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Acute respiratory illness and return to sport: a systematic review and meta-analysis by a subgroup of the IOC consensus on 'acute respiratory illness in the athlete'

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ABSTRACT

Objective To determine the days until return to sport (RTS) after acute respiratory illness (ARill), frequency of time loss after ARill resulting in >1 day lost from training/competition, and symptom duration (days) of ARill in athletes.

Design Systematic review and meta-analysis.

Data sources PubMed, EBSCOhost, Web of Science, January 1990–July 2020.

Eligibility criteria Original research articles published in English on athletes/military recruits (15–65 years) with symptoms/diagnosis of an ARill and reporting any of the following: days until RTS after ARill, frequency (%) of time loss >1 day after ARill or symptom duration (days) of ARill.

Results 767 articles were identified; 54 were included (n=31 065 athletes). 4 studies reported days until RTS (range: 0–8.5 days). Frequency (%) of time loss >1 day after ARill was 20.4% (95% CI 15.3% to 25.4%). The mean symptom duration for all ARill was 7.1 days (95% CI 6.2 to 8.0). Results were similar between subgroups: pathological classification (acute respiratory infection (ARinf) vs undiagnosed ARill), anatomical classification (upper vs general ARill) or diagnostic method of ARinf (symptoms, physical examination, special investigations identifying pathogens).

Conclusions In 80% of ARill in athletes, no days were lost from training/competition. The mean duration of ARill symptoms in athletes was 7 days. Outcomes were not influenced by pathological or anatomical classification of ARill, or in ARinf diagnosed by various methods. Current data are limited, and future studies with standardised approaches to definitions, diagnostic methods and classifications of ARill are needed to obtain detailed clinical, laboratory and specific pathogen data to inform RTS.

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INTRODUCTION

The International Olympic Committee is committed to protecting the health of the athlete.[1] Acute illness threatens athlete health and well-being, and can lead to interruption of training, withdrawal from competition and financial loss for professional athletes.[2 3] An acute illness causing delayed time to return to sport (RTS) (training and/or competition) is referred to as a 'time loss' illness.[4]

In athletes, the respiratory tract accounts for ~50% of all acute illness episodes,[5–9] and the majority of acute respiratory illnesses (ARill) in athletes are acute respiratory infections (ARinf).[6–10] The annual incidence of ARinf in the general adult population is about 2–3 episodes per year.[11] Physically active individuals typically have a lower incidence of ARinf compared with sedentary individuals, but competitive athletes may be more susceptible to ARinf, especially during periods of intense training and competition (J-shaped curve).[12] Elite athletes accustomed to very high training and competition loads may be less prone to ARinf (S-shaped curve).[13–15]

The sport and exercise medicine (SEM) physician is responsible for guiding the athlete with recent ARill to full and safe sports participation in the shortest possible time, while minimising the risk of potential medical complications. Evidence-based clinical guidelines to assist the SEM physician to decide on RTS after ARinf are lacking. RTS can be defined as 'the time (days after the onset of an injury or illness), when the ill or injured athlete can return to preillness/injury level of activity and full training and competitive sports activities, with no limitation in performance or additional risk of medical complications'.[16 17]

Symptoms of an acute illness are widely used in RTS decision making, specifically for ARinf.[18–20] Historically, athletes with localised symptoms of ARinf above the neck (eg, sore throat, rhinorrhoea or nasal congestion) were advised that exercise can resume at a low intensity for a short duration, and if exercise is well tolerated, training can continue. If symptoms are below the neck (eg, fever, myalgia or cough), the athlete was advised to rest until symptoms have resolved. These guidelines are referred to as the 'neck check'.[19] There is no scientific evidence for these guidelines and the validity of the 'neck check' as a guide for RTS has been challenged.[21] Despite the lack of data, the presence and nature (type) of regional/systemic symptoms is still a key component of most clinical decision-making guidelines for RTS following ARinf in athletes.[22–24]

Several studies report the frequency (%) of ARill that result in interruption from training/competition for >1 day (% of time loss ARill), while other studies report the duration of symptoms (days) of ARill. The frequency (%) of time loss ARill is defined as the number of ARill that resulted in time

loss >1 day from training or competition (numerator) divided by all the ARill (denominator), expressed as a %. Few studies report the actual days until RTS following ARill in athletes. Data from all these studies have not been reviewed systematically.

A systematic review with a meta-analysis was undertaken to determine the effects of ARill on RTS in athletes. Specific outcomes were days to RTS, frequency (%) of time loss ARill (ARill resulting in interruption of training/competition >1 day), and the mean duration of symptoms (days) of ARill. We also sought to determine outcomes in subgroups of ARill in athletes, based on the method used for the diagnosis of ARill, pathology (ARinf vs undiagnosed ARill), and predominant anatomical region affected [upper vs lower respiratory tract or general (upper/lower)]. The impact of ARill on other training/competition variables was also explored.

METHODS

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses[25] guidelines were used.

Study selection and eligibility criteria

Articles that fulfilled the following criteria were included:

1. Male or female participants (15–65 years), athletes at any level (recreational to elite), or military recruits engaged in training.
2. Participants with a diagnosis of ARinf (suspected or confirmed) or a mixed ARill (infective and non-infective).
3. Studies reporting any of the following variables: days lost to training/competition or RTS following an ARill, % ARill's in athletes resulting in time loss >1 day lost from training or competition (time loss ARill), the duration of symptoms of ARill or the time to recovery from ARill (days).
4. Original research journal articles.
5. Full-text articles published in English between 1 January 1990 and 31 July 2020.

Articles in non-human studies, those that reported chronic respiratory illness (including malignancy) or only non-infective ARill (eg, allergic rhinitis or asthma), review articles, expert opinions, position statements, single case-studies, conference abstracts, book chapters and commentaries were excluded.

