	✓	✓	✓	✓	
Netherlands, 2010[52]	✓					
Germany, 2010[44]	✓	✓				
Canada, 2011[29]	✓	✓		✓	✓	
USA, 2011[79]	✓	✓				
Germany, 2012[46]	✓	✓				
USA, 2012[80]‡						
China, 2013[31]	✓					
Netherlands, 2013[53]	✓					✓
Germany, 2013[92]	✓	✓				
Scotland, 2013[60]	✓					
USA, 2014[47]	✓	✓		✓	✓	
Germany, 2014[93]	✓					
Canada, 2015[30]				✓		
USA, 2014[83]		✓		✓	✓	
South Africa, 2015[19]	✓					
USA, 2016[82]	✓	✓		✓		
Belgium, 2017[13]✓		✓		✓	✓	

*If after 10 days, fracture still suspected, or multiple sites of pain, consider bone scan and consultation before defining anatomy with CT.
†Appropriate investigations are indicated in cases of acute low back pain when alerting features ('red flags') of serious conditions are present.
‡The therapist should inform the patient of this, and advise them to contact their family doctor.

For exercise medicine clinicians, the inconsistency between guidelines also creates uncertainty for managing these patients.[25 26] With the growing popularity of masters sports, sports physicians will increasingly see patients who are older and a subset of the red flags identified will be applicable to them (specifically: 'older age', 'trauma', 'use of steroids', 'female gender', 'previous fracture' and a 'combination of flags'). And finally, our findings suggest that guideline developers need to pay more attention to diagnostic research when framing recommendations for the use of red flags and that many existing guidelines need urgent revision.

Unanswered questions and future research
The inconsistency between guidelines for red flags creates uncertainty over their application and utility within clinical practice.[4 85 86 89] Some commentators suggest that screening for red flags is a popular idea that did not work and should be removed from guidelines.[85 86 89] Our review supports the use of red flags with caution as the majority of them are based on evidence from single studies.[4] Therefore, an important extension of our research would be to evaluate combinations of red flags. Few studies[88 89] have reported on the accuracy of combinations of factors, and none have been validated in independent samples. Furthermore, our review showed that most guidelines contain little information on the diagnostic accuracy of the red flags. This lack of strong evidence to support the diagnostic capacity of the red flags is concerning and highlights the need for more high-quality diagnostic research on the topic.

What is already known

▶ Clinical practice guidelines endorse red flags as the ideal method to identify patients with a higher likelihood of vertebral fracture.
▶ The total number of red flags endorsed in clinical guidelines is large.

What are the new findings

▶ The number of red flags endorsed in guidelines to screen for fracture has risen over time.
▶ Most guidelines do not endorse the same set of red flags.
▶ Most red flags presented in guidelines are not supported by research or accompanied by diagnostic accuracy data.

CONCLUSION
The number of red flags endorsed in guidelines to screen for fracture has risen over time. Most guidelines do not endorse the same set of red flags, with the majority of recommendations not

supported by research or accompanied by diagnostic accuracy data.

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