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Physical Activity and Immunity in Pediatric Populations: A Comprehensive Review

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Abstract:

Physical activity in childhood is a powerful, scalable determinant of immune health that complements vaccination, nutrition, and sleep in pediatric care. Regular moderate exercise enhances mucosal, innate, and adaptive immunity, while sedentary behavior and obesity promote chronic inflammation and impaired host defense. These changes reduce upper respiratory tract infections (URTIs) and improve vaccine response[1-4].

Mechanistically, moderate exercise mobilizes natural killer and $CD8^+$ T cells, enhances neutrophil function, and increases salivary secretory IgA, improving viral clearance without causing prolonged immunosuppression seen in adults. Children show blunted stress hormone responses and rapid immune recovery, suggesting lower immunosuppressive risk[5-8].

Epidemiologic studies show each additional 1,000 daily steps reduces URTI symptoms by about 4 days, explaining a significant portion of infection variability. Higher training frequency links to fewer infections; higher screen time increases lower respiratory infections. These findings support daily movement as a core infection prevention strategy.[1,9]

Clinically, age-appropriate aerobic activity (~60 minutes moderate-to-vigorous daily) should be prescribed alongside vaccination and nutrition. For children with obesity or chronic illness, tailored exercise programs reduce inflammation and restore immune homeostasis. As research advances, integrating mechanistic and practical approaches will optimize “movement as immune medicine” through childhood and adolescence.

Keywords: physical activity; pediatric exercise immunology; innate immunity; secretory IgA; natural killer cells; childhood obesity; upper respiratory tract infection; vaccination; sedentary behavior.

Introduction:

Physical inactivity has emerged as a critical global health threat to pediatric populations, now recognized as one of the leading risk factors for worldwide mortality[10]. Despite decades of public health messaging, the epidemic of sedentary behavior continues to accelerate. Contemporary epidemiological data reveal that approximately one in five adolescents globally does not meet WHO physical activity guidelines, with female adolescents particularly affected, showing inactivity prevalence of 84.7% compared to 77.6% in males. This alarming trend establishes the foundation for understanding how sedentary lifestyles during formative years create cascading immunological consequences that persist into adulthood[11].

Concurrently, the prevalence of childhood obesity has reached epidemic proportions, with obesity affecting immune homeostasis throughout development. Childhood obesity is characterized by persistent chronic, low-grade sterile inflammation that fundamentally dysregulates immune function—altering baseline immune cell activation states, compromising pathogen defense capacity, impairing vaccine responsiveness, and paradoxically increasing susceptibility to both infections and autoimmune disease. The chronic inflammatory adipokine milieu in obese children—characterized by elevated leptin, decreased adiponectin, and infiltration of pro-inflammatory adipose tissue macrophages—creates an immunologically hostile environment that extends beyond metabolic dysfunction to impair CD4+ and CD8+ T cell function, reduce regulatory T cell (Treg) populations, and suppress mucosal immunity. Physical activity emerges as a potentially modifiable, cost-effective, and widely accessible intervention capable of reversing obesity-induced immune dysregulation through reductions in

visceral adiposity, normalization of adipokine signaling, and restoration of immune cell populations[3].

The relationship between sedentary behavior and immune competence is paradoxical: children are biologically equipped with larger lymphoid tissues relative to body size than adults, yet contemporary sedentary behaviors appear to underutilize and ultimately attenuate this immunological potential. Current guidelines specify that children and adolescents aged 5–17 years should accumulate an average of 60 minutes daily of moderate-to-vigorous intensity aerobic physical activity across the week, reduce the time spent sitting or lying down and aim to spread activity throughout the day[12]. Yet the growing evidence base reveals that children failing to meet these thresholds are at risk of diminished vaccine-induced antibody titers and increased susceptibility to upper respiratory tract infections (URTIs)[1,13].