Search strategy

PubMed, EBSCOhost and Web of Science (Core Collection) databases were searched for articles. Search terms were combined in three search strings of key terms relating to (1) ARill, (2) athletes/active individuals and (3) RTS, joined with 'AND'. The terms within the strings were joined by 'OR', and those not deemed relevant to the study question were excluded by using 'NOT' (online supplemental file 1). Search results were combined, and duplicate articles removed. Article screening and selection was conducted with the online tool CADIMA (V.2.2.1).[26] Two independent reviewers (CS and DBP) screened all articles, first by title and abstract, and then by full text. References and reviews were searched manually to identify additional articles. Disagreement among reviewers were resolved by consensus. The final selection of articles was cross-checked by two additional reviewers (MS and NS).

Data extraction

We used the term 'athletes' to combine diverse levels of sports participation and included military recruits (trainees regarded as active individuals). Participant demographics and details of data extracted for analyses from each article are summarised in online supplemental tables A and B, respectively. The following data were extracted: participants (number, age, sex), study design, type of sport or sporting event/military, level of participation (recreational/amateur/military or elite/professional/international/national), length of study surveillance, method used for the diagnosis of ARill and classification of ARill (pathological/anatomical classification), number days lost (>1) from training/competition due to ARill, duration of ARill symptoms, and the possible impact of ARill on training/competition variables. In randomised control studies, only results from control group were extracted.

Definitions and classification of subgroups of ARill

Pathological classification

Methods to diagnose an ARill, and specifically an ARinf vary substantially and include typically symptoms, findings on clinical examination and/or special investigations to identify a specific pathogen. We developed a classification system to categorise the methods to diagnose ARill in each study as follows: (1) self-reported symptoms of ARill only, (2) self-reported symptoms combined with an algorithm at least partially validated for ARinf, (3) self-reported symptoms of an ARinf reviewed by a physician, but without clinical or laboratory evaluation, (4) clinical diagnosis of an ARinf by a physician, based on history and clinical examination and (5) clinical diagnosis of ARinf by a physician confirmed by laboratory investigation to identify a specific pathogen(s) as follows: PCR testing on specimen(s), culture of an organism(s) from specimen(s) or serology (eg, rise in antibody titres). Data were extracted for each study and agreed by consensus (CS, DBP, NS and MS). Once studies were classified by the five methods of diagnosis, all ARill studies were included in one of the following main and subgroups of ARill, based on a pathological classification (table 1).

Anatomical classification

ARill (including ARinf) frequently present with both upper and lower respiratory tract symptoms/signs, and it is not always possible to clearly distinguish between these main anatomical regions when classifying ARill. A limitation of this anatomical classification is that several pathogens that cause predominantly upper ARinf can, in some cases, present with lower respiratory and/or systemic symptoms. In most studies of ARill in athletes, there is a clear distinction between upper and lower ARill, and upper ARinf (suspected or confirmed) is the most common acute illness in athletes.[6–10] Thus, from a clinical/pragmatic point of view we deemed it relevant to include an anatomical classification of ARill in the review. We classified studies into the following subgroups, based on the predominant anatomical region affected:

- Upper (ARill or ARinf): Studies where the predominant symptoms, signs, or confirmed pathology was mainly related to the upper respiratory tract (ie, above the larynx), or if the study specifically referred to athletes with upper ARill or ARinf. A few studies referred to ARinf with non-specific terms such as 'influenza', 'influenza symptoms', 'common cold', 'symptoms suggestive of influenza', 'influenza symptoms' or 'influenza like'. Studies referring to these clinical syndromes were also included in this broad anatomical classification because they are caused by pathogens that all present with predominantly upper respiratory tract symptoms.[27–30] Notably, this includes the influenza viruses, which predominantly present with upper respiratory tract

Table 1 Pathological classification (main and subgroups) of acute respiratory illness (ARill) by diagnostic method

Pathological classification			
Main group	**Subgroup**	**Methods to diagnose ARill**	**Description**
Undiagnosed ARill		► Self-reported symptoms of ARill only ► Self-reported symptoms combined with an algorithm at least partially validated for ARill ► Self-reported symptoms of an ARill reviewed by a physician, but without clinical or laboratory evaluation ► Clinical diagnosis of an ARill by a physician, based on history and clinical examination	► General symptoms of an ARill where the pathology could not be attributed specifically to an infection ► ARill studies could include illnesses that are due to either infective or non-infective causes but were not specified in the study design
ARinf	Suspected acute respiratory tract infection (ARinf)	► Self-reported symptoms combined with an algorithm at least partially validated for ARinf ► Self-reported symptoms of an ARinf reviewed by a physician, but without clinical or laboratory evaluation ► Clinical diagnosis of an ARinf by a physician, based on history and clinical examination	► General symptoms and/or physical signs suggestive of an ARinf, but where the pathology of an infection was not confirmed ► The validated questionnaires that were used including the Wisconsin Upper Respiratory Symptom Survey-21,[93] the Jackson Cold Scale,[94] or other questionnaires in which the severity of the symptoms were scored to provide a quantitative assessment,[35 95]
	Confirmed ARinf	► Clinical diagnosis of ARinf by a physician and confirmed by laboratory investigation to identify a specific pathogen as follows: PCR testing on specimen(s), culture of an organism from specimen(s), or serology (eg, rise in antibody titres)	► In some cases, a diagnosis of an ARinf caused by a specific pathogen can also be regarded as confirmed when diagnostic clinical features with a high sensitivity and specificity are present in suspected cases ► In such case there is also a high pretest probability of an ARinf (eg, a history and typical rash in an athlete where there is a confirmed viral outbreak in a travelling team or during an epidemic/pandemic)

ARinf, acute respiratory infection.

symptoms[31] and are listed as a cause of upper respiratory tract infections.[27–29]

- Lower (ARill or ARinf): Studies where the predominant symptoms or signs were below the larynx (including chest symptoms that is, cough, chest pain), or if a confirmed diagnosis specifically referred to athletes with mainly lower respiratory illness (tracheal, bronchial or lung pathology, eg, pneumonia).
- General (upper/lower) (ARill or ARinf): Studies where there were no data to clearly distinguish between predominantly upper/lower respiratory ARill. These studies could include upper, lower or both.

