



# Acute and chronic effects of physical exercise on IgA and IgG levels and susceptibility to upper respiratory tract infections: a systematic review and meta-analysis

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## Abstract

This systematic review and meta-analysis aimed at evaluating acute and chronic effects of physical exercise on IgA and IgG levels, as well as its relationship with the susceptibility to develop upper respiratory tract infections (URTI). This systematic review and meta-analysis was conducted and reported in accordance with PRISMA statement. A systematic search of PubMed, Web of Science, and EMBASE was performed in July 2020. This systematic review and meta-analysis included studies in which participants performed acute exercise or chronic physical training and were subjected to analyses of URTI incidence and concentrations of IgA and IgG. The selected studies for systematic review were divided into the following three groups: (I) trials that evaluated the effects of acute exercise in sedentary subjects, (II) trials that evaluated the effects of acute exercise in athletes/trained individuals, and (III) trials that evaluated the effects of chronic physical training on the incidence of URTI, as well as on the levels of IgA and IgG. Acute exercise increases the IgA levels in trained subjects but does not affect its levels in untrained subjects. Such increase in IgA levels induced by acute exercise is greater in trained individual that performed ultramarathon. On the other hand, chronic physical training reduces IgA levels in both trained and untrained subjects, does not change IgA levels in non-military subjects, besides from not affecting IgG levels. The present systematic review and meta-analysis indicates that acute exercise positively influences IgA levels in trained individuals, being this effect pronounced when a strenuous exercise such as ultramarathon is executed. Chronic physical training, in turn, does not affect IgG levels.

**Keywords** Immunoglobulins · Immune system · Physical training · Respiratory tract

## Introduction

The COVID-19 pandemic is a global crisis of unprecedented scale in modern times [83]. The social distancing measures employed to curtail the impact of the infection are likely to reduce the amount of usual physical activity being performed by most individuals [2, 28]. However, regular practice of physical exercise is known to induce multiple benefits on physical and mental health, including the improvement of the body's ability to combat infections [2]. Thus, in addition to personal hygiene and social distancing, maintaining a healthy and active lifestyle can reduce the risk of COVID-19 infection [82]. A very important question emerges on the topic in this context, the regular practice of moderate physical exercise or even vigorous chronic physical training can increase the susceptibility to severe cases of COVID-19?

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The immune system protects the body against infectious diseases through the recognition, attack and destruction of foreign elements to the body, being the resistance to infections associated with the effectiveness of such immune actions [21]. Physical exercise influences the immune system in a dual way, as illustrated by the “J”-shaped curve that models the relationship between exercise and susceptibility to infection [50]. While several evidences indicate that moderate intensity physical training is associated with several benefits to the immune system, such as reduction of chronic inflammation and elevation of immunological markers related to various diseases [14, 22, 76], others indicate that high-intensity physical exercise can result in mucosal and cellular immunosuppression, associated with increased incidence of upper respiratory tract infections (URTI) [55, 65].

URTI episodes result from the invasion of microorganisms (i.e., viruses, bacteria or fungi), specifically in the airways above the glottis or vocal cords, that can manifest itself as tonsillitis, pharyngitis, laryngitis, sinusitis, otitis media, flu, and cold [25, 78]. Studies indicate that during periods of intense training and competitions, athletes may experience immunosuppression and, consequently, increased susceptibility to URTI [16, 27]. One body's immune response to exercise is the production and secretion of immunoglobulins, whose serum levels and secretion, especially the antigen-specific antibodies IgA and IgG, are associated with resistance to infection [54].

IgA is the most abundant antimicrobial protein that protects the mucosal surfaces [6], region where most infections are initiated [5, 32, 42, 49]. It is proposed that secretory IgA provides an immunological barrier by neutralizing and preventing viral pathogens from penetrating the body through the mucosal surfaces [32, 42, 49]. Based on the above mentioned, low concentrations of SIgA in athletes may in fact be associated with the increased susceptibility to URTI [23, 46, 49]. However, in sedentary individuals, moderate chronic exercise training has been shown to increase SIgA levels, which may have contributed to the apparent reduced susceptibility to URTI [23].

Immunoglobulin G (IgG) is the most common type of antibody found in blood circulation. It is also one of the most abundant proteins in the human serum, accounting for about 10–20% of all plasma proteins. IgG appears during the first and second immune responses by activating the complement system and macrophages [6, 80]. A recent study demonstrated that serum IgG levels were increased in pre-frailty elderly women after 12-weeks of aquatic moderate exercise [34]. Previous study also reported that acute moderate exercise, such as 45 min bout of walking, is associated with a transient rise in serum immunoglobulin (IgA, IgG, and IgM) levels [54].

The studies that have examined exercise-associated changes in the levels of immunoglobulin isotypes often have contradictory results. As such, this interesting research area, which could potentially impact the practical guidelines for recommending exercise, remains open. While some studies have shown that exercise may decrease immunoglobulins in athletes [19, 20], others have reported, instead, an increase in its levels [44, 75]. No association between immunoglobulins and exercise has been described as well [35]. In face of such inconsistencies, and taking into account the apparent value of IgA and IgG as a potential biomarkers of URTI susceptibility in the context of exercise, the present systematic review intended to update the knowledge about the effects of acute exercise and exercise training, the two situations in which URTI mostly often occur, on IgA and IgG levels. The relationship between secretory immunoglobulins and the susceptibility to develop the diseases was also evaluated. Taking into account that COVID-19 is an infection that also affects the respiratory tract, it seems relevant to better understand the beneficial effects of exercise in fighting URTI through modulation of immunoglobulin levels. This analysis could eventually be useful as guidance on prescribing physical exercise safely.

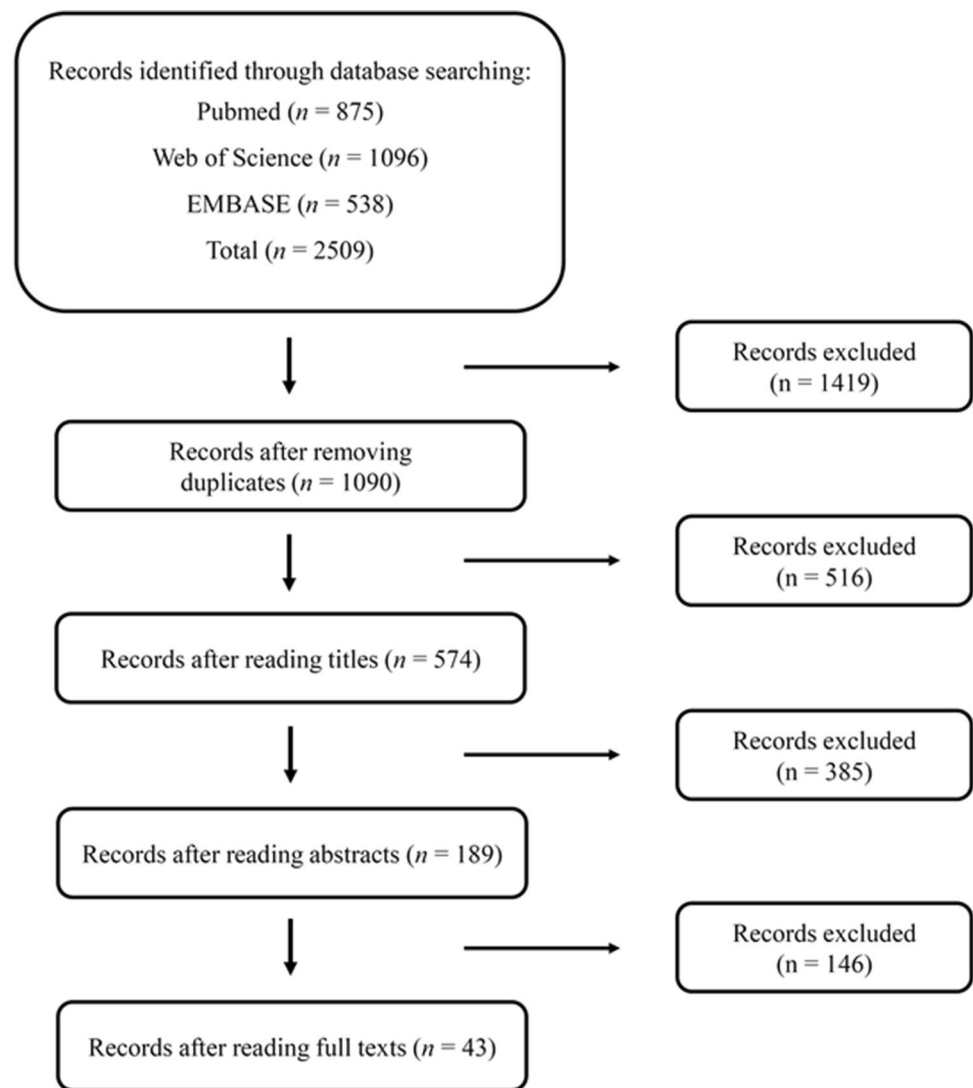
## Methods

### Search strategy

This systematic review and meta-analysis was conducted and reported according to the guidelines outlined in the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) statement [36, 43, 64]. A systematic search in electronic databases, including PubMed, Web of Science and EMBASE was performed in July 2020 without any date restrictions. The search strategy used combinations of the following keywords: respiratory tract, exertion, physical effort, firefighters, military, immune system, infection, exercise, physical training, and sport. This review was not registered.

### Study selection

This systematic review and meta-analysis included studies in which participants performed acute exercise or chronic physical training and were subjected to analyses of URTI incidence and concentrations of IgA and IgG. Furthermore, all included studies were written in English. Reviews, summaries, case studies, and letters were disregarded, although this bibliography was consulted. Based on the search and inclusion/exclusion criteria, 43 studies (112 trials,  $n = 1291$  individuals) were selected for inclusion in this systematic review (Fig. 1). For inclusion in the meta-analysis, only

**Fig. 1** Summary of the study selection process

the 29 studies (85 trials,  $n = 662$  individuals) that assessed IgA and IgG concentrations after acute exercise or chronic physical training were selected. Notably, several studies measured more than one physical performance parameter. Therefore, since all data addressing the effect of exercise on each parameter were included, the number of trials was greater than the number of studies.

### Data grouping

The selected studies for systematic review were divided into the following three groups: (I) trials that evaluated the effects of acute exercise in sedentary subjects (11 trials; 83 individuals, Table 1), (II) trials that evaluated the effects of acute exercise in athletes/trained individuals (64 trials; 345 individuals, Table 2), and (III) trials that evaluated the effects of chronic exercise training (42 trials; 748

individuals, Table 3) on the incidence of URTI, as well as on the levels of IgA and IgG.

The studies included in the meta-analysis were divided into studies that evaluated the concentrations of IgA or IgG. IgA analysis was performed in the following groups: (I) untrained individuals that performed acute exercise, (II) trained individuals that performed acute exercise, (III) trained individuals that performed acute exercise in ultramarathon, (IV) trained individuals that performed acute exercise in triathlon, and (V) non-military trained individuals that performed acute exercise. IgG analysis was only performed in chronic physical trained individuals.

### Risk of bias assessment

Two independent reviewers assessed the risk of bias using an adapted Grading of Recommendations Assessment, Development and Evaluation (GRADE) instrument [26].