Importantly, acute immune responses to exercise differ substantially between children and adults, with pediatric subjects demonstrating considerably smaller magnitude NK cell mobilization, absent or minimal post-exercise lymphopenia (in contrast to the classical "open window" immunosuppression seen in adults), and smaller cytokine responses to identical exercise stimuli. While adult exercise immunology has characterized high-intensity exercise as producing transient immunosuppression through lymphopenia and sIgA suppression—phenomena attributed to the magnitude of catecholamine surge and cortisol elevation—pediatric populations show markedly blunted versions of these responses, reflecting developmental differences in neuroendocrine axis maturation. This developmental-age interaction is clinically significant: it suggests that exercise-induced immunosuppression (the proposed mechanism for the "open window" phenomenon in which athletes experience elevated URTI risk post-competition) may be substantially less pronounced in pediatric athletes, potentially explaining epidemiological observations that regular child athletes experience fewer infections than non-athletes despite occasional exposure to intense training loads[6].

This review synthesizes current evidence on the mechanisms by which physical activity modulates immune function across pediatric populations. We further contextualize physical activity within the constellation of pediatric health determinants: as a cost-effective, sustainable, and widely accessible non-pharmacological intervention with potential applications across preventive medicine.

How Physical Activity Modulates Immunity in Pediatric Populations

Natural killer cells represent the primary innate immune defense against viral pathogens and constitute a major mechanism by which physical activity reduces upper respiratory tract infection (URTI) susceptibility in pediatric populations. NK cells recognize and eliminate virus-

infected or transformed cells through perforin and granzyme-mediated cytotoxicity, independent of prior antigen exposure or major histocompatibility complex (MHC) recognition[14].

During acute exercise, NK cells undergo rapid mobilization from lymphoid tissues and bone marrow into the bloodstream through catecholamine-mediated β_2-adrenergic receptor (β_2-AR) signaling. This mechanism demonstrates remarkable specificity: Graff et al. (2018), publishing in *Brain, Behavior, and Immunity*, documented that β_2-AR blockade with nadolol (which crosses the blood-brain barrier) selectively prevented mobilization of NK cells, non-classical monocytes, and differentiated CD8+ T cell subsets while leaving other immune cell types (CD4+ T cells, naive CD8+ T cells, classical monocytes) unaffected. This finding unequivocally demonstrates that NK cell mobilization depends on direct catecholamine signaling through β_2-AR, independent of indirect sympathetic nervous system influences on other cell types[7].

The sustained mobilization of NK cells into the post-exercise recovery period (lasting 60+ minutes) creates a prolonged window of enhanced immunosurveillance. When these mobilization episodes repeat daily (as in regularly active children), cumulative NK cell surveillance directly explains the 4.1-day reduction in URTI symptoms per 1,000 daily steps observed in prospective epidemiological studies[1].

Unlike adults who demonstrate marked post-exercise lymphopenia during recovery (the classical "open window" immunosuppression hypothesis), children show minimal lymphopenia and actually demonstrate sustained NK mobilization into recovery. This developmental difference may explain why pediatric athletes experience fewer URTIs than sedentary children despite occasional intense training loads—the immunosuppressive mechanisms that limit adult athletes may operate less forcefully in children due to maturational differences in neuroendocrine axis responsiveness[6].

Neutrophils represent the most abundant leukocyte population and play critical roles in bacterial defense through mechanisms including phagocytosis and production of reactive oxygen species (ROS). Critically, pediatric neutrophil responses to exercise differ fundamentally from adult responses.

De Almeida-Neto et al. (2023), publishing in *Frontiers in Pediatrics*, documented that neutrophil levels in children do not elevate significantly after intense exercise compared to adults; however, the intracellular oxidative stress response of neutrophils is substantially higher in children than in adults. This age-specific difference appears mediated by greater oxygen cost of exercise in children relative to body size and greater dependence on mitochondrial

metabolism for energy production, both of which increase the possibility to generate more RONS during exercise than adults do[6].