Quality assessment and risk of bias

The Downs and Black tool[32] was modified by removing questions pertaining to randomised controlled trials as this review only included studies using participants and outcomes. A score out of 13 (online supplemental file 2) was used to determine the quality of articles. The tool consisted of items as follow: reporting, external validity, internal validity (bias and selection bias). Each item was scored as 'yes' (score=1), 'no' (score=0) or 'undetermined' (score=0). Two reviewers (CS, DP) independently scored articles, and after discussions agreed on the final score for each article by consensus (online supplemental table C). The level of evidence was determined using the Oxford Centre for Evidence Based Medicine (2009)[33] (online supplemental table C).

Outcome measures

There were four outcome measures as follows:

Days until RTS after an ARill

The number of days to RTS after an ARill was taken as the reported days lost in training/competition due to the ARill.

Frequency (%) of time loss ARill

Another outcome variable was the frequency (%) of ARill in athletes resulting in time loss >1 day from training/competition (time loss ARill). The frequency (%) of time loss ARill is defined as the number of ARill that resulted in time loss >1 day from training or competition (numerator) divided by all the ARill (denominator), expressed as a %. This variable is reported for all ARill and in subgroups as follows: pathological classification (suspected ARinf vs undiagnosed ARill), and anatomical classification (upper ARill/ARinf vs general (upper/lower) ARill).

Duration of symptoms of ARill (days)

The mean duration of symptoms (days) of ARill in athletes is reported in the following subgroups: pathological classification (suspected ARinf vs confirmed ARinf vs undiagnosed ARill), and methods to diagnose ARinf (physician diagnosed with confirmed PCR/special investigation(s) vs physician diagnosis by history and clinical examination vs self-reported symptoms with algorithm). In studies reporting a specific causative pathogen for ARinf, the duration of symptoms for the common pathogens is reported (where available).

The effect of ARill on other training/competition variables

Studies reporting on the effect of an ARill on other training/competition variables were also reviewed. Variables included % of ARill resulting in training modification for example, training reduction/discontinuation and illness burden of ARill (illness episode resulting in the inability of player to participate fully in training/competition).[34]

Data synthesis and statistical analysis

Qualitative synthesis was performed on all 54 included articles that met the criteria for the outcome variables: days to RTS, frequency of time loss ARill, and duration of ARill symptoms. Qualitative synthesis was also performed on other training/competition variables. The frequency (%) of time loss ARill and mean duration of symptoms (days) of ARill were estimated using a DerSimonian-Laird Binary random effects model to account for heterogeneity in the cohorts (eg, differences in method of diagnosis, level of athlete) and weighting of studies. Heterogeneity was measured using I^2 statistics. For frequency, analyses of

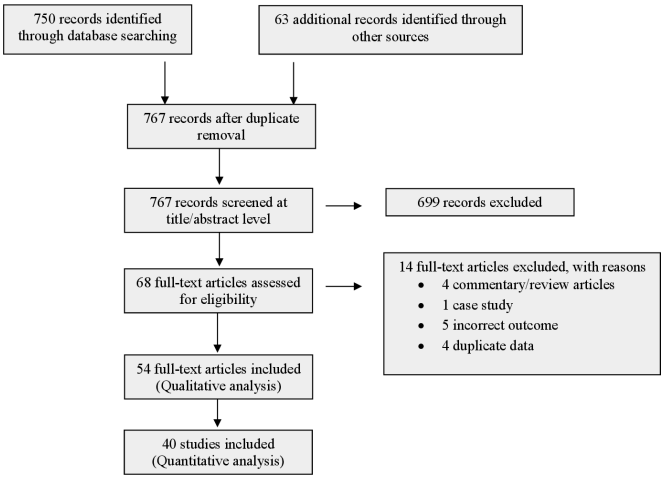

Figure 1 Study selection flow diagram.

the subcategories of pathological and anatomical classifications of ARill were performed. For duration of symptoms, subgroup analyses for pathological classification and by methods to diagnose ARinf were performed. Differences between subgroups were determined by comparing 95% CIs. Forest plots illustrate the results. All meta-analyses were conducted using Open Meta-Analyst. Publication bias statistics including Egger tests and funnel plots for each analysis are presented (online supplemental file 3) and were analysed using ProMeta V.3. A significance level of 0.05 was accepted, and all statistical tests were two tailed.

RESULTS

Study selection

Electronic database searches identified 767 articles. After duplicates/non-eligible articles were excluded, 68 remained and 54 met the inclusion criteria for analysis of data. Reasons for exclusion at each stage of the selection process are outlined (figure 1).

Study characteristics

Data were extracted from the 54 articles[8 9 34–85] (online supplemental table A). These studies included 31 065 athletes (including military recruits), 10 706 days of surveillance, and a sex distribution of 67% males and 33% females. No articles specifically reported the days until RTS after ARill. Four studies reporting the number of days lost in training/competition due to ARill were included in the review, but not the meta-analysis given the small number and heterogeneity in reporting of the results. Eleven articles were included in the analysis of the frequency of time loss ARill, and 29 articles were included in the quantitative synthesis of duration of symptoms of ARill.

Level of evidence and quality assessment

The Oxford Level of Evidence for articles included in this review ranged from 1b to 3b (online supplemental table C). The modified Downs and Black quality assessment of the articles resulted in a total score ranging from a minimum score of 7 (fair) to the highest score of 13 (excellent) (online supplemental table C).