**Table 1** Studies characteristics — acute exercise in sedentary subjects

Reference	N° of subjects (♂/♀)	Characteristics of subjects	Exercise protocol			Days with exercise	Exercise environment	Exercise protocol	Modality	Variable of infection		Result
			Duration	Intensity	Exercise protocol					sgA ( $\mu\text{g}\cdot\text{mL}^{-1}$ )	sgA ( $\mu\text{g}\cdot\text{mL}^{-1}$ )	
Eda et al. [15]	23 (0/23)	Healthy women	90 min	–	Yoga stretching for 90 min	1	–	–	Yoga	sgA ( $\mu\text{g}\cdot\text{mL}^{-1}$ )	Pre: $26.3 \pm 10.3$ Post: $31.5 \pm 13.4^*$	
Gleeson et al (1) [19]	26 (11/15)	Healthy people involved in regular physical activities	–	High intensity	–	1	–	–	Swimming	sgA ( $\mu\text{g}\cdot\text{mL}^{-1}$ )	Pre: $41.7 \pm 1.8$ Post: $46.1 \pm 1.8$	
Gleeson et al. (2) [19]	26 (11/15)	Healthy people involved in regular physical activities	–	High intensity	–	1	–	–	Swimming	sgG ( $\mu\text{g}\cdot\text{mL}^{-1}$ )	Pre: $3.9 \pm 20.9$ Post: $5.8 \pm 14.7$	
Mackinnon et al. (1) [38]	10 (–/–)	Recreational joggers	40 min	$55\% \text{VO}_{2\text{peak}}$	Treadmill runs	1	$22\text{--}23^\circ\text{C}$	$55\% \text{VO}_{2\text{peak}}$	Running	IgA secretion rate ( $\mu\text{g}\cdot\text{min}^{-1}$ )	Pre: $52.2 \pm 9.0$ Post: $40.5 \pm 9.0$	
Mackinnon et al. (2) [38]	10 (–/–)	Recreational joggers	40 min	$75\% \text{VO}_{2\text{peak}}$	Treadmill runs	1	$22\text{--}23^\circ\text{C}$	$75\% \text{VO}_{2\text{peak}}$	Running	IgA secretion rate ( $\mu\text{g}\cdot\text{min}^{-1}$ )	Pre: $61.2 \pm 10.0$ Post: $48.8 \pm 9.7$	
Murase et al. (1) [47]	16 (16/0)	Sedentary young	59 min	$75\% \text{VO}_{2\text{max}}$	Cycling exercise	1	$25^\circ\text{C}$	Cycling exercise	Cycling	sgA secretion rate ( $\mu\text{g}\cdot\text{min}^{-1}$ )	Pre: $26.9 \pm 12.6$ Post: $20.3 \pm 10.4$	
Murase et al. (2) [47]	16 (16/0)	Sedentary young	59 min	$75\% \text{VO}_{2\text{max}}$	Cycling exercise	1	$25^\circ\text{C}$	Cycling exercise	Cycling	sgA ( $\mu\text{g}\cdot\text{mL}^{-1}$ )	Pre: $22.8 \pm 8.5$ Post: $18.5 \pm 7.6$	
Sari-Sarraf et al. (1) [72]	8 (8/0)	Healthy	90 min	$\text{VO}_{2\text{max}}$ : $56.6 \pm 12.0\%$ RPE: $11.9 \pm 0.8$	Intermittent exercise specific to soccer	1	$16 \pm 1^\circ\text{C}$ $47 \pm 8\% \text{RH}$	Intermittent exercise specific to soccer	Soccer	sgA secretion rate ( $\mu\text{g}\cdot\text{min}^{-1}$ )	Pre: $78.7 \pm 44.5$ Post: $113.9 \pm 85.7$	
Sari-Sarraf et al. (2) [72]	8 (8/0)	Healthy	90 min	$\text{VO}_{2\text{max}}$ : $56.6 \pm 12.0\%$ RPE: $11.9 \pm 0.8$	Intermittent exercise specific to soccer	1	$16 \pm 1^\circ\text{C}$ $47 \pm 8\% \text{RH}$	Intermittent exercise specific to soccer	Soccer	sgA ( $\text{mg L}^{-1}$ )	Pre: $131.6 \pm 61.2$ Post: $148.4 \pm 82.5$	
Sari-Sarraf et al. (3) [72]	8 (8/0)	Healthy	90 min	$\text{VO}_{2\text{max}}$ : $56.6 \pm 12.0\%$ RPE: $11.9 \pm 0.8$	45-min exercise + 15-min half-time + 45-min exercise	1	$16 \pm 1^\circ\text{C}$ $47 \pm 8\% \text{RH}$	45-min exercise + 15-min half-time + 45-min exercise	Soccer	sgA secretion rate ( $\mu\text{g}\cdot\text{min}^{-1}$ )	Pre: $78.9 \pm 56.3$ Post: $101.8 \pm 70.1$	
Sari-Sarraf et al. (4) [72]	8 (8/0)	Healthy	90 min	$\text{VO}_{2\text{max}}$ : $56.6 \pm 12.0\%$ RPE: $11.9 \pm 0.8$	45-min exercise + 15-min half-time + 45-min exercise	1	$16 \pm 1^\circ\text{C}$ $47 \pm 8\% \text{RH}$	45-min exercise + 15-min half-time + 45-min exercise	Soccer	sgA ( $\text{mg L}^{-1}$ )	Pre: $146.4 \pm 07.6$ Post: $229.2 \pm 159.6$	

♂, Male; ♀, female.  $\text{VO}_{2\text{peak}}$  peak oxygen uptake,  $\text{VO}_{2\text{max}}$  maximal oxygen uptake,  $\text{RPE}$  rate of perceived exertion,  $\text{RH}$  relative humidity. Results showed as mean values and standard deviations  
\*Statistical difference

**Table 2** Studies characteristics—acute exercise in trained (athletes) subjects

Reference	N° of subjects (♂/♀)	Characteristics of subjects	Training protocol			Session protocol			Variable of infection	Result
			Duration of protocol	Frequency	Intensity	Duration of session	Exercise environment	Exercise protocol		
Canto et al. (1) [11]	47 (28/19)	Healthy non-elite marathon runners	–	–	–	Mean finishing time was 3 h and 38 min (±41 min)	–	Marathon	Pre: 2.34 ± 1.16 Post: 2.37 ± 0.37	
Canto et al. (2) [11]	47 (28/19)	Healthy non-elite marathon runners	–	–	–	Mean finishing time was 3 h and 38 min (±41 min)	–	Marathon	Pre: 0.39 ± 0.25 Post: 0.35 ± 0.24	
Costa et al. (1) [13]	32 (32/0)	Healthy triathletes (Olympic and Ironman Triathlon)	20.9 ± 5.8 h/week	6 day/week	70% VO <sub>2max</sub>	1 h	–	Run for 1 h/day	Pre: 184.6 ± 67.4 Post: 167.9 ± 62.1	
Costa et al. (2) [13]	32 (32/0)	Healthy triathletes (Olympic and Ironman Triathlon)	20.9 ± 5.8 h/week	6 day/week	70% VO <sub>2max</sub>	1 h	–	Run for 1 h/day	Pre: 153.4 ± 45.7 Post: 165.9 ± 82.4	
Costa et al. (3) [13]	32 (32/0)	Healthy triathletes (Olympic and Ironman Triathlon)	20.9 ± 5.8 h/week	6 day/week	70% VO <sub>2max</sub>	1 h	–	Run for 1 h/day	Pre: 168.8 ± 55.3 Post: 157.1 ± 73.7	
Gleeson et al. (1) [19]	26 (11/15)	Elite swimmers	6 months	20–25 h of training in the pool and 5 h of training on dry land per week	High intensity	–	–	–	Pre: 50.4 ± 1.6 Post: 45.2 ± 1.7	
Gleeson et al. (2) [19]	26 (11/15)	Elite swimmers	6 months	20–25 h of training in the pool and 5 h of training on dry land per week	High intensity	–	–	–	Pre: 8.1 ± 13.2 Post: 5.2 ± 18.5	

Table 2 (continued)

Reference	N° of subjects (♂/♀)	Characteristics of subjects	Training protocol		Session protocol		Variable of infection	Result	
			Duration of protocol	Frequency	Intensity	Duration of session			Exercise environment
Gleeson et al. (1) [20]	22 (12/10)	Elite swimmers	12 weeks	10 to 25 h/week	High intensity	–	Mean air temperature 24 °C, mean water temperature 27 °C	Training in the pool and of training on land (resistance, flexibility and circuits)	slgA (mg L) Pre: 55.3 Post: 37.11
Gleeson et al. (2) [20]	22 (12/10)	Elite swimmers	12 weeks	10 to 25 h/week	High intensity	–	Mean air temperature 24 °C, mean water temperature 27 °C	Training in the pool and of training on land (resistance, flexibility and circuits)	slgG (mg L) Pre: 15.8 Post: 13.9
Kunz et al. (1) [30]	17 (13/4)	Healthy and experienced cyclists	Minimum period of 12 months	At least three times per week	–5% blood lactate threshold	30 min	10-min warm-up + 30 min of exercise	Cycling	slgA (µg/mL) Pre: 290 ± 219 Post: 297 ± 169*
Kunz et al. (2) [30]	17 (13/4)	Healthy and experienced cyclists	Minimum period of 12 months	At least three times per week	+5% blood lactate threshold	30 min	10-min warm-up + 30 min of exercise	Cycling	slgA (µg/mL) Pre: 283 ± 204 Post: 319 ± 202*
Kunz et al. 2015 (3) [30]	17 (13/4)	Healthy and experienced cyclists	Minimum period of 12 months	At least three times per week	+15% blood lactate threshold	30 min	10-min warm-up + 30 min of exercise	Cycling	slgA (µg/mL) Pre: 264 ± 268 Post: 386 ± 260*
Libicz et al. (1) [37]	8 (8/0)	Elite triathletes	–	–	Extended intense exercise	40 min	14.5 – 27,2 °C	Run 2.5 km, bike 20 km, run 2.5 km	slgA (µg/ml) Pre: 61.9 ± 36.5 Post: 88.1 ± 53.3
Libicz et al. (2) [37]	8 (8/0)	Elite triathletes	–	–	Extended intense exercise	20 min	14.5 – 27,2 °C	Swim 400 m, bike 10 km, run 2,5 km	slgA (µg/ml) Pre: 77.3 ± 47.5 Post: 82.2 ± 50.8
Libicz et al. (3) [37]	8 (8/0)	Elite triathletes	–	–	Extended intense exercise	1 h 40 min	14.5 – 27,2 °C	Swim 1500 m, bike 40 km, run 10 km	slgA (µg/ml) Pre: 101.0 ± 51.6* Post: 85.6 ± 82.0
Libicz et al. (4) [37]	8 (8/0)	Elite triathletes	–	–	Extended intense exercise	40 min	14.5 – 27,2 °C	Swim 750 m, bike 20 km, run 5 km	slgA (µg/ml) Pre: 56.8 ± 30.6 Post: 69.2 ± 32.1
Libicz et al. (5) [37]	8 (8/0)	Elite triathletes	–	–	Extended intense exercise	1 h	14.5 – 27,2 °C	Swim 750 m, bike 20 km, run 5 km	slgA (µg/ml) Pre: 75.8 ± 54.9 Post: 58.3 ± 14.3