Exercise upregulates serum total antioxidant capacity (TAC), catalase activity, and markers of lipid peroxidation (thiobarbituric acid-reactive substances [TBARS]), while typically reducing reduced glutathione (GSH). These responses are transient, with oxidative stress markers returning to baseline within 24 hours of recovery. Critically, antioxidant reserves such as GSH may be lower in children, especially those in chronic intensive training programs, suggesting that children may be susceptible to exercise-induced oxidative damage during periods of excessive training without adequate recovery. This observation has implications for understanding exercise-induced immune changes in pediatric athletes: insufficient antioxidant capacity coupled with overtraining may temporarily compromise neutrophil antimicrobial function through oxidative depletion[15].

Secretory IgA (sIgA) is the primary mucosal defense barrier present in saliva and all respiratory and gastrointestinal secretions. sIgA plays dual anti-bacterial and anti-viral roles at mucosal surfaces, making it the first line of defense against respiratory pathogens. Exercise effects on sIgA demonstrate a clear dose-response relationship with direct clinical implications for URTI susceptibility[8].

Starzak et al. (2016), publishing in *Pediatric Exercise Science*, demonstrated that poor cardiorespiratory fitness (CRF) and/or obesity in children are associated with compromised mucosal immunity, as measured by reduced salivary sIgA secretion rate. This effect was independent of other confounders and appears driven by elevated sympathetic nervous system activation and altered autonomic regulation in low-fitness children[16].

The clinical implications for URTI protection are direct: elevated sIgA concentrations enhance the probability of pathogen neutralization at mucosal entry points (respiratory epithelium) before systemic infection can establish. Children with higher baseline sIgA levels and activity-enhanced sIgA secretion demonstrate reduced URTI symptom duration, whereas sedentary children with suppressed sIgA levels experience prolonged symptom duration upon respiratory pathogen exposure[1,16].

The HPA axis orchestrates endocrine responses to physical and psychological stress through release of corticotropin-releasing hormone (CRH), adrenocorticotropic hormone (ACTH), and finally cortisol from the adrenal cortex.

Wegner et al. (2019), in *Psychoneuroendocrinology*, investigated effects of different exercise training interventions on cortisol awakening response (CAR) in children and found that cardiovascular and motor exercise exert different effects on HPA axis activity. In 9–10-year-old

children, cardiovascular exercise training increased CAR (reflecting HPA axis hyperresponsiveness), while motor exercise training decreased CAR (reflecting downregulation). These divergent responses likely reflect different neuromuscular demands and stress signaling pathways activated by different exercise modalities[17].

Another significant study demonstrated that children with highest levels of overall physical activity showed minimal cortisol responses to a standardized psychosocial stressor (Trier Social Stress Test for Children), whereas sedentary children showed significant cortisol increases. This finding indicates that regular exercise training enhances stress resilience and reduces HPA axis reactivity to psychosocial stressors—a mechanism that indirectly enhances immunity by preventing stress-induced immunosuppression[18].

Article in *Frontiers in Pediatrics*, documented that the immune system may be more prepared to protect the body from possible infections during puberty, when the period of peak lymphoid tissue expansion occurs. This period is associated with expansion of the thymus gland, which produces and promotes maturation of T lymphocytes (CD4+ and CD8+) and secretion of immunoglobulins (particularly IgG through thymic plasma cells)[6].

Regular physical activity appears to enhance lymphoid tissue preservation during the post-pubertal involution phase. Active children show slower rates of thymic involution and greater lymph node volumes compared to sedentary peers, resulting in maintenance of expanded immune surveillance capacity into late adolescence[6].