Days until RTS

The number of training/competition days lost due to ARill as a proxy for days until RTS was determined from data in four articles.[42 56 58 68] Training/competition days lost due to upper ARinf varied as follows: 1.7±2.3 days[56] and 3.5±5.0 days of training lost.[68] Only one study[58] reported the training/competition days lost due to lower ARinf (mean of 2.5 days per illness episode). In one study,[42] days lost were reported in two subgroups: upper ARinf and ARinf with multiple systemic symptoms (including muscle or joint pain, vomiting, diarrhoea and productive cough). In the upper ARinf subgroup, 0 days were lost, while in the systemic ARinf subgroup, up to 7 training/competition days were lost.[42] In two other studies,[72 73] total training/competition days lost due to ARill, accounted for 60%–63% of total days with all illnesses.

Frequency (%) of time loss ARill

There were 11 unique studies[8 9 36 41–45 58 62 73] reporting the frequency of time loss ARill. These studies included 18 730 participants over 1966 surveillance days. The estimated pooled % (95% CI) of all time loss ARill (>1 day) was 20.4% (15.3% to 25.4%) (I^2=69.6%) (figure 2).

The estimated pooled % of time loss ARill was similar for suspected ARinf (17.9%; 11.8–23.9) and undiagnosed ARill (21.6%; 13.6–29.7) (I^2=69.6%) as depicted in figure 3.

The number of studies distinguishing between upper and lower ARill were too few to include in the meta-analysis on % of time loss ARill. The estimated pooled % time loss ARill was similar for studies referring specifically to upper ARill (18.4%;

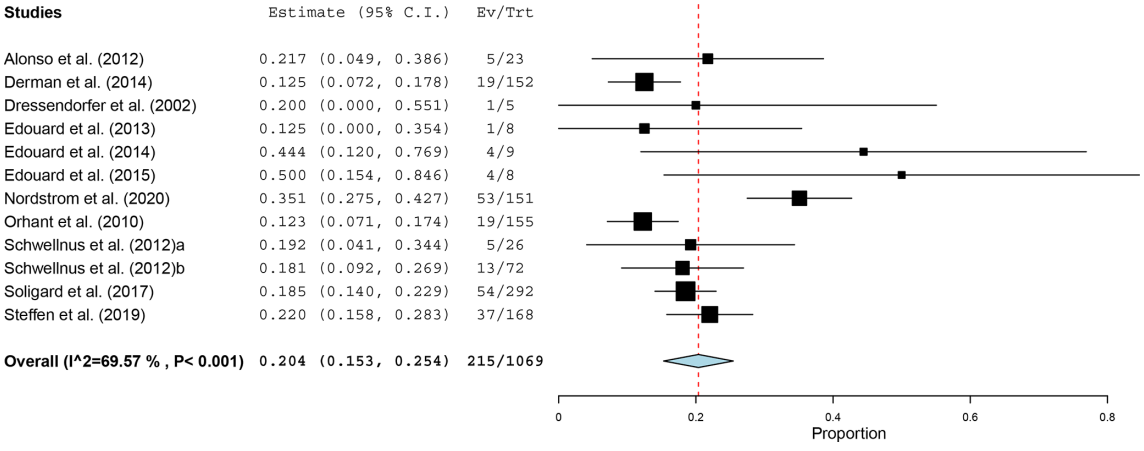

Figure 2 Frequency (%) of all time loss ARill (>1 day). The diamond shape represents the point estimate and CIs when an average is indicated for all the individual studies are combined. Proportions are reported as %. ARill, acute respiratory illness; Ev, event=number of time loss ARill, Trt, treatment=total number of ARill.

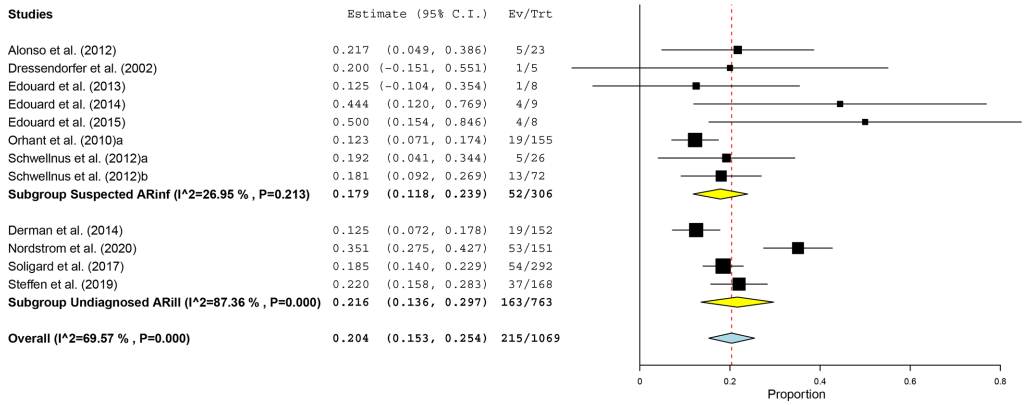

Figure 3 Frequency (%) of time loss acute respiratory illness (ARill) (>1 day) by pathological classification: suspected acute respiratory infection (ARinf), undiagnosed ARill. The diamond shape represents the point estimate and 95% CIs when an average is indicated for all the individual studies are combined. Proportions are reported as %. Ev, event=number of time loss ARill, Trt, treatment=total number of ARill.

10.7–26.1) when compared with studies where no distinction could be made based on the anatomical classification of ARill, that is, general (upper/lower) ARill (21.3%; 14.1–28.5) (I^2=72.3%). Studies in these two groups (upper vs general) were not combined and deemed mutually exclusive (online supplemental figure 1). There was no significant publication bias to note in the frequency analysis (online supplemental file 3).