**Table 2** (continued)

Reference	N° of subjects (♂/♀)	Characteristics of subjects	Training protocol		Session protocol		Variable of infection	Result	
			Duration of protocol	Frequency	Intensity	Duration of session			Exercise environment
Libicz et al. (6) [37]	8 (8/0)	Elite triathletes	–	–	Extended intense exercise	2 h 20 min	14.5 – 27.2 °C	51.5 km Tri	Pre: 53.6 ± 22.5 Post: 70.1 ± 39.8
Libicz et al. (7) [37]	8 (8/0)	Elite triathletes	–	–	Extended intense exercise	40 min	14.5 – 27.2 °C	Run 2.5 km, bike 20 km, run 2.5 km	Pre: 20.7 ± 15.7 Post: 12.8 ± 6.0
Libicz et al. (8) [37]	8 (8/0)	Elite triathletes	–	–	Extended intense exercise	20 min	14.5 – 27.2 °C	Swim 400 m, bike 10 km, run 2.5 km	Pre: 31.4 ± 21.6 Post: 8.4 ± 4.0
Libicz et al. (9) [37]	8 (8/0)	Elite triathletes	–	–	Extended intense exercise	1 h 40 min	14.5 – 27.2 °C	Swim 1500 m, bike 40 km, run 10 km	Pre: 47.3 ± 40.7 Post: 11.1 ± 2.6
Libicz et al. (10) [37]	8 (8/0)	Elite triathletes	–	–	Extended intense exercise	40 min	14.5 – 27.2 °C	Swim 750 m, bike 20 km, run 5 km	Pre: 14.9 ± 9.9 Post: 16.1 ± 7.4
Libicz et al. (11) [37]	8 (8/0)	Elite triathletes	–	–	Extended intense exercise	1 h	14.5 – 27.2 °C	Swim 750 m, bike 20 km, run 5 km	Pre: 14.6 ± 7.1 Post: 15.8 ± 7.7
Libicz et al. (12) [37]	8 (8/0)	Elite triathletes	–	–	Extended intense exercise	2 h 20 min	14.5 – 27.2 °C	51.5 km Tri	Pre: 21.6 ± 13.4 Post: 12.7 ± 3.4
Mackinnon et al. (1) [40]	8 (8/0)	Elite kayakers	–	–	7.5 (1 to 10)	30 min	2-min efforts of increasing intensity, at 70%, 80%, 90%, and 100% (HR <sub>max</sub> ), with 30-s rest	Kayaking	Pre: 41.1 ± 5.3 Post: 33.4 ± 5.2
Mackinnon et al. (2) [40]	8 (8/0)	Elite kayakers	–	–	7.5 (1 to 10)	30 min	2-min efforts of increasing intensity, at 70%, 80%, 90%, and 100% (HR <sub>max</sub> ), with 30-s rest	Kayaking	Pre: 25.3 ± 9.5 Post: 28.7 ± 7.1

Table 2 (continued)

Reference	N° of subjects (♂/♀)	Characteristics of subjects	Training protocol		Session protocol		Variable of infection	Result	
			Duration of protocol	Frequency	Intensity	Duration of session			Exercise environment
Mackinnon et al. (3) [40]	8 (8/0)	Elite kayakers	–	–	8.0 (1 to 10)	24 min	Three 8-min efforts, at 70%, 80% and 90% ( $HR_{max}$ ) with 30-s rest	Kayaking	sIgA (relative to total protein) (µg/mg) Pre: $37.4 \pm 6.7$ Post: $32.2 \pm 5.0$
Mackinnon et al. (4) [40]	8 (8/0)	Elite kayakers	–	–	8.0 (1 to 10)	24 min	Three 8-min efforts, at 70%, 80%, and 90% ( $HR_{max}$ ) with 30-s rest	Kayaking	sIgA (relative to total protein) (µg/mg) Pre: $30.7 \pm 9.9$ Post: $36.8 \pm 9.9$
Mackinnon et al. (5) [40]	8 (8/0)	Elite kayakers	–	–	8.5 (1 to 10)	40 min	Two 20-min efforts at an intensity eliciting FC determined in critical power testing sessions	Kayaking	sIgA (relative to total protein) (µg/mg) Pre: $27.1 \pm 3.7$ Post: $25.8 \pm 5.3$
Mackinnon et al. (6) [40]	8 (8/0)	Elite kayakers	–	–	8.5 (1 to 10)	40 min	Two 20-min efforts at an intensity eliciting FC determined in critical power testing sessions	Kayaking	sIgA (relative to total protein) (µg/mg) Pre: $19.7 \pm 5.8$ Post: $24.6 \pm 6.3$
Mackinnon et al. (1) [38]	8 (–/–)	Competitive endurance athletes	–	–	55% $VO_{2peak}$	90 min	22 – 23 °C	Treadmill running	sIgA secretion rate (µg/min) Pre: $45.3 \pm 9.6$ Post: $46.6 \pm 8.0$
Mackinnon et al. (2) [38]	8 (–/–)	Competitive endurance athletes	–	–	75% $VO_{2peak}$	90 min	22 – 23 °C	Treadmill running	sIgA secretion rate (µg/min) Pre: $62.0 \pm 12.6$ Post: $51.5 \pm 12.2$
Mackinnon et al. (1) [38]	7 (–/–)	Competitive marathon runners and triathletes	–	–	75% $VO_{2peak}$	90 min	22 – 23 °C	Treadmill running	sIgA secretion rate (µg/min) Pre: $59.1 \pm 9.8$ Post: $48.9 \pm 12.5$



**Table 2** (continued)

Reference	N° of subjects (♂/♀)	Characteristics of subjects	Training protocol		Intensity	Session protocol		Variable of infection	Result
			Duration of protocol	Frequency		Duration of session	Exercise environment		
Mackinnon et al. (2) [38]	7 (–/–)	Competitive marathon runners and triathletes	–	–	75% VO <sub>2peak</sub>	90 min	22 – 23 °C	Treadmill running	Pre: 53.2 ± 5.0 Pos: 30.8 ± 9.6*
Mackinnon et al. (3) [38]	7 (–/–)	Competitive marathon runners and triathletes	–	–	75% VO <sub>2peak</sub>	90 min	22 – 23 °C	Treadmill running	Pre: 52.3 ± 10.6 Pos: 36.2 ± 7.5
Moreira et al. (1) [44]	10 (10/–)	Professional top-level Brazilian futsal players	–	–	Highly competitive games	40 min	–	Futsal match	Pre: 175 ± 43 Post: 99 ± 17*
Moreira et al. (2) [44]	10 (10/–)	Professional top-level Brazilian futsal players	–	–	Highly competitive games	40 min	–	Futsal match	Pre: 14 ± 2 Post: 7 ± 1*
Nieman et al. (1) [58]	45 (–/–)	Ultramarathon runners	–	–	–	27 ± 0.4 h	Running 90 km	Ultramarathon	Pre: 508 ± 40 Post: 287 ± 39*
Nieman et al. (2) [58]	45 (–/–)	Ultramarathon runners	–	–	–	27 ± 0.4 h	Running 160 km	Ultramarathon	Pre: 508 ± 40 Post: 254 ± 30*
Nieman et al. (3) [58]	45 (–/–)	Ultramarathon runners	–	–	–	27 ± 0.4 h	Running 90 km	Ultramarathon	Pre: 530 ± 37 Post: 577 ± 59
Nieman et al. (4) [58]	45 (–/–)	Ultramarathon runners	–	–	–	27 ± 0.4 h	Running 160 km	Ultramarathon	Pre: 530 ± 37 Post: 562 ± 75
Nieman et al. (5) [58]	45 (–/–)	Ultramarathon runners	–	–	–	27 ± 0.4 h	Running 90 km	Ultramarathon	Pre: 611 ± 57 Post: 567 ± 59
Nieman et al. (6) [58]	45 (–/–)	Ultramarathon runners	–	–	–	27 ± 0.4 h	Running 160 km	Ultramarathon	Pre: 611 ± 57 Post: 523 ± 51
Nieman et al. (7) [58]	45 (–/–)	Ultramarathon runners	–	–	–	27 ± 0.4 h	Running 160 km	Ultramarathon	Incidence URTI (15 days post-race) Post: 26%

Table 2 (continued)

Reference	N° of subjects (♂/♀)	Characteristics of subjects		Training protocol		Session protocol		Variable of infection	Result
		Duration of protocol	Frequency	Intensity	Duration of session	Exercise environment	Exercise protocol		
Novas et al. (1) [60]	17 (0/17)	Tennis players	12 weeks	–	RPE: 6.7 ± 1.5 HR: 145 ± 13 bpm %HRR: 61 ± 9%	60 min	–	Tennis	Pre: 308.3 ± 150 Post: 326.8 ± 156.3
Novas et al. (2) [60]	17 (0/17)	Tennis players	12 weeks	–	RPE: 6.7 ± 1.5 HR: 145 ± 13 bpm %HRR: 61 ± 9%	60 min	–	Tennis	Pre: 369 ± 167 Post: 361.1 ± 185.1
Novas et al. (3) [60]	17 (0/17)	Tennis players	12 weeks	–	RPE: 6.7 ± 1.5 HR: 145 ± 13 bpm %HRR: 61 ± 9%	60 min	–	Tennis	Pre: 287 ± 165 Post: 222 ± 152*
Novas et al. (4) [60]	17 (0/17)	Tennis players	12 weeks	–	RPE: 6.7 ± 1.5 HR: 145 ± 13 bpm %HRR: 61 ± 9%	60 min	–	Tennis	Pre: 395 ± 223 Post: 398 ± 211
Owen et al. (1) [62]	10 (10/–)	Elite professional soccer players	1 week	4 session/week	High-intensity RPE: 15.1 – 16.3	–	–	Tactical and technical soccer training	Pre: 67.89 ± 41.53 Post: 58.11 ± 44.98
Owen et al. (2) [62]	10 (10/–)	Elite professional soccer players	1 week	4 session/week	High-intensity RPE: 15.1 – 16.3	–	–	Tactical and technical soccer training	Pre: 156.11 ± 111.01 Post: 101.11 ± 38.76
Owen et al. (3) [62]	10 (10/–)	Elite professional soccer players	1 week	4 session/week	High-intensity RPE: 15.1 – 16.3	–	–	Tactical and technical soccer training	Pre: 125.00 ± 87.30 Post: 85.33 ± 42.53
Owen et al. (4) [62]	10 (10/–)	Elite professional soccer players	1 week	4 session/week	High-intensity RPE: 15.1 – 16.3	–	–	Tactical and technical soccer training	Pre: 64.44 ± 43.50 Post: 59.15 ± 54.92
Owen et al. (5) [62]	10 (10/–)	Elite professional soccer players	1 week	4 session/week	Low-intensity RPE: 9.4 – 10.3	–	–	Tactical and technical soccer training	Pre: 132.44 ± 71.26 Post: 86.56 ± 63.78
Owen et al. (6) [62]	10 (10/–)	Elite professional soccer players	1 week	4 session/week	Low-intensity RPE: 9.4 – 10.3	–	–	Tactical and technical soccer training	Pre: 127.33 ± 43.68 Post: 124.56 ± 49.21