Upper Respiratory Tract Infections (URTIs):

Upper respiratory tract infections (URTIs) represent the most common acute illness in pediatric populations, with profound impacts on family quality of life, school absenteeism, and healthcare resource utilization. Ostrzyżek-Przeździecka et al. (2019), in *The Association of Physical Activity and Sedentary Behaviors with Upper Respiratory Tract Infections and Sleep Duration in Preschool Children*, documented that recurrent respiratory infections are the primary reason for general practitioner intervention in pediatric populations, and that "children of all ages spend more time on sedentary behavior, eat less nutritious food and spend less time sleeping...adversely affecting the immune system."[19]

The most rigorously designed prospective study examining the relationship between physical activity and URTIs in pediatric populations was conducted by Ostrzyżek-Przeździecka et al. (2023), published in *Pediatric Research*, studying 104 Polish children aged 4–7 years.

This study employed objective, continuous measurement of physical activity using accelerometer technology (Garmin Vivo Fit 1 pedometer worn 24 hours/day for 40 days) combined with standardized, daily parental symptom reporting using the validated Wisconsin

Upper Respiratory System Survey for Kids for 60 consecutive days. This prospective design with continuous monitoring represents the gold standard for establishing relationships between activity and infection frequency, avoiding the recall bias inherent in retrospective reports[1].

The central finding was quantitatively striking: each increase of 1,000 daily steps was associated with a 4.1-day reduction in URTI symptom days over the 60-day observation period. More statistically important, the average daily step count on healthy days was a significant determinant of total URTI symptom days, accounting for 43.5% ($p<0.001$) of the variance in infection burden. This represents extraordinarily high explanatory power for a single behavioural variable and far exceeds typical effect sizes for pediatric health interventions[1].

To translate this into clinical context: among 47 children whose average daily step count during the initial 14-day "run-in" period was only 5,668 steps ("less-active group"), the cumulative number of person-days with URTI symptoms over the following 46 days was 947 days. In contrast, among 47 children whose initial average daily steps numbered 9,368 ("active group"), the cumulative person-days with URTI symptoms over the same 46-day period was 724 days—a difference of 223 person-days, representing a 19% reduction in infection burden based on baseline activity levels alone[1].

Melunović et al. (2024), published in *Medicinski Glasnik* independently confirmed the sedentary behavior-infection association in a separate, geographically distinct cohort of preschool children. The study enrolled **1**29 preschool children with a mean age of 72.2±4.2 months (approximately 6 years), with slightly higher male representation (65 males, 50.4%; 64 females, 49.6%). The study was conducted across multiple pediatric departments in Sarajevo, Bosnia and Herzegovina, representing an independent population from a different geographic region, healthcare system, and socioeconomic context compared to the Ostrzyżek-Przeździecka Polish cohort. Upper respiratory tract infections showed statistically significant negative correlations with training frequency—meaning increased physical activity directly predicted reduced URTI frequency[9].

The stronger association on weekends ($p=0.005$ vs. $p=0.041$ for weekdays) suggests that weekend physical activity—which is typically more discretionary and intensive—provides particularly strong URTI protection. This pattern aligns with mechanistic expectations: weekend physical activity often involves more vigorous exercise and outdoor exposure, generating stronger NK cell mobilization and enhanced mucosal immunity compared to weekday activity[9].

Global health organizations recommend specific exercise parameters that optimize immune benefit while minimizing suppression risk: *"Exercise at recommended workloads (150–300*

minutes per week as defined by multiple public health agencies) has proven effective in enhancing immune cell function, strengthening the body's anti-infection capacity, and improving overall defense." Regular moderate-intensity training demonstrates: lower risk of upper respiratory tract infections (URTIs), improved survival rates with acute pneumonia, mitigation of age-related immune decline, consistent enhancement of immune cell function without suppression[20].

Obesity-related immune dysfunction: Chronic Inflammation, Adipokine Dysregulation, and Restoration Through Exercise

Childhood obesity has become an epidemic affecting approximately 200 million school-age children globally, with 40–50 million classified as obese. Critically, 70% of obese adolescents progress to obesity in adulthood, establishing childhood as the critical window for intervention. Beyond metabolic complications, pediatric obesity fundamentally dysregulates immune function, creating a state of chronic low-grade systemic inflammation that perpetuates infection susceptibility and vaccine nonresponse[21].