Duration of symptoms (days) of ARill

There were 29 unique studies[35 37–39 46–57 59–61 63–71 82] that reported the duration of symptoms of ARill involving 1428 participants over 6212 surveillance days. Duration of symptoms in one study, could not be included in this analysis because of bias—as only participants with symptoms >72 hours (3 days) were included.[74] The estimated pooled mean (95% CI) duration of symptoms for all ARill was 7.1 (6.2 to 8.0) days.

The duration of symptoms in subgroups of ARill by pathological classification (undiagnosed ARill, suspected ARinf or confirmed ARinf) is shown in figure 4. In one study reporting ARinf, the population included both athletes and sedentary controls.[66] We included this study in the meta-analysis on symptom duration because the majority of ARinf (28/37=76%) were reported in athletes.

The estimated pooled mean (95% CI) duration of symptoms (days) of ARill of subgroups by pathological classification was similar for undiagnosed ARill (6.8: 4.8 to 8.7), suspected ARinf (7.0: 6.0 to 8.0) and confirmed ARinf (8.3: 6.2 to 10.3) (I^2=99.2%).

The duration of symptoms (days) of suspected ARinf (diagnosed by self-reported symptoms with algorithm and checklist) vs suspected ARinf (physician diagnosed by history and clinical examination) versus confirmed ARinf (physician diagnosis with pathology confirmed by PCR, culture or serology) are shown in figure 5.

The estimated pooled mean (95% CI) duration of symptoms (days) of ARinf by method of diagnosis was 7.2 days (6.3 to 8.2) and for individual subgroups were as follows: suspected ARinf diagnosed by self-reported symptoms with algorithm and checklist (6.7; 5.7 to 7.8), suspected ARinf diagnosed by a physician on history and clinical examination (8.0; 4.7 to 11.3) and ARinf confirmed by laboratory investigation(s) using PCR, culture or serology tests (8.3: 6.2 to 10.3) (I^2=99.3%).

The duration of symptoms in athletes with confirmed ARinf was only reported in three studies.[64 66 67] In two prospective studies over several months,[66 67] a pathogen could only be identified in ~30% of ARinf. In athletes with confirmed ARinf, symptom severity and functional impairment were most severe on day 3 and 4 of illness.[66] Rhinovirus was the most common pathogen in both studies. Time loss days were not reported in these two studies. In the third study[64] of 44 athletes participating in the Winter Olympic Games, 20 athletes presented with symptoms of the 'common cold'. A pathogen was identified in 75% of cases, and the most common pathogens causing ARinf were respiratory syncytial virus A (RSV A) followed by metapneumovirus with a mean duration of symptoms of 8.7 days and 4.0 days, respectively. Both these viruses appeared in clusters within a team travelling and living together during the Games. The next most common pathogens causing ARinf were coronaviruses 229E and OC43, each with a mean duration of symptoms of 13.5 and 18.0 days, respectively. In this study, one athlete lost time during a competition on 1 day due to an ARinf. There was significant publication bias to note in the symptom duration analysis (online supplemental file 3).

Other outcome measures

The effect of ARill on other training/competition variables

In six studies,[34 38 52 56 67 68] the effect of ARill on selected training/competition variables was reported but variables were not standardised. The main observations from these studies were as follows: 42%–70% of participants[52 56] reported that ARill negatively affected or impaired training, 14%–19% of athletes[38 67] reported reduced training volume or intensity after ARill, weekly training load was reduced by 24% in athletes[52] after ARill, training was modified in up to 50% of athletes[67] after ARill, up to 31% of elite athletes[67] ceased all training during the acute phase of their ARill, and in endurance athletes, training was reduced for 3.4±5.1 days.[68] In one study over a 4-year period, 3.2 absence days were recorded per 1000 player-days.[34]

DISCUSSION

There are several important outcomes of this systematic review and meta-analysis. The first observation is that accurate data detailing the actual number of days to RTS after ARill in athletes are very limited. Second, from the best available data,