**Table 2** (continued)

Reference	N° of subjects (♂/♀)	Characteristics of subjects	Training protocol		Session protocol		Variable of infection	Result
			Duration of protocol	Frequency	Intensity	Duration of session		
Owen et al. (7) [62]	10 (10/–)	Elite professional soccer players	1 week	4 session/week	Low-intensity RPE: 9.4 – 10.3	–	Tactical and technical soccer training	Pre: 121.00 ± 52.22 Post: 113.56 ± 56.52
Owen et al. (8) [62]	10 (10/–)	Elite professional soccer players	1 week	4 session/week	Low-intensity RPE: 9.4 – 10.3	–	Tactical and technical soccer training	Pre: 119.44 ± 57.02* Post: 129.00 ± 58.60*
Pacque et al. (1) [63]	17 (13/4)	Healthy race participants	–	4.5 – 15 h/week	–	1 h 25 min ± 1 h 32 min	Ultramarathon	Pre: 252 Post: 106*
Pacque et al. (2) [63]	17 (13/4)	Healthy race participants	–	4.5 – 15 h/week	5 – 18 °C Minimal rain	1 h 25 min ± 1 h 32 min	Ultramarathon	Pre: 2142 ± 817 Post: 1640 ± 766*
Pacque et al. (3) [63]	17 (13/4)	Healthy race participants	–	4.5 – 15 h/week	5 – 18 °C Minimal rain	1 h 25 min ± 1 h 32 min	Ultramarathon	Pre: 4 Post: 3
Peters et al. (1) [68]	14 (0/14)	Ultramarathon runners	Until 5 km/week	–	–	9:33 ± 1:04 h	86.5 km	Pre: 27.24 ± 17.86 Post: 44.18 ± 19.47
Peters et al. (2) [68]	14 (0/14)	Ultramarathon runners	Until 5 km/week	–	–	9:33 ± 1:04 h	86.5 km	URT I incidence Post: 71%
Steenberg et al. [75]	42 (36/6)	Triathletes	–	–	–	2–2.5 h	1000–1500 m swimming, 40 km cycling and 10 km running	Pre: 500 Post: 308
Zakovska et al. [84]	15 (12/3)	Ultra-marathoners	91.4 ± 27.0 h/week or 10.7 ± 3.7 h/week	–	6:18 ± 1:42 min·km	–	100 km ultramarathon running (completing 60 km at least)	Pre: 21.09 ± 90.52 Post: 24.0 ± 13.56

♂, Male; ♀, female.  $VO_{2peak}$  peak oxygen uptake,  $VO_{2max}$  maximal oxygen uptake,  $HR_{max}$  maximum heart rate,  $HRR_{max}$  maximum heart rate reserve,  $RPE$  rate of perceived exertion,  $RH$  relative humidity. Results showed as mean values and standard deviations

\*Statistical difference

**Table 3** Studies characteristics—chronic exercise training

Reference	N° of subjects (♂/♀)	Characteristics of subjects	Exercise training protocol						Result	
			Exercise pro- tocol	Duration of protocol	Intensity	Duration of ses- sion	Frequency	Exercise envi- ronment		Variable of infection
Blume et al. [3]	274 (175/99)	Young athletes (cross-country skiing, cycling, figure skating, gymnastics, high diving, soccer, speed skating, swimming, tennis and volleyball)	–	2010–2014	–	–	14.9 ± 5.6 h weekly	–	URTI	30.7%
Borges et al. [4]	12 (6/6)	Elite kayakers	Kayaking (60–140 km/ week), running (20– 35 km/week), swimming (4–6 km/ week), strength (90–140 tons/ week) and calisthen- ics (100– 220 min/ week)	November to June	–	–	–	–	URTI	9 episodes
Brisola et al. [8]	20 (0/20)	Young female water polo players	First session of the day was only for dry and training and second session of the day included swimming routine and specific water polo exercises	January to April of the competitive season	–	–	General cycle: 118.6 ± 27.0 min Specific cycle: 118.8 ± 17.0 min Competitive cycle: 109.9 ± 13.6 min	6 times a week with 2 daily sessions	URTI	General cycle: 4.00 ± 2.0 a.u.* Specific cycle: 2.00 ± 1.2 a.u Competi- tive cycle: 2.00 ± 1.3 a.u

**Table 3** (continued)

Reference	N° of subjects (♂/♀)	Characteristics of subjects	Exercise training protocol				Frequency	Exercise environment	Variable of infection	Result
			Exercise protocol	Duration of protocol	Intensity	Duration of session				
Broadbent et al. [9]	15 (15/0)	Ironman triathletes	3–4 swim sessions per week (12–16 km) 3–4 cycle sessions per week (300–400 km) 3–5 run sessions per week (60–90 km)	12 months	–	–	–	URTI	2 episodes	
Brunelli et al. [10]	11 (11/0)	Adolescent basketball athletes	Technical and functional skills according to the objectives of training	20 weeks	–	–	98.7 ± 4.5 min	URTI	Preparatory period: 28,8% Competitive period: 61,7%*	
Fahlman et al. (1) [16]	75 (75/0)	University football team	–	12 months	Moderate	–	–	URTI	Pre: 6% Post: 59%	
Fahlman et al. (2) [16]	75 (75/0)	University football team	–	12 months	Moderate	–	–	IgA to protein (µg mg <sup>-1</sup> )	Pre: 96 ± 7 Post: 92 ± 10	
Fahlman et al. (3) [16]	75 (75/0)	University football team	–	12 months	Moderate	–	–	IgA to osmolality (mg mOsmol <sup>-1</sup> )	Pre: 2.8 ± 0.8 Post: 1.9 ± 1.8	
Fahlman et al. (4) [16]	75 (75/0)	University football team	–	12 months	Moderate	–	–	Secretion rate of sIgA (µg min <sup>-1</sup> )	Pre: 54.9 ± 1.3 Post: 38.3 ± 1.5	
Filaire et al. (1) [17]	20 (20/0)	Professional football players	Running (70–75% VO <sub>2max</sub> ), physical training, and technical training sessions	12 months	High intensity	–	27 h a week	IgA	Pre: 2.3 ± 0.2 Post: 2.3 ± 0.1	

Table 3 (continued)

Reference	N° of subjects (♂/♀)	Characteristics of subjects	Exercise training protocol				Frequency	Exercise envi- ronment	Variable of infection	Result
			Exercise pro- tocol	Duration of protocol	Intensity	Duration of ses- sion				
Filjaire et al. (2) [17]	20 (20/0)	Professional football play- ers	Running (70–75% VO <sub>2max</sub> ), physical training, and technical training ses- sions	12 months	High intensity	27 h a week	–	IgG	Pre: 11.9 ± 0.4 Post: 11.8 ± 0.2	
Gleeson et al. (1) [19]	26 (11/15)	Elite swimmers	20–25 h of training in the pool and 5 h of training on dry land per week	6 months (April to October)	High intensity	6 h/day	–	Serum IgA	Athletes: 1.51 ± 1.39 Control: 1.73 ± 1.62*	
Gleeson et al. (2) [19]	26 (11/15)	Elite swimmers	20–25 h of training in the pool and 5 h of training on dry land per week	6 months (April to October)	High intensity	6 h/day	–	Serum IgG	Athletes: 10.28 ± 1.26 Control: 10.80 ± 1.21*	
Gomez- Merino et al. [24]	21 (21/0)	Cadets	1 week – sea phase 2 and 3 week – mountain phase 5 days combat course – rough terrain	3 weeks of training and 5 days com- bat course	High	–	12 – 25 °C	URTI	14 episodes	
Ihalainen et al. [29]	25 (25/0)	Recreational male endur- ance runners	Running	12 weeks	1 to 2 incre- mental run: 65–85% HR <sub>max</sub> 1 long run: 60–65% HR <sub>max</sub> 1 interval run: 20 – 25 min 80–85% HR <sub>max</sub> 1 to 2 light run: 60–65% HR <sub>max</sub>	1 to 2 incremen- tal run: 35 – 45 min 1 long run: 70 – 120 min 1 interval run: 20 – 25 min 1 to 2 light run 35 – 40 min	4–6 sessions/ week	Average tem- perature: –7 to –1 °C	URTI	13 episodes

**Table 3** (continued)

Reference	N° of subjects (♂/♀)	Characteristics of subjects	Exercise training protocol				Frequency	Exercise environment	Variable of infection	Result
			Exercise protocol	Duration of protocol	Intensity	Duration of session				
Mackinnon et al. [39]	24 (8/16)	Elite swimmers	Intensified training	4 weeks	> 80% HR <sub>max</sub>	–	–	URTI	10 episodes	
Moreira et al. (1) [45]	15 (15/0)	Basketball players under-19	–	–	–	90–120 min	–	sIgA (µg ml <sup>-1</sup> )	Pre: 587 ± 94 Post: 720 ± 153	
Moreira et al. (2) [45]	15 (15/0)	Basketball players under-19	–	–	–	90–120 min	–	sIgA secretion rate (µg min <sup>-1</sup> )	Pre: 106 ± 20 Post: 92 ± 21*	
Martins et al. (1) [41]	21 (8/13)	Elderly	Aerobic exercise training	16 weeks	40 – 85% HRR	45 min	–	sIgA (mg dL <sup>-1</sup> )	Pre: 8.40 ± 7.09 Post: 6.25 ± 4.25	
Martins et al. (2) [41]	21 (8/13)	Elderly	Aerobic exercise training	16 weeks	40 – 85% HRR	45 min	–	IgA (g L <sup>-1</sup> )	Pre: 1.08 ± 0.51 Post: 2.40 ± 0.86*	
Martins et al. (3) [41]	21 (8/13)	Elderly	Aerobic exercise training	16 weeks	40 – 85% HRR	45 min	–	IgG (g L <sup>-1</sup> )	Pre: 4.95 ± 2.09 Post: 12.44 ± 2.91*	
Nehlsen-Cannarella et al., 2000 (1) [48]	20 (0/20)	Elite rowers	–	–	–	90–120 min training/week	–	Days with URTI symptoms	Rowers: 5.2 ± 1.2 Nonathletes: 3.3 ± 1.1	
Nehlsen-Cannarella et al. (2) [48]	20 (0/20)	Elite rowers	–	–	–	90–120 min training/week	–	sIgG (µg ml <sup>-1</sup> )	Rowers: 14.7 ± 1.9 Nonathletes: 11.4 ± 1.6	
Nehlsen-Cannarella et al. (3) [48]	20 (0/20)	Elite rowers	–	–	–	90–120 min training/week	–	Saliva protein IgA concentration (µg mg <sup>-1</sup> )	Rowers: 425 ± 20 Nonathletes: 409 ± 96	
Nehlsen-Cannarella et al. (4) [48]	20 (0/20)	Elite rowers	–	–	–	90–120 min training/week	–	Saliva protein IgG concentration (µg mg <sup>-1</sup> )	Rowers: 15.4 ± 1.6 Nonathletes: 21.6 ± 6.7	
Nehlsen-Cannarella et al. (5) [48]	20 (0/20)	Elite rowers	–	–	–	90–120 min training/week	–	sIgA secretion rate (µg min <sup>-1</sup> )	Rowers: 63.0 ± 12.3 Nonathletes: 47.1 ± 7.6	

Table 3 (continued)