Obese children demonstrate abnormal autonomic nervous system dysfunction characterized by elevated sympathetic nervous system activity combined with reduced parasympathetic activity. This dual dysfunction (elevated SNS + reduced parasympathetic) directly impairs mucosal immunity. Recall that sIgA secretion requires sympathetic ANS stimulation of salivary glands. While obese children have elevated baseline SNS tone, the dysregulated ANS fails to provide acute exercise-induced sIgA elevation—a paradoxical failure of the very system that should be hyperactive[22].

While sIgA concentrations were elevated (likely due to ANS dysregulation-mediated compensatory overproduction), sIgA secretion rate (the functional measure of mucosal defense) was significantly reduced. Perez et al. (2018), in a correlation study published in a peer-reviewed journal, directly measured this relationship: *"Overweight/obese children showed higher salivary immunoglobulin A (s-IgA) values, with correlations between BMI and body fat percentage [$p<0.05$].* This finding reveals a fundamental dysfunction: despite elevated sIgA concentrations (suggesting attempted compensation), the actual secretion rate and functional mucosal protection are compromised, explaining why obese children experience higher infection rates despite paradoxically elevated baseline sIgA levels[23].

Limitations & Research Gaps

Most of the current understanding of how exercise shapes immune function is still extrapolated from adult studies, and pediatric-specific evidence remains relatively sparse. Even within the available pediatric literature, only a modest number of rigorous randomized controlled trials

(RCTs) exist, and these are often underpowered, disease-specific, and heterogeneous in design. In addition, concerns about publication bias—where positive findings are more likely to be published than neutral or negative results—further limit the reliability and generalizability of the current evidence base[24].

High-quality pediatric RCTs remain scarce, and those that exist are concentrated in narrow clinical niches. In a systematic review of exercise interventions in pediatric oncology, Beller et al. screened 1,448 articles and found only eight eligible studies with 400 children and adolescents with cancer plus 17 healthy controls, of which just three were randomized controlled trials. Although these trials suggested that exercise enhances NK cytotoxicity and may reduce infections and hospital days, the authors explicitly concluded that data were "very limited" and called for more research across different training modalities, intensities, treatment phases, and diagnoses. Outside oncology, key pediatric infection-prevention data such as the Ostrzyżek-Przeździecka URTI study rely on a single-country cohort with 104 preschoolers and short follow-up (60 days), which limits confidence in global generalizability and long-term causal inference[1,25]

Clinical Implications & Translational Recommendations:

Clinical translation of pediatric exercise immunology supports a clear, actionable message: regular, developmentally appropriate physical activity should be prescribed as a core immune-supportive intervention alongside vaccination, nutrition, and infection-prevention measures. Below, recommendations are organized for healthy children and for key clinical populations (obesity, asthma, cancer), with practical guidance on dosing, safety, and integration into routine care[2].

or otherwise healthy children, clinical evidence supports recommending at least 60 minutes per day of mostly aerobic, moderate-to-vigorous physical activity, consistent with WHO and AAP guidance. This volume is associated with fewer days of URTI symptoms in preschoolers, improved mucosal immunity (sIgA), better vaccine responses, and lower long-term NCD risk. Pediatricians should assess physical activity at every well-child visit and provide a concrete "exercise prescription" specifying type (aerobic + muscle-/bone-strengthening), duration (≥60 min/day), and moderate intensity[1,4].

For school-aged children and adolescents, epidemiological and mechanistic work indicates that regular moderate activity lowers ARI risk and severity, including COVID-19, via enhanced innate and adaptive responses and reduced chronic inflammation. Clinicians should frame physical activity as part of "respiratory hygiene": in addition to handwashing, vaccines, and sleep, daily moderate movement meaningfully lowers infection risk.[26]

In all groups, clinicians should reinforce that consistency over months and years matters more than short bursts of intensive activity, and that exercise is a cornerstone, not an optional add-on, for building and maintaining robust immune health in childhood and beyond[2].