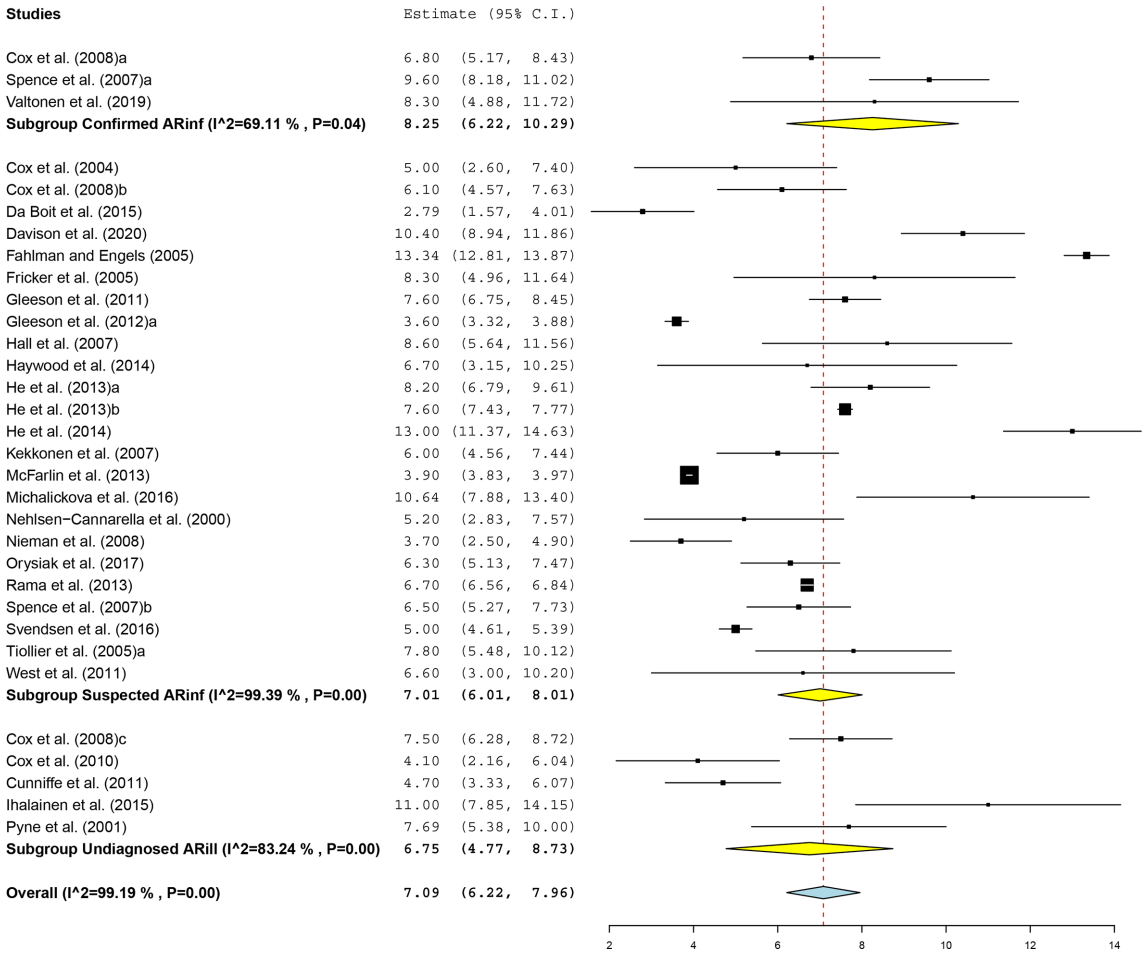

Figure 4 The duration of symptoms (days) of subgroups of acute respiratory illness (ARill) by pathological classification: undiagnosed ARill, suspected ARinf or confirmed acute respiratory infection (ARinf). The diamond shape represents the point estimate and 95% CIs when an average is indicated for all the individual studies are combined.

approximately one in five ARill in athletes result in time loss from training/competition. Third, the estimated pooled mean duration of symptoms of ARill in athletes is 7 days. Finally, for other outcome variables related to the effect of ARill on training/competition, data are very limited, but it appears that ARill negatively affects training.

Days until RTS after an ARill

Few studies report days lost due to ARill in athletes, duration, and types of symptoms, and the reason for time loss was not verified (due to the illness or on advice from medical or coaching staff not to train while ill). The number of training/competition days lost due to suspected upper ARinf was reported in only four studies, and varied between 0 and 8.5 days.[42 56 58 68] In only one study on lower ARinf, four episodes of illness resulted in a mean of 2.5 days lost per illness.[58] Limitations of these studies are that the causative pathogen was not confirmed and the severity of infection not reported. It is likely that days until RTS after an ARinf will depend on the causative pathogen and severity of illness, as some pathogens mostly cause mild disease affecting a localised area of the respiratory tract, while others are associated with regional/systemic effects, including multiorgan involvement (moderate to severe disease). This assertion is supported by data from two recent studies on return to training (sport) after ARinf in athletes.[86 87] Both these studies could not be included in the systematic review because they fell outside the time frame (dates) of the inclusion criteria. In the first of these studies days-until-return-to-play (sport) for subcategories of ARill were reported in rugby players over five seasons (102 738 player days). ARinf resulted in significantly more days to RTS per single illness compared with non-infective ARill ($p<0.001$) (days to RTS ratio: 10.4; 95% CI 4.3 to 25.3). Lower ARinf resulted in the highest number of days to RTS per single illness followed by influenza-like illness.[86] In a second study of 84 athletes with recent ARinf, athletes with confirmed COVID-19 (n=45) had more severe disease (greater number, more severe and more prolonged symptoms), and the median days until RTS was three times longer than the subgroup with other ARinf (30 days vs 10 days).[87] In summary, there are too few data to make firm conclusions or recommendations on days until RTS after ARill or ARinf. Limited data show that days until RTS after ARinf in athletes varied from 0 to 30 days and is likely dependent on multiple factors including the definition of RTS, type of sport, individual athlete factors (susceptibility to ARinf, presence of comorbidities, immune response), the specific pathogen and the severity of the ARinf by pathology (localised upper vs regional lower ARinf vs ARinf with multiorgan involvement). More studies are needed and in future we recommend accurate recording and reporting of days until RTS, general medical history including comorbidities, symptoms (type, duration and severity) and clinical signs, evidence of regional or systemic (multiorgan) involvement and laboratory confirmation of specific pathogens.