Reference	N° of subjects (♂/♀)	Characteristics of subjects	Exercise training protocol				Frequency	Exercise environment	Variable of infection	Result
			Exercise protocol	Duration of protocol	Intensity	Duration of session				
Nehlsen-Canarella et al. (6) [48]	20 (0/20)	Elite rowers	–	–	–	–	–	slgG secretion rate ( $\mu\text{g min}^{-1}$ )	Rowers: $2.3 \pm 0.5$ Nonathletes: $2.7 \pm 0.5$	
Nieman et al. [56]	32 (0/32)	Healthy elderly women	Walking	12 weeks	60% heart rate reserve	30–40 min	5 days/week	URTI	Callisthenic: 8/16 (50%) Walking: 3/14 (21%) Highly conditioned: 1/12 (8.3%)*	
Nieman et al. [57]	39 (0/39)	Elite female rowers	Rower	–	–	90–120 min	12–13 sessions/week	URTI days	Rowers: $5.2 \pm 1.2$ Nonathletes: $3.3 \pm 1.1$	
Novas et al. (1) [60]	17 (0/17)	Female tennis player	–	12 weeks	–	$104 \pm 32$ min	–	IgA ( $\mu\text{g ml}^{-1}$ )	Pre: $395 \pm 223$ Post: $398 \pm 211$	
Novas et al. (2) [60]	17 (0/17)	Female tennis player	–	12 weeks	–	$104 \pm 32$ min	–	slgA rate ( $\mu\text{g min}^{-1}$ )	Pre: $287 \pm 165$ Post: $222 \pm 152^*$	
Novas et al. (3) [60]	17 (0/17)	Female tennis player	–	12 weeks	–	$104 \pm 32$ min	–	URTI episodes	$1.5 \pm 1.4$	
Novas et al. (4) [60]	17 (0/17)	Female tennis player	–	12 weeks	–	$104 \pm 32$ min	–	URTI days	$10 \pm 10.3$	
Orysiak et al. (1) [61]	12 (12/0)	Young ice hockey players	Strength training, training on ice and friendly match	17 days	–	–	–	URTI	Training camp 42% During the tournament 0% After the World Championship 8%	
Orysiak et al. (2) [61]	12 (12/0)	Young ice hockey players	Strength training, training on ice and friendly match	17 days	–	–	–	slgA concentration (g/ml)	Pre: $116.17 \pm 51.66$ Post: $122.84 \pm 82.67$	
Orysiak et al. (3) [61]	12 (12/0)	Young ice hockey players	Strength training, training on ice and friendly match	17 days	–	–	–	slgA secretion rate ( $\mu\text{g/min}$ )	Pre: $84.93 \pm 32.30$ Post: $73.69 \pm 45.75$	



**Table 3** (continued)

Reference	N° of subjects (♂/♀)	Characteristics of subjects	Exercise training protocol					Frequency	Exercise environment	Variable of infection	Result
			Exercise protocol	Duration of protocol	Intensity	Duration of session	Frequency				
Rama et al. [70]	19 (13/6)	Elite swimmers	–	29 weeks	–	–	8–11 sessions/week	–	URTI	31 episodes	
Tiollier et al. (1) [79]	21 (21/0)	Male cadets from the French Military	–	3 weeks of commando training followed by a 5-day combat course	–	–	–	Minimum temperature: 1–12.7 °C, maximum temperature: 7–27.2 °C	URTI	14 episodes	
Tiollier et al. (2) [79]	21 (21/0)	Male cadets from the French Military	–	3 weeks of commando training followed by a 5-day combat course	–	–	–	Minimum temperature: 1–12.7 °C, maximum temperature: 7–27.2 °C	IgA	Pre: 113 ± 11 Post: 120 ± 14	
Whitham et al. (1) [81]	14	PARA recruits	10- and 20-mile foot races carrying a 35-lb bergan and weapon, a 1.8-mile log race in teams of six to nine, and a 5-mile stretcher race	19 weeks	–	–	–	Ambient temperatures of > 25 °C	URTI	4.1 ± 0.3	
Whitham et al. (2) [81]	14	PARA recruits	10- and 20-mile foot races carrying a 35-lb bergan and weapon, a 1.8-mile log race in teams of six to nine, and a 5-mile stretcher race	19 weeks	–	–	–	Ambient temperatures of > 25 °C	sIgA concentration (mg/L)	Pre: 66 ± 15 Post: 347 ± 79	

Table 3 (continued)

Reference	N° of subjects (♂/♀)	Characteristics of subjects	Exercise training protocol				Variable of infection	Result
			Exercise pro- tocol	Duration of protocol	Intensity	Duration of ses- sion		
Whitham et al. (3) [81]	14	PARA recruits	10- and 20-mile foot races carry- ing a 35-lb bergan and weapon, a 1.8-mile log race in teams of six to nine, and a 5-mile stretcher race	19 weeks	-	-	Ambient temperatures of > 25 °C	slgA secretion rate (µg/min) Pre: 14 ± 3 Post: 27 ± 6

♂, male; ♀, female.  $HR_{max}$  maximum heart rate,  $HRR$  heart rate reserve. Results showed as mean values and standard deviations

\*Statistical difference

Discrepant evaluations were settled via discussion with a third reviewer. Using this approach, it was possible to evaluate the risk of bias in each study included in the present systematic review. Domains reflecting sequence generation, allocation concealment, blinding of participants and personnel, incomplete outcome data, selective outcome reporting and other sources of bias were evaluated. The lack of one of these domains characterizes the reduction in the individual methodological quality of each study in the following sequence: high, moderate, low and very low.

Furthermore, the GRADE approach was used to assess the overall quality with levels of evidence. This analysis was performed using a GRADE profiler software, available online (<https://gdt.grade.pro.org/app/>), which was used to summarize our findings on the certainty of the evidence. Thus, for each outcome analyzed in the meta-analysis, the global assessment of the level of evidence was performed and classified into four levels: high (GRADE A), moderate (GRADE B), low (GRADE C), and very low (GRADE D) [26].

## Statistical analysis

The mean and SD values of the IgA and IgG levels after acute and chronic exercise were obtained from the data provided in the consulted research papers. Heterogeneity was evaluated using the  $\chi^2$  test for homogeneity and the  $I^2$  statistic. The effect size (Cohen's  $d$  or Hedges'  $g$ ) was calculated for the physical performance indexes in each study. Then, a weighted-mean estimate of the effect size was calculated to account for differences in the sample sizes. The mean unweighted effect size and associated 95% CI were also calculated. We used Cohen's classification of the effect size magnitude, where  $d < 0.20$  = negligible effect;  $d = 0.20$ – $0.49$  = small effect;  $d = 0.50$ – $0.79$  = moderate effect; and  $d > 0.8$  = large effect [12].

## Results

### Systematic review

In total, 2509 studies were identified through the database and reference searches. After removing the duplicates and excluding papers that did not meet the eligibility criteria following a review of their titles, abstracts and full texts, 43 studies (117 trials,  $n = 1176$  individuals) were selected for inclusion in the systematic review (Fig. 1). The characteristics of the subjects, the exercise/physical training protocols and the infection parameter evaluated in each study are summarized in Tables 1, 2, and 3.

## Meta-analyses

Twenty-nine studies (85 trials,  $n = 662$  individuals) were included in the meta-analysis.

### Untrained: acute exercise – IgA levels (GRADE C)

After pooling the data from 9 trials, the mean effect size was 0.16 (95% CI:  $-0.32$  to  $0.64$ ), which indicates that acute exercise has a non-significant effect on IgA levels ( $p > 0.05$ ; Fig. 2). According to a random effects analysis, medium heterogeneity was observed among these studies ( $I^2 = 62.1\%$ ;  $Q = 21.1$ ,  $df = 8$ ,  $p = 0.07$ ).

### Trained: acute exercise – IgA levels (GRADE B)

After pooling the data from 50 trials, the mean effect size was 0.68 (95% CI:  $0.34$  to  $1.02$ ), which indicates that acute exercise induces a moderate and significant increase on IgA levels ( $p < 0.05$ ; Fig. 3). According to a random effects analysis, high heterogeneity was observed among these studies ( $I^2 = 90.2\%$ ;  $Q = 500.8$ ,  $df = 49$ ,  $p = 0.00$ ). The subsequent analysis consisted of subdividing the trained subjects into two different sports: ultramarathon and triathlon. These sports were chosen based on their higher frequency on the trials. In addition, these sports are known to impose a high burden on the organism, challenging the immune system.

### Trained: acute exercise—IgA levels in ultramarathon (GRADE A)

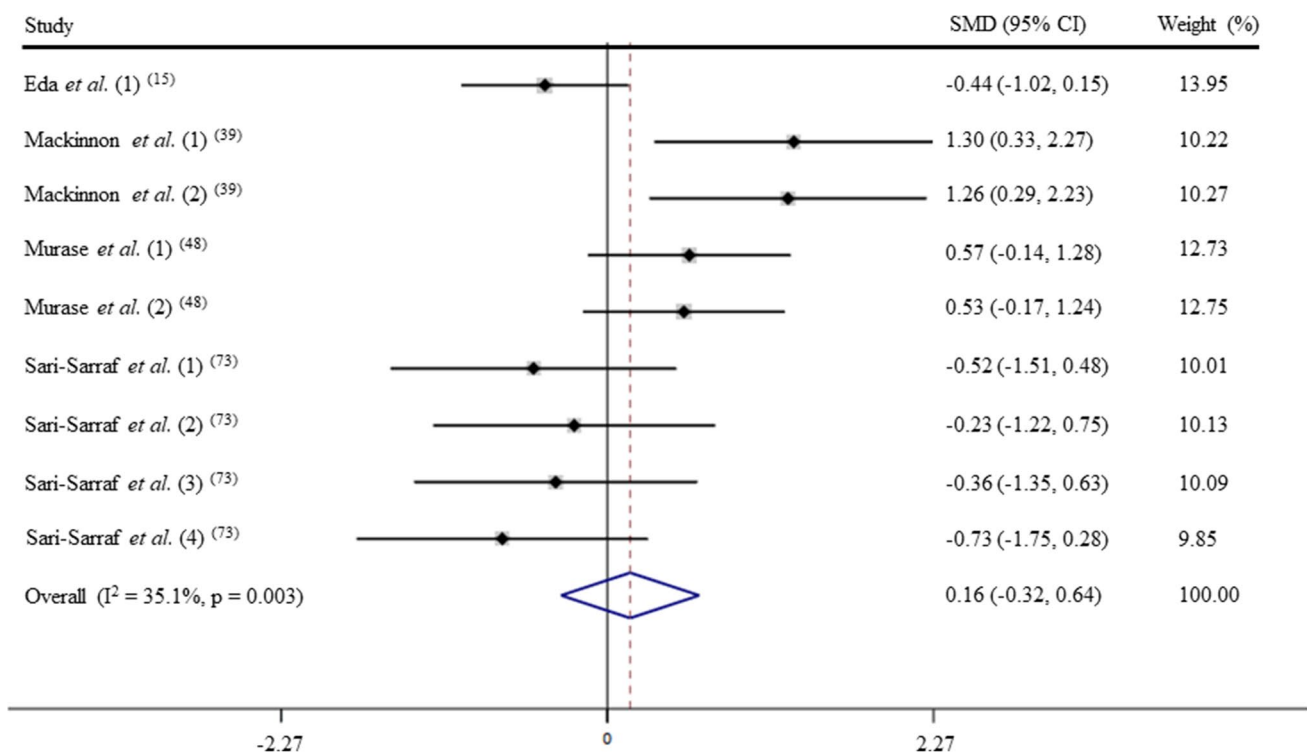
After pooling the data from 8 trials, the mean effect size was 1.60 (95% CI:  $0.20$  to  $3.01$ ), which indicates that ultramarathon induces a large and significant increase on IgA levels ( $p < 0.05$ ; Fig. 4). According to a random effects analysis, high heterogeneity was observed among these studies ( $I^2 = 97.5\%$ ;  $Q = 358.8$ ,  $df = 9$ ,  $p = 0.00$ ).