Future Research Directions:

Future work needs to move beyond demonstrating that "exercise is good for immunity" toward defining who benefits most, at what dose, via which mechanisms, and under what developmental and disease contexts. Several converging position papers now call for more rigorous, pediatric-specific, mechanistically anchored and clinically oriented research agendas. Systematic reviews in pediatric oncology underscore that current evidence is based on a handful of small trials, often underpowered and focused on surrogate markers. Future research should prioritize adequately powered randomized controlled trials across broader pediatric populations (healthy, obese, asthmatic, autoimmune, cancer, congenital heart disease), with standardized, well-described exercise prescriptions (modality, duration, intensity, frequency), objective physical activity measurement (accelerometry/wearables) instead of parental report, clinically meaningful primary endpoints: validated URTI diaries, pathogen-confirmed ARIs, days of hospitalization, antibiotic courses, vaccine seroconversion and GMT, and disease-specific outcomes (e.g. asthma exacerbations, neutropenic fever)[25].

If these methodological and conceptual advances are implemented, pediatric exercise immunology can progress from promising but fragmented evidence toward a mature, clinically actionable science that defines precise, equitable, and developmentally informed exercise prescriptions for immune health across childhood and adolescence.

Conclusion:

Regular, developmentally appropriate physical activity emerges from this review as a cornerstone, non-pharmacological strategy for strengthening immune competence and reducing infection burden across pediatric populations. Evidence from epidemiological cohorts, mechanistic studies, and early interventional trials converges on the conclusion that moderate habitual exercise enhances mucosal, innate, and adaptive immune function in children, while sedentary behavior and obesity induce chronic low-grade inflammation and immune dysregulation that increase susceptibility to both acute infections and non-communicable diseases.

At the population level, the most compelling pediatric data link daily movement to fewer upper respiratory tract infections (URTIs). In preschoolers, objectively measured physical activity showed a clear dose–response: each additional 1,000 steps per day was associated with roughly

four fewer days of URTI symptoms over two months, with average daily step count explaining more than 40% of the variance in infection days. Independent data from a separate preschool cohort confirmed that higher training frequency correlated with fewer acute respiratory infections, while greater screen time predicted more lower respiratory tract infections. Together, these studies establish low physical activity and high sedentariness as independent, modifiable risk factors for common childhood infections, and support prescribing daily movement as part of routine infection prevention[1,9].

Clinically, these findings justify integrating structured physical activity assessment and counseling into routine pediatric care, in line with WHO recommendations for at least 60 minutes per day of mostly aerobic, moderate-to-vigorous activity for children and adolescents. For healthy youth, this level of activity appears sufficient to support robust mucosal defenses, improve innate and adaptive immune function, and reduce URTI burden. For children with obesity, asthma, cancer, or other chronic conditions, exercise should be framed not as optional lifestyle advice but as a core, evidence-based adjunct therapy that can mitigate inflammation, improve functional capacity, and likely enhance resilience to infections when appropriately tailored and supervised. In this way, paediatric exercise immunology provides a mechanistic foundation for what should become routine clinical practice: prescribing movement as immune medicine from early childhood onward, while continuing to refine dose, modality, and timing through more rigorous, child-focused research.

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Author's contribution

Conceptualization: : M.I.Sroka ; methodology: M.I.Sroka; check: W.Wasiniewska; formal analysis: S.Kosek; investigation: J.Klonowska; resources: T.Kandefer; data curation: M.Barański; writing - rough preparation: R.J.Walkowski; writing - review and editing: M.I.Sroka; visualization: J.Klonowska; supervision: W. Wasiniewska; project administration: T.Kandefer; receiving funding- no specific funding.

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