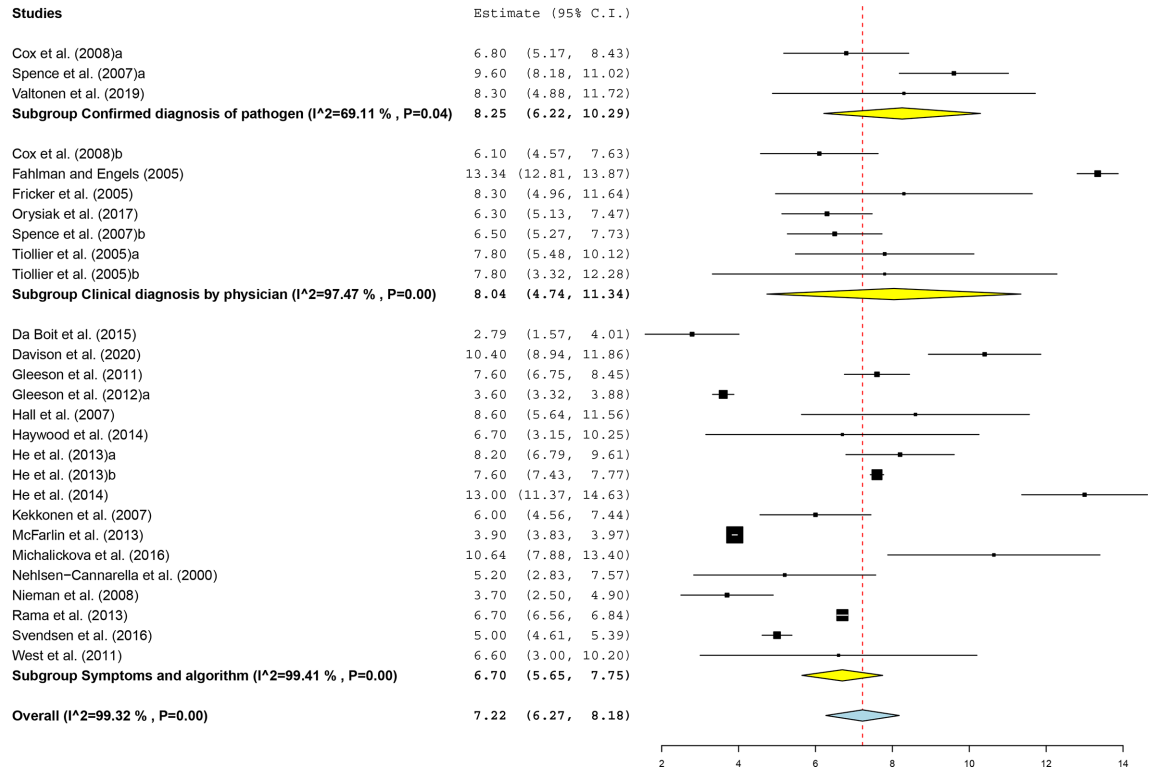

Figure 5 The duration of symptoms (days) of suspected and confirmed ARinf by method of diagnosis. The diamond shape represents the point estimate and 95% CIs when an average is indicated for all the individual studies are combined. ARinf, acute respiratory infection

Frequency (%) of time loss ARI's

There were significant limitations in the methods used in studies included in this analysis: in some studies, the decision on time loss was estimated by the physician at the time of initial presentation and therefore not confirmed, in most cases the specific diagnosis and the causative pathogen was not confirmed, and in several studies the predominant anatomical area (upper or lower respiratory tract) affected by the ARill/ARinf was not clear. The main observation is that the % of time loss ARill (illness episodes resulting in time loss >1 day from training or competition) is low (20%) and accordingly, by inference, that the large majority (ie, 80%) of ARill are not severe, because they are associated with no time loss. The % of time loss ARill was similar in subgroups based on the pathological and anatomical classification (suspected ARinf 17.9%; undiagnosed ARill 21.6%; upper ARill 18.4%; general (upper/lower) ARill 21.3%). Although the low % of time loss ARill indicates that most ARill are not severe, there are data from other studies that clearly show a significant burden (a measure of both severity and incidence) of acute illness in athletes, particularly ARill/ARinf.[40 73 88] Future studies in this area are needed, addressing these limitations.

Duration of symptoms of ARill (days)

The mean symptom duration of any ARill in athletes was 7 days. The duration of symptoms of ARill was similar in subgroups based on the method used to diagnose ARinf: suspected ARinf diagnosed by self-reported symptoms with algorithm and checklist (6.7 days), suspected ARinf diagnosed by a physician on history/clinical examination (8.0 days) and confirmed ARinf by laboratory investigations (8.3 days). The duration of symptoms results must be interpreted with caution due to the large heterogeneity in data (I^2 >99%). In two studies, the pathogen could only be identified in ~30% of ARinf[66 67] and the most common pathogen in these studies was rhinovirus. This is also the most common pathogen causing ARinf in the general population.[89 90] A study[64] on Finnish athletes participating in the 2018 Winter Olympic Games, identified the causative pathogen in 75% of cases of ARill. The pathogens occurred in clusters of athletes travelling and living together and this might differ from the normal distribution of pathogen occurrence. In one study,[67] participants with confirmed upper ARinf the duration of symptoms was 6.8±3.8 days. In suspected ARinf (PCR/culture negative but abnormal full blood count) the duration was 6.1±3.4 days, and in the ARill subgroup (negative PCR and normal laboratory investigations) the duration of symptoms was 7.5±3.4 days. In our review, data on duration of symptoms in athletes with confirmed ARinf were, therefore, limited to a few specific pathogens that cause ARinf: rhinovirus, RSV or coronaviruses (229E and OC43).[64 66 67]

A further limitation in all the studies documenting symptoms is that the duration of specific or regional symptoms of ARill were not reported. To distinguish between symptoms is important in clinical RTS decision making[87] for example, rhinorrhoea (localised) as the only symptom may not prevent RTS, while the presence of chest pain (regional) or generalised myalgia (systemic) might delay RTS. There are data from three recently published studies (not included in the systematic review as they were published outside the time frame) documenting symptom duration in athletes infected with the specific pathogen (SARS-CoV-2) causing COVID-19. In a case series of 90 athletes with confirmed COVID-19, 23% were asymptomatic and 77% mildly symptomatic. The mean (±SD) duration of symptoms in the mildly symptomatic subgroup was 9±14 days.[91] In another study, symptoms of 'mild' COVID-19 lasted <1 week in a group of 15 symptomatic football players.[92] In the third study, individual and regional symptom duration was reported in 84 athletes with

ARinf (45 confirmed COVID-19, and 30 suspected ARinf).[87] This is the first study to report duration of specific individual symptoms in athletes with ARinf. For all the athletes with ARinf (n=84) the duration (median days) of symptoms was: localised (nose and throat) symptoms (9–10 days), regional (chest and neck) symptoms (14 days), and systemic symptoms (11 days). In this study, specific individual symptoms, and a particular symptom cluster, were associated with more prolonged return to training.[87] This symptom cluster also included symptoms 'above the neck' such as headache and altered/loss sense of smell. These symptoms were, together with 'excessive fatigue' and 'fever/chills' significantly related to prolonged return to training. These early data do not support the 'neck check' as a clinical tool for RTS decision making. In future studies, we recommend accurate recording and reporting of the duration and severity of each specific symptom, regional symptoms (such as localised, regional or systemic symptoms), as well as the specific pathogen causing an ARinf.