### Trained: acute exercise—IgA levels in triathlon (GRADE C)

After pooling the data from 16 trials, the mean effect size was 0.13 (95% CI:  $-0.06$  to  $0.33$ ), which indicates that triathlon has a non-significant effect on IgA levels ( $p > 0.05$ ; Fig. 5). According to a fixed effects analysis, no heterogeneity was observed among these studies ( $I^2 = 28.1\%$ ;  $Q = 20.87$ ,  $df = 15$ ,  $p = 0.14$ ).

### Chronic physical training and IgA levels (GRADE B)

After pooling the data from 16 trials, the mean effect size was  $-0.51$  (95% CI:  $-0.95$  to  $-0.07$ ), which indicates that the chronic physical training induces a moderate and significant decrease on IgA levels ( $p < 0.05$ ; Fig. 6). According to a random effects analysis, high heterogeneity was



**Fig. 2** Forest plot of IgA levels in response of acute exercise in untrained subjects. SMD: standardized mean difference

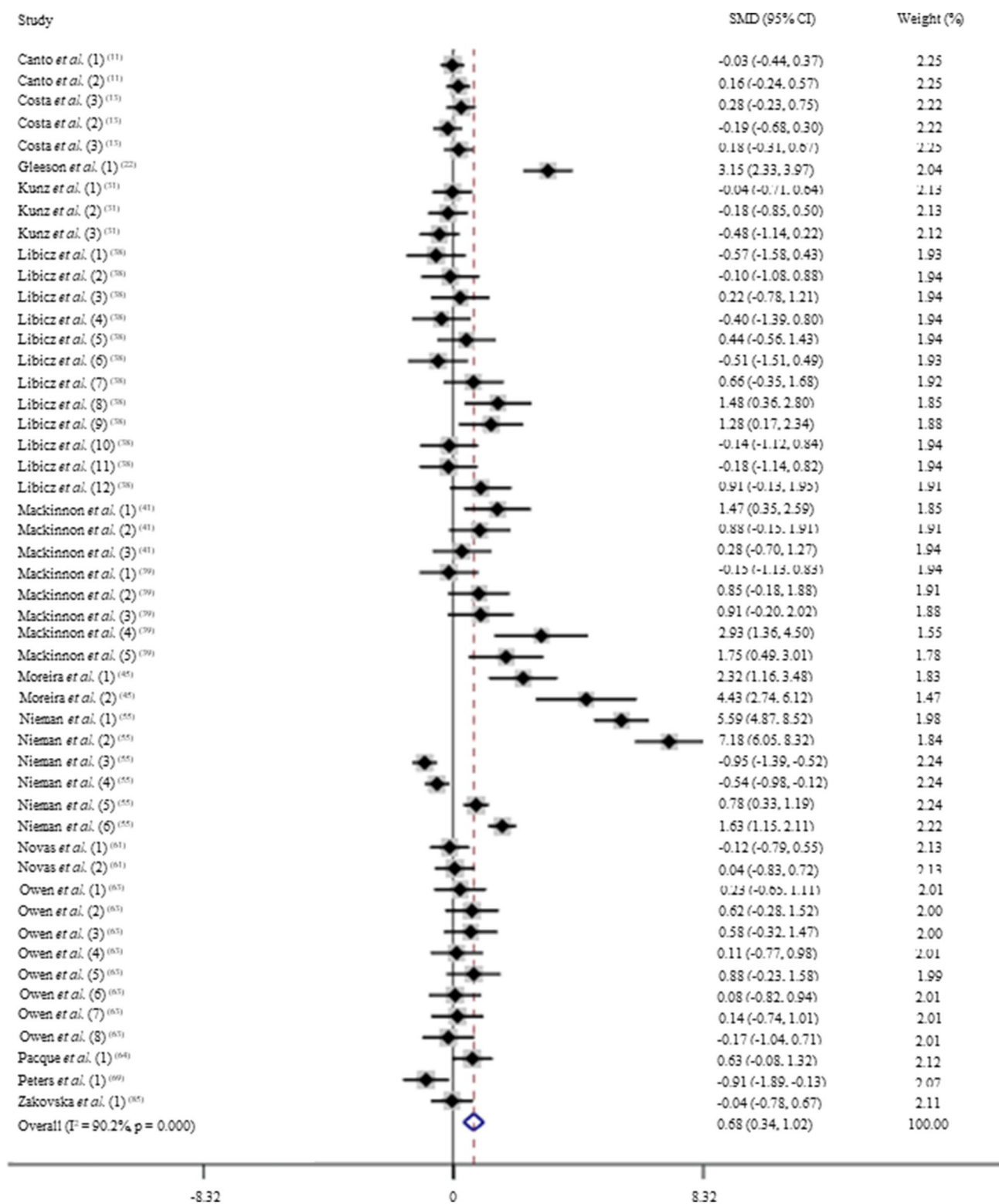
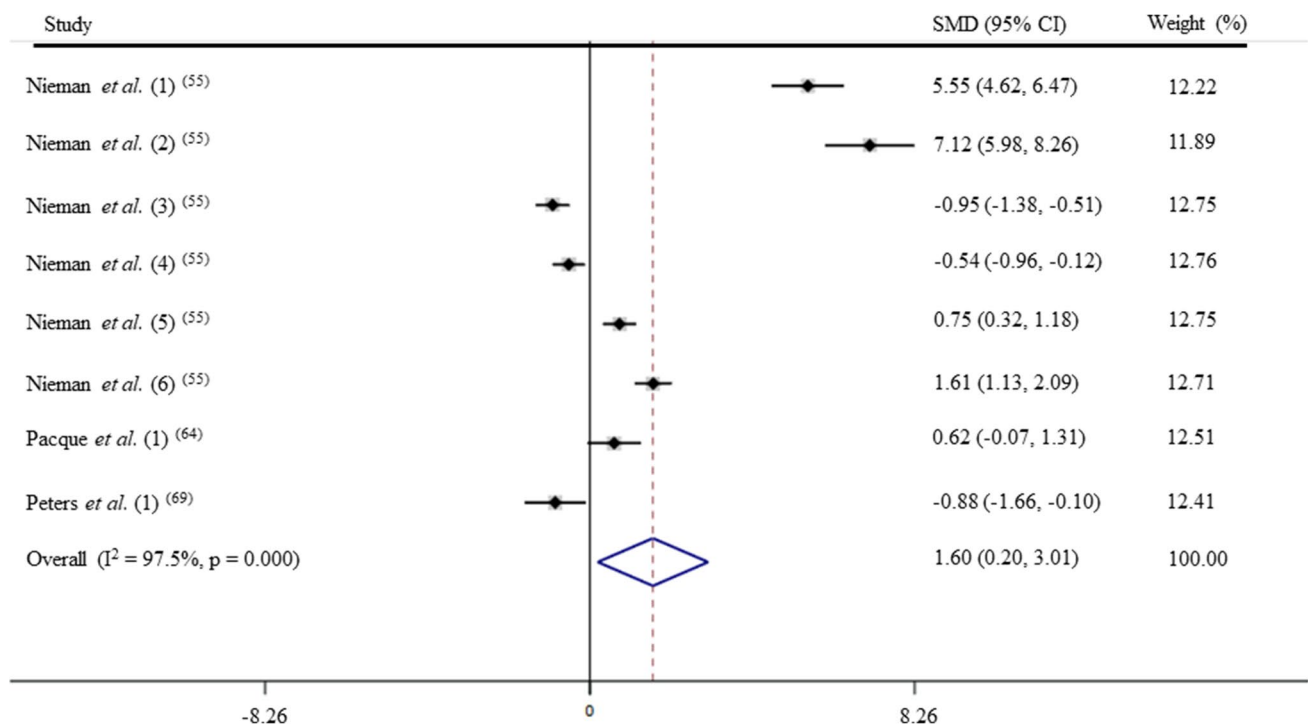


Fig. 3 Forest plot of IgA levels in response of acute exercise in trained subjects. SMD: standardized mean difference



**Fig. 4** Forest plot of IgA levels in response of acute exercise in ultramarathoner. SMD: standardized mean difference

observed among these studies ( $I^2 = 89.6\%$ ;  $Q = 144.1$ ,  $df = 15$ ,  $p = 0.00$ ).

### Chronic physical training and IgA levels non-military personnel (GRADE C)

Due to the fact that the IgA response to chronic physical training was greatly affected by military coaching, IgA levels were analysed in non-military trained individual separately. After pooling the data from 14 trials, the mean effect size was  $-0.17$  (95% CI:  $-0.53$  to  $0.18$ ), which indicates that the chronic physical training has a non-significant effect on IgA levels ( $p > 0.05$ ; Fig. 7). According to a random effects analysis, high heterogeneity was observed among these studies ( $I^2 = 83.3\%$ ;  $Q = 78.0$ ,  $df = 13$ ,  $p = 0.00$ ).

### Chronic physical training and IgG levels (GRADE C)

After pooling the data from 6 trials, the mean effect size was  $-0.31$  (95% CI:  $-1.49$  to  $0.88$ ), which indicates that the chronic physical training has a non-significant effect on IgG levels ( $p > 0.05$ ; Fig. 8). According to a random effects analysis, high heterogeneity was observed among these studies ( $I^2 = 94.0\%$ ;  $Q = 83.5$ ,  $df = 5$ ,  $p = 0.00$ ).

### Relation between IgA levels and URTI incidences

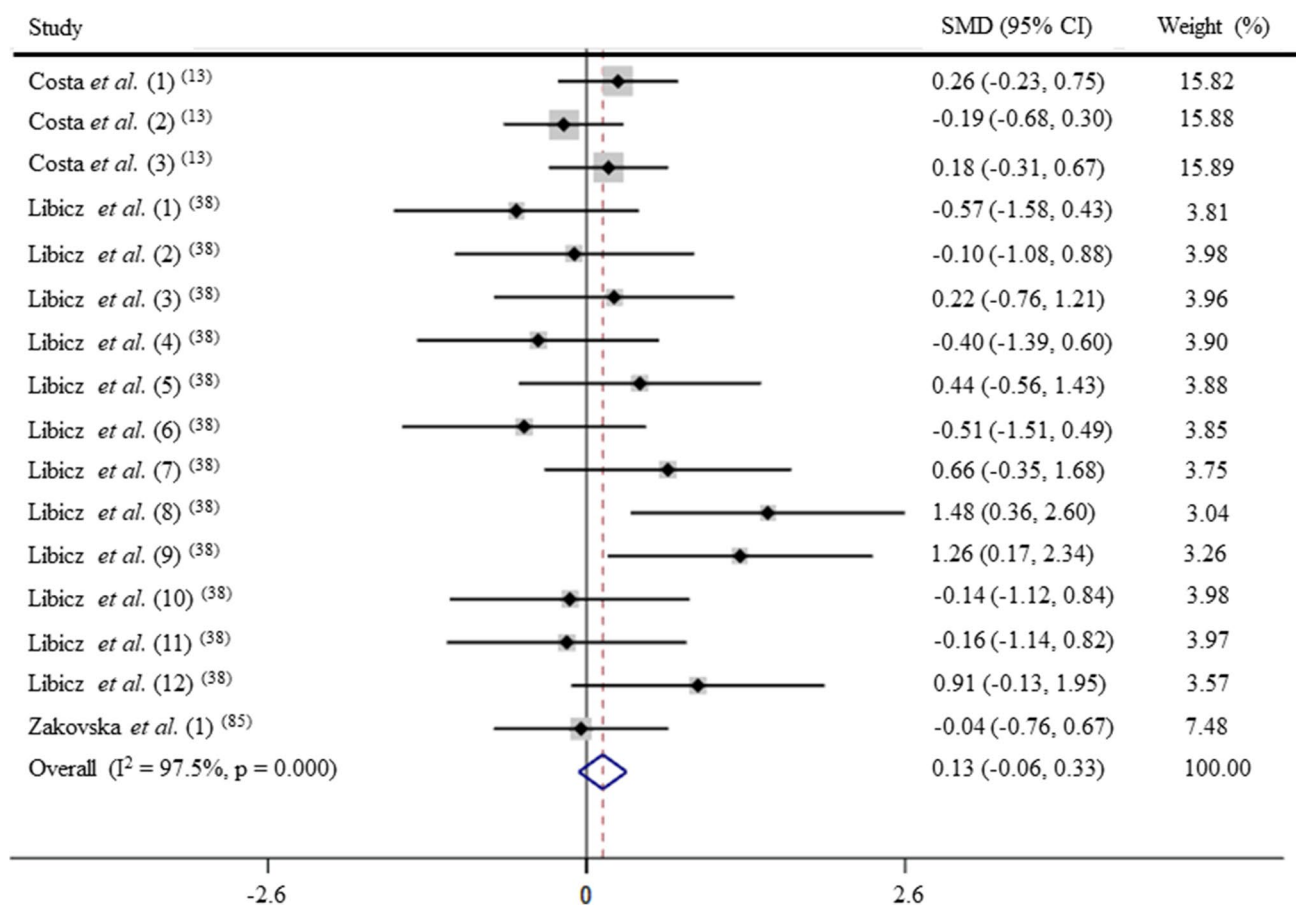
A correlation between the URTI incidence and IgA levels in response to exercise was performed with data from three studies that simultaneously analyzed these variables. A strong negative correlation between the variables was found ( $r = -0.97$ ,  $p = 0.13$ ; Fig. 9).

### Risk of bias

The risk of bias was assessed in 43 studies in the systematic review. Approximately 25% (11 studies) of them did not blind the participants or researchers. This limitation seems to be related to the characteristics of the studies' experimental protocols. Nevertheless, most of the studies evaluated in the present systematic review consistently controlled the risk of bias and, therefore, were deemed moderate to high quality (Supplementary Table 1).

### Discussion

The present systematic review and meta-analysis demonstrates that acute exercise increases the IgA levels in trained subjects, but does not affect its levels in untrained subjects. Such increase in IgA levels induced by acute exercise is greater in trained individual that performed ultramarathon in comparison with those that executed triathlon. Although,



**Fig. 5** Forest plot of IgA levels in response of acute exercise in triathletes. SMD: standardized mean difference

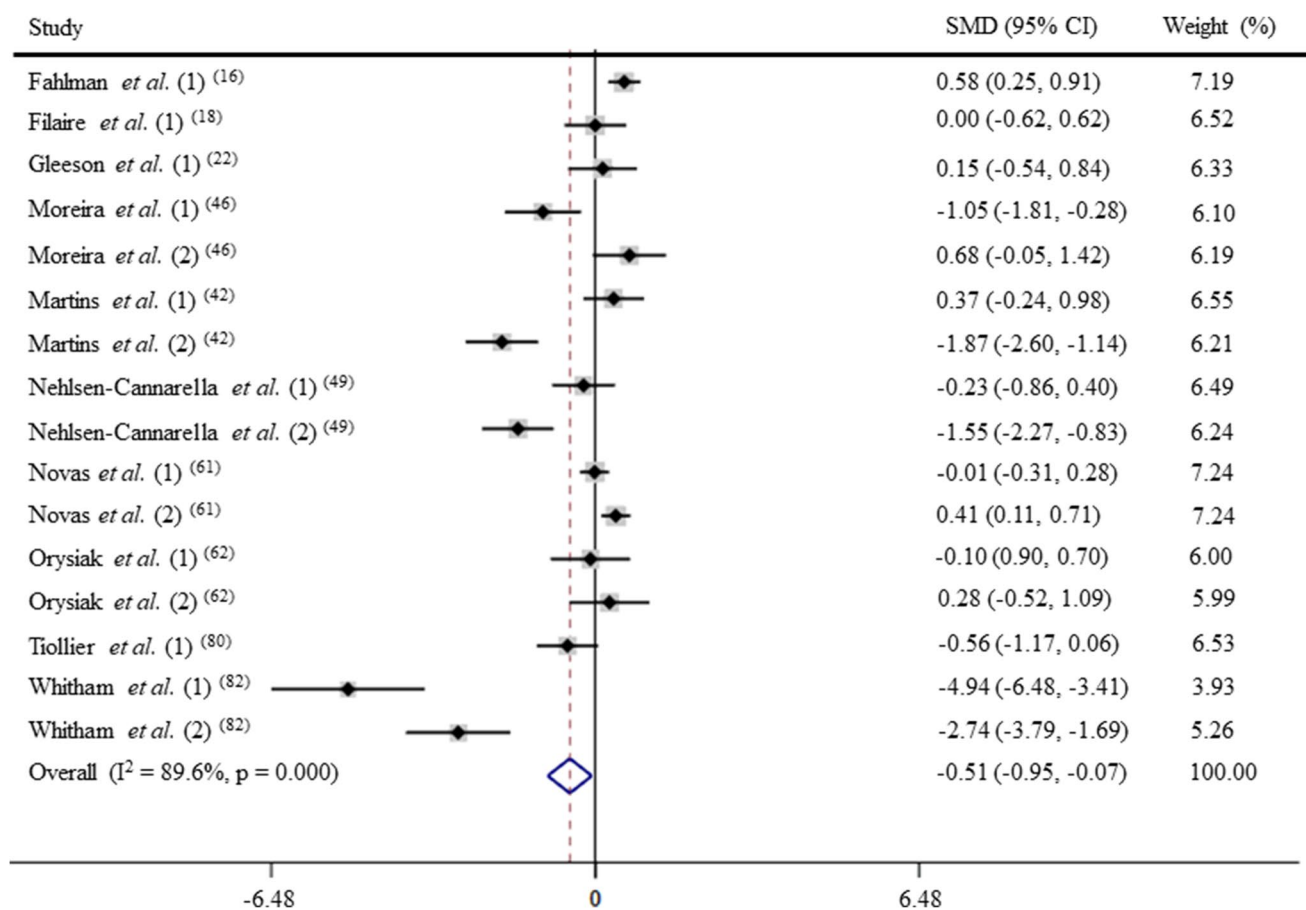
trained individuals' present elevated IgA response to acute exercise, these individuals have decreased IgA baseline. On the other hand, the basal IgA levels were reduced by chronic physical training. However, when data from non-military personnel are excluded from the trained individuals group, the remaining data reveals that chronic physical training does not alter IgA levels. In addition, chronic physical training does not change IgG levels. These data indicate that acute exercise positively influences IgA levels in trained individuals, being this effect pronounced when a strenuous exercise such as ultramarathon is executed. Moreover, chronic physical training response over IgA levels seems to depend on the characteristics of the subject's chronic physical training since non-military personnel presented unchanged IgA levels. The present analysis brings important information for exercise practitioners and athletes and provide support for the better understanding of the beneficial effects of exercise in fighting infections such as URTI through modulation of immunoglobulin levels.

The execution of acute, moderate and vigorous aerobic exercise of less than 60 min duration is known to enhance the recirculation of agents that play critical roles in immune

defense activity and metabolic health, including immunoglobulins [55]. Thus, this type of exercise is now seen as an immune system adjuvant. However, in response to prolonged and intensive exercise, and in competition events, salivary IgA output and other biomarkers of immune function are altered for several hours to days [52, 59]. These immune changes occur in different body sites such as the upper respiratory tract mucosal tissue and the lungs [55]. Secretory IgA plays an important role in the organism's defense against respiratory illness through immune exclusion at mucosal surfaces, intra-epithelial viral naturalization and immune elimination across mucosal surfaces [7, 20, 42].

The results of the present study indicate that acute exercise does not modify IgA levels in untrained individuals. It does only when acute exercise is performed by trained subjects, particularly after a strenuous bout of exercise. It is difficult to provide a definitive description of the acute effects of exercise on salivary IgA concentration [20]. Evidence demonstrated that athletes seem to experience a transitory decrease in s-IgA for up to 24 h post strenuous training sessions or competition [66]. It is during this "open window" period of immune depression that athletes are thought to be





**Fig. 6** Forest plot of IgA levels in response of physical training. SMD: standardized mean difference

at greatest risk of URTI [49]. In fact, low IgA concentration and secretion rate have been associated with increased incidence of URTI in athletes [16, 20]. On the other hand, basketball players have shown an increase of IgA after competitive games [77]. This increase in IgA levels possibly represents a beneficial effect of chronic physical training on immunity [20].

Upper respiratory tract infection during a critical training period may have a deleterious effect on the athlete's ability to train and compete [20, 69]. The increase in the incidence of URTI in athletes is still under debate in the literature. However, it is known that URTIs are the most common infection in highly trained athletes [67, 71]. Therefore, it is plausible to predict that chronic exercise training protocols that cause a reduction in IgA levels increase the incidence of URTI mostly in athletes than in the general sedentary population. In the present study, trained athletes present such a reduction of IgA levels. Interestingly, this response is unaffected in non-military trained individuals. Among the studies evaluated in the present review, only three simultaneously assessed the incidence of URTI and IgA levels. Despite of the few

studies, the relationship between IgA levels and the incidence of URTI seems clear (Fig. 9). Even though no significant response was found, probably as a consequence of the small number of available studies, the sample of individuals ( $n = 125$ ) is substantial. Therefore, to better establish this relationship between URTI incidence and IgA levels, a higher number of trials would be necessary.

Military training environment is a situation associate with several stressors such as intense physical training, energy deficit, psychological pressure, and sleep deprivation. The combination of these stressors enhances the susceptibility of detrimental effects on the immune system [79]. In the present study, military trained individuals show a greater reduction in IgA levels compared to non-military ones, probably due to an immune reaction to the combined actions of these stressors.

Small changes in IgG levels may be relevant for mucosal resistance to infections in the respiratory tract [7, 20]. The results of the meta-analysis indicate that chronic physical training does not alter baseline IgG levels. However, it should be noted that the number of studies and trials that carried out this type of evaluation was also small.