The effect of ARill on other training/competition variables

The effect of ARill on training could not be analysed due to small number of studies with heterogeneous reporting of results. However, from six studies[34 38 52 56 67 68] reporting on the effects of ARill on training, it is evident that an ARill potentially has a negative impact on the ability to continue with a regular training schedule. The reason/s for modification/cessation of training was not recorded and may relate to several factors including: the direct consequence of the illness process, symptoms (type, duration, severity), decrease in exercise/ sporting performance directly due to the pathology of an acute infection, and advice by medical personnel or coaching staff to modify training intensity or not to train at all.

Strengths and limitations

To our knowledge, this is the first systematic review to determine the effects of ARill on RTS in athletes. We registered the review with PROSPERO and followed a systematic approach using an online tool, CADIMA. We developed a classification system, based on methods to diagnose an ARill, and performed analyses using a pathological and anatomical classification. We believe this approach provides a more comprehensive clinical picture to inform management strategies and RTS protocols. This review has clinical importance and relevance given that ARill is the most common illness affecting athletes resulting in time loss.

The main limitations of this systematic review are related to the studies that could be included. Although we included 54 studies, these were only in the English language, and did not include recently published studies related to the COVID-19 pandemic as these fell outside the predefined time frame of the review. There is also a potential risk of publication bias that we cannot account for. Egger's tests and funnel plots indicated a higher risk for publication bias for the duration of symptoms results, compared with the prevalence of time loss data. Among studies that were included, there was inconsistency in the definition and reporting of outcome variables and heterogeneity in athletic populations studied. There was no consensus on pathological and anatomical classification and definition of ARill subgroups. We could only include a small sample of studies that reported outcome variables in subgroups (eg, confirmed ARinf). We also acknowledge that one of our outcome variables, the duration of symptoms, does not necessarily predict days until RTS after an ARill. Finally, in most studies reporting the % of time loss ARill, this was an estimated time loss ARill that physicians recorded at the time of initial diagnosis, and not necessarily verified.

The risk of publication bias was difficult to assess given poorly defined outcome variables to measure RTS and the heterogeneous methods and reporting of results. The I^2 results (I^2 >99% for duration of symptom analyses), indicates the high level of heterogeneity, and although effort was made to categories ARill in subgroups, the results were still varied. The authors acknowledge the impact this might have on the research findings. A uniform approach to the definition of variables, methods to diagnose ARill, and classification of ARill in the athletic setting is needed. In this review, we propose such classifications. We believe this framework will assist both clinicians and researchers to better characterise variables to measure RTS and their time course. This approach is important for development of evidence-based guidelines on RTS in athletes with ARill.

SUMMARY AND CLINICAL IMPLICATIONS

Respiratory illnesses are common in athletes, but to make an accurate pathological diagnosis is challenging and costly. An ARill in the athlete raises two major clinical concerns; first, the athlete and coach are concerned about the athlete's ability to train and perform, and second, the SEM physician is required to provide safe RTS guidelines for an athlete after an ARill. Such guidelines should include monitoring athletes for potential medical complications after RTS and to limit possible transmission of infective agents to team members and staff. In this systematic review and meta-analysis, we identified that~20% of ARill resulted in more than 1 day of time loss from training. The mean duration of symptoms of ARill was 7 days, regardless of pathological (infective vs undiagnosed), anatomical (upper vs general)

What is already known?

⇒ Acute respiratory illness (ARill) is the most common illness affecting athletes, and these are mostly acute respiratory infections (ARinf).
⇒ ARill can result in time loss from training and competition.
⇒ Return to sport (RTS) criteria after ARill in athletes are largely based on broad criteria related to symptoms 'above' or 'below' the neck.

What are the new findings?

⇒ The actual days to RTS after ARill is under-researched and not well documented, with large individual athlete variation.
⇒ The majority of ARill do not result in >1 day of time loss from training or competition.
⇒ The mean symptom duration of an ARill in athletes is 7 days (both ARinf and other ARill of unknown cause).
⇒ ARinf and ARill can have a negative impact on ability to train and compete.
⇒ In clinical practice and for future studies, we recommend a standardised approach to the:
Classification and definition of ARill/ARinf.
Method of diagnosing ARill/ARinf.
Uniform documentation of both individual and regional symptoms of ARill/ARinf.
Accurate recording and reporting of outcome variables (RTS, physical signs, laboratory confirmation of pathogen(s) causing ARinf).

classification or subcategories based on the method used to diagnose ARinf. In a few studies where individual and regional symptoms were recorded and a specific pathogen causing the ARinf identified, there was considerable variability in the duration of symptoms of the ARinf. Moreover, there is early evidence that discrete symptoms that are both 'above' and 'below' the neck, as well as subgroups of ARinf are associated with more prolonged time to RTS. This individual variability highlights the fact that future studies are needed where days until RTS, individual and regional symptoms (and severity of symptoms) are accurately recorded and reported in athletes with a confirmed diagnosis of ARinf (pathogen identified). This information will refine future RTS clinical decision making, which we anticipate will be highly customised and based on the individual athlete response to infection from a specific pathogen that causes ARinf.

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