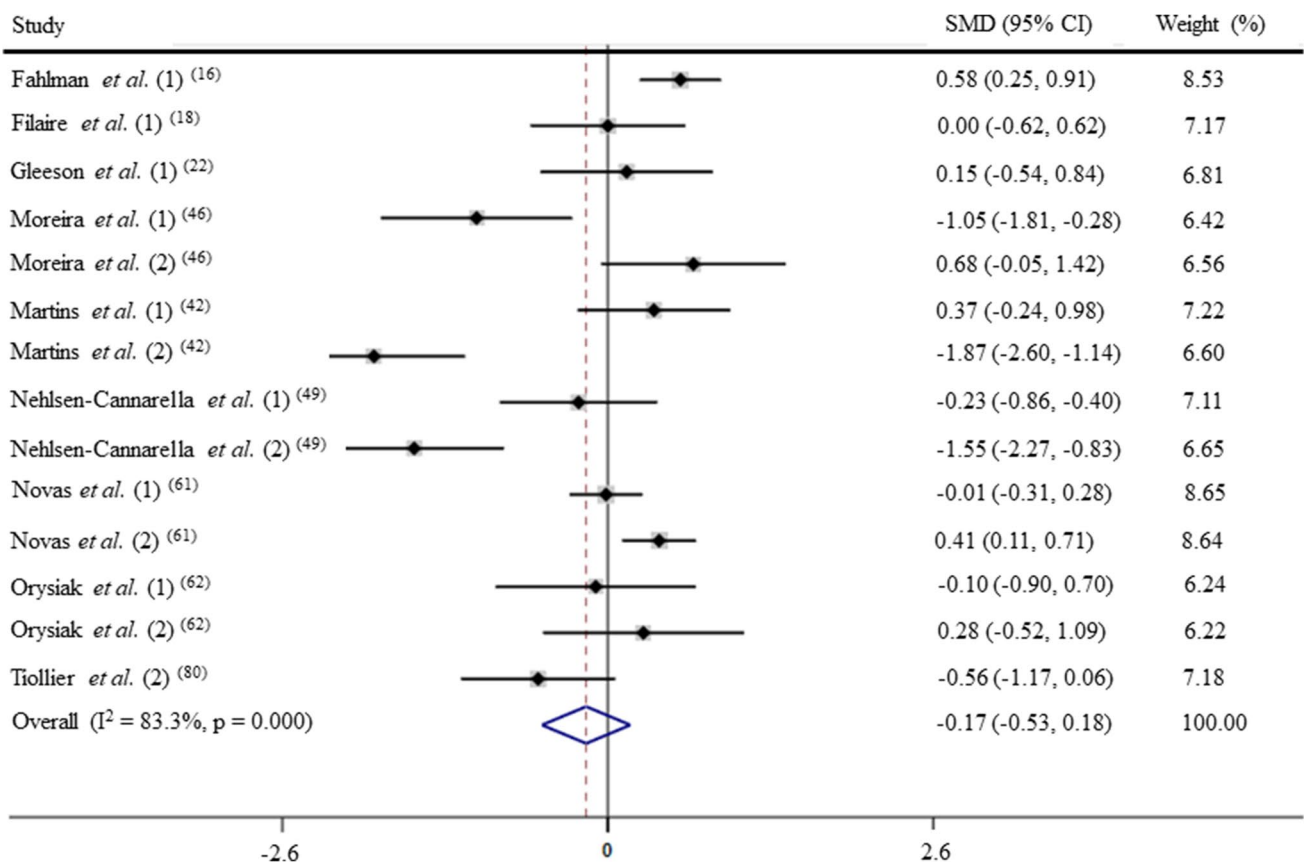


Fig. 7 Forest plot of IgA levels in response of physical training in non-military personnel. SMD: standardized mean difference

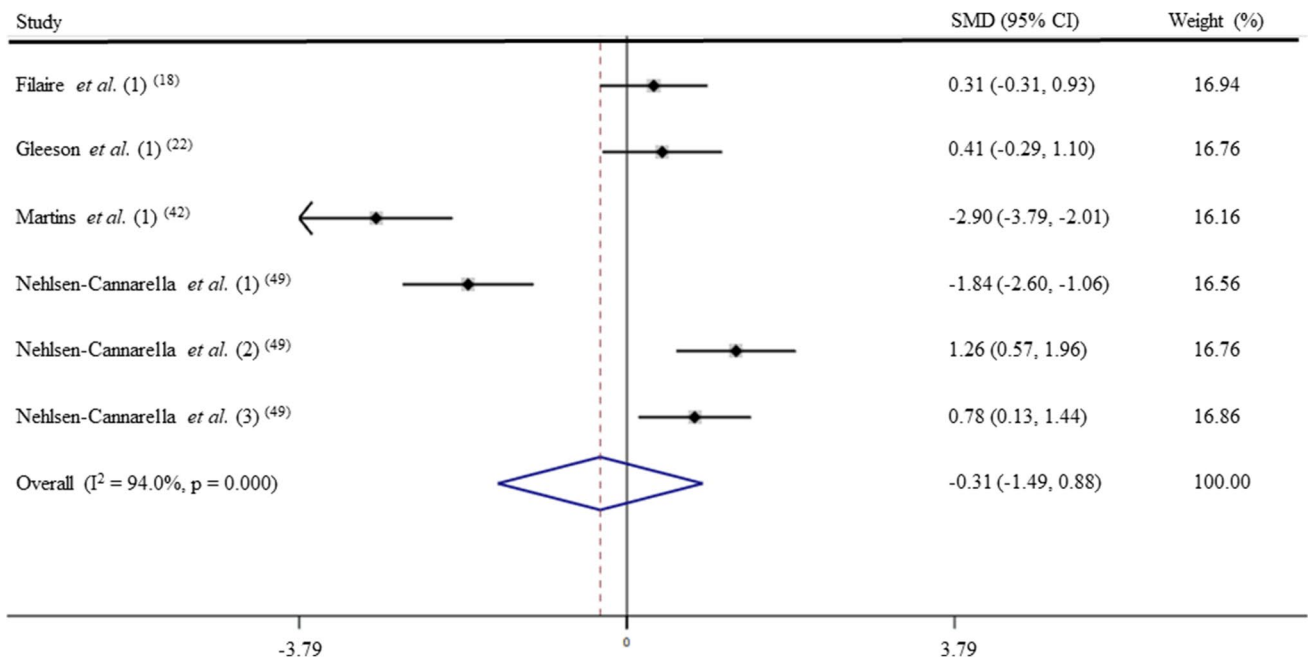
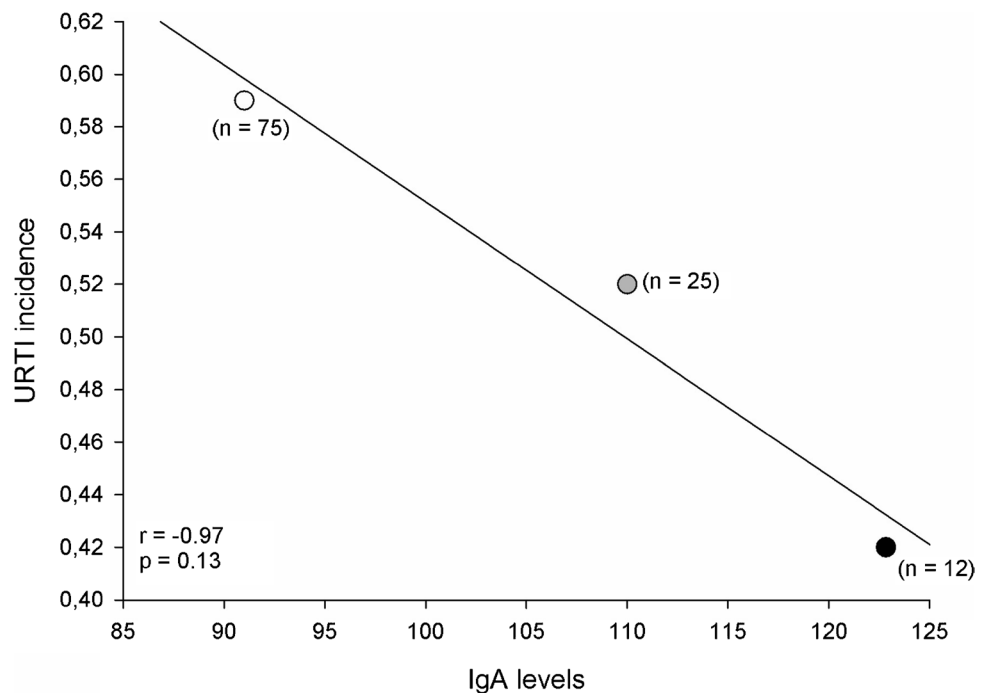


Fig. 8 Forest plot of IgG levels in response of physical training. SMD: standardized mean difference



**Fig. 9** Correlation between IgA levels and the incidence of URTI in athletes



Exercise-induced immunomodulation appears to be dependent on the relationship between exercise intensity, duration and frequency [74]. As suggested by Nieman [53], the risk of upper tract infection is lower in the case of moderate-intensity exercise. This is supported by the concept that the relationship between the exercise load and the risk of URTI has the shape of the letter “J.” This means that both too little and too much physical activity may increase the risk of upper respiratory tract infection [51]. Therefore, while regular practice of moderate physical exercise can be considered as a tool to prevent respiratory infections, vigorous intensity physical exercise is usually associated with adverse events [31, 73]. Such scenario implies that the effect of physical exercise on immunoglobulin levels may take into account the subject’s physical training. In fact, elite athletes frequently report upper respiratory symptoms associated with decreased efficiency of humoral immune response on a mucosal level, manifesting predominantly as lowered secretory IgA levels [31].

In this context, the present study demonstrated that military trained individuals showed a greater reduction in IgA levels compared to non-military ones. We propose that this is probably due to the military training environment, which mimics a strenuous training load. Similarly, to elite athletes, who have an increased chance of URTIs associated with decreased IgA [31], this creates the possibility that military personnel may experience URTI symptoms as a result of greater infection susceptibility due to vigorous intensity physical exercise. Still, the issue of exercise load-related infection susceptibility requires further research.

Leandro et al. [33] state that exercise of long duration and/or intense exercise (> 2 h and/or > 80% of maximal oxygen uptake,  $VO_{2max}$ ) is associated with markers of immunosuppression, including reduced production of salivary IgA and plasma IgM and IgG. Therefore, long duration and/or intense exercise can make people more susceptible to infections (mainly URTI), which can increase the risk of contamination and worsening of COVID-19 symptoms [33]. COVID-19’s high morbidity and mortality is more prevalent in older people (> 60 years), but the health of a young and well-fit population or even athletes should also be noted since there are still many answers to be given in relation to COVID 19 [28]. Thus, understanding whether acute exercise or even chronic physical training increases the susceptibility to URTI or even COVID is very important. And for that, it is necessary that adequate guidance becomes available [28].

Although we found it interesting/important to compare gender and age, this was not possible in the present study, because the number of studies was insufficient for this analysis to be carried out. We point out that Fondell et al. [18], whose study included 1509 subjects divided into groups of men and women aged 20–60 years, found that physical activity reduces the incidence of upper respiratory tract illness in both gender, regardless of age. In another study, Akimoto et al. [1] demonstrated that regular physical training increases salivary IgA levels in healthy subjects (18 males and 27 females) over 60 years of age.

## Conclusion

The present systematic review and meta-analysis indicates that acute exercise positively influences IgA levels in trained individuals, being this effect pronounced when a strenuous exercise such as ultramarathon is executed. Moreover, chronic physical training response over IgA levels seems to depend on the characteristics of the subject's physical training since non-military personnel present unchanged IgA levels.

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**Author contribution** All authors have contributed to the development of the research question and study design. LRD, HOC, FRD, and GMO developed the literature search. LRD, HOC, FRD, GMO, JGRP, RPA, MCM, HFGL, LHRL, and CCC performed the study selection. LRD, HOC, and FRD analyzed the data. LRD, HOC, FRD, GMO, JGRP, RPA, MCM, HFGL, LHRL, and CCC performed the study selection. LRD, HOC, and FRD interpret the results and wrote the manuscript. All authors reviewed and approved the manuscript.

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**Data availability** Not applicable.

**Code availability** Not applicable.

## Declarations

**Ethics approval** Not applicable.

**Consent to participate** Not applicable.

**Consent for publication** Not applicable.

**Competing interests** The authors declare no competing interests.

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