research

Physical activity monitors and their effect in adults p 143

Impact of covid-19 pandemic on outcomes from childhood infections p 144

Vitamin D and omega 3 fatty acids and risk of autoimmune disease p 146

ORIGINAL RESEARCH Systematic review and meta-analysis

Effectiveness of physical activity monitors in adults

Larsen RT, Wagner V, Korfitsen CB, et al

Cite this as: *BMJ* 2022;376:e068047
Find this at doi: 10.1136/bmj-2021-068047

Study question What is the effectiveness of physical activity monitor (PAM) based interventions among adults?

Methods For this systematic review and meta-analysis, the electronic databases Medline, Embase, SPORTDiscus, CINAHL, and the Cochrane Central Register of Controlled Trials were searched for randomised controlled trials comparing interventions in which adults received feedback from PAMs with control interventions in which no feedback was provided. Two reviewers independently extracted data and assessed risk of bias. The results were synthesised using random effects meta-analyses. The certainty of evidence was rated by the Grading of Recommendations Assessment and Evaluation (GRADE) approach. The three primary outcomes of interest were physical activity, moderate to vigorous physical activity, and sedentary time.

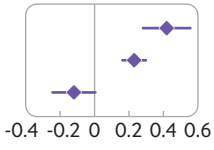
Study answer and limitations 121 randomised controlled trials with 141 study comparisons, including 16 743 participants, were included. The PAM based interventions showed a moderate effect on physical activity, equivalent to 1235 daily steps; a small effect on moderate to vigorous physical activity, equivalent to 48.5 weekly minutes; and a small insignificant effect on sedentary time, equal to 9.9 daily minutes. The certainty of evidence was low for the effect on physical activity, and moderate for the effect on moderate to vigorous physical activity and sedentary time. The effect on physical activity and moderate to vigorous physical activity is well established but might be overestimated owing to publication bias.

What this study adds This study provides evidence for using PAMs for enhancing physical activity and moderate to vigorous physical activity at a time when large, feasible, and scalable interventions are urgently needed.

Funding, competing interests, and data sharing
This project received funding from the European Union's Horizon 2020 research and innovation programme. No competing interests reported. The dataset is available from the corresponding author on reasonable request.

Systematic review registration PROSPERO CRD42018102719.

Outcome	No of studies	No of participants	SMD (95% CI)	SMD (95% CI)	I^2 (%)
Physical activity	103	12 840		0.42 (0.28 to 0.55)	81
Moderate to vigorous physical activity	63	8250		0.23 (0.16 to 0.30)	67
Sedentary time	38	5634		-0.12 (-0.25 to 0.01)	66



Random effects meta-analysis adjusted to Hedges' g on effect of interventions on physical activity, moderate to vigorous physical activity, and sedentary time. SMD=standardised mean difference

Covid-19 control measures and paediatric infections

ORIGINAL RESEARCH Population based observational study

FAST TRACK

Indirect effects of the covid-19 pandemic on childhood infection in England

Kadambari S, Goldacre R, Morris E, Goldacre MJ, Pollard AJ

Cite this as: *BMJ* 2022;376:e067519
Find this at doi: 10.1136/bmj-2021-067519

Study question What is the impact of the covid-19 pandemic on hospital admission rates and mortality outcomes for respiratory infections, severe invasive infections, and vaccine preventable disease among children in England?

Methods This study of 19 childhood infections compared hospital admission rates and mortality outcomes before and after the onset of the covid-19 pandemic in England. Hospital admission data for children aged 0-14 years were obtained for every NHS trust in England. These records were linked to national mortality data collected by the Office for National Statistics. The main outcome measures were numbers of hospital admissions for each infection from 1 March 2017 to 30 June 2021, percentage changes in the number of hospital admissions before and after 1 March 2020, and 60 day case fatality outcomes before and after 1 March 2020.

Study answer and limitations After 1 March 2020, substantial and sustained reductions in hospital admissions were found for all but one of the 19 infective conditions studied. Among the respiratory infections, the greatest percentage reductions were for influenza (mean annual number admitted between 1 March 2017 and 29 February 2020 was 5379 and number of children admitted from 1 March 2020 to 28 February 2021 was 304, 94% reduction, 95% confidence interval 89% to 97%), and bronchiolitis (from 51 655 to 9423, 82% reduction, 79% to 84%). Among the severe invasive infections, the greatest reduction was for meningitis (50% reduction, 47% to 52%). For the vaccine preventable infections, decreases ranged from 53% (32% to 68%) for mumps to 90% (80% to 95%) for measles. Reductions were seen across all demographic subgroups and in children with underlying comorbidities. Corresponding decreases were also found for the absolute numbers of 60 day case fatalities, although the proportion of children admitted for pneumonia

COMMENTARY Admissions fell substantially, probably reflecting a real decrease in non-covid infections

The covid-19 pandemic upended virtually all aspects of society, not least patterns of healthcare use. In their paper, Kadambari and colleagues report dramatic decreases in hospital admissions due to a range of 19 childhood infections in UK children in the 16 months after the start of the covid-19 pandemic.[1] Almost all studied infections declined, including common respiratory viruses, vaccine preventable infections, and common bacterial infections. These findings support and expand data from the United States showing major decreases in childhood respiratory viruses.[2]

One surprising finding was the decrease in sporadic bacterial infections, osteomyelitis and septic arthritis, most commonly caused by *Kingella kingae*, *Staphylococcus aureus*, and *Streptococcus pyogenes*. Although progression from pathogen acquisition to symptomatic infection in bacterial musculoskeletal infections is not well understood, conditions such as acute haematogenous osteomyelitis probably begin with colonisation of mucosal sites with the causative pathogen.[3] Encounters with such pathogens were probably less frequent during the study period.

Zachary Willis zwillis@med.unc.edu
Annabelle de St Maurice
See bmj.com for author details

Another finding of interest was that although the absolute number of hospital admissions for pneumonia decreased by 60% during the pandemic, the proportion of patients admitted for pneumonia who died within 60 days increased from 1% to 2%, with an adjusted odds ratio of 1.71. While this could be secondary to disruptions in care due to a healthcare system under pressure, these data could also reflect changes in clinical practice; for example, children with less severe pneumonia being managed outside hospital. Reassuringly, no increases in mortality were observed for children admitted with any other infection type.

Some limitations must be acknowledged when interpreting this study. First, it is difficult to determine if some illnesses that might have ordinarily resulted in hospital admission were managed as outpatients. Second, Kadambari and colleagues' analyses relied on ICD-10 (international classification of diseases, 10th revision) codes of clinical diagnoses, but there is no reason to suspect that their findings can be attributed to changes in coding accuracy.

If decreased care seeking were the primary driver of the reduction in infection related hospital admissions reported here, we might expect a corresponding rise in infection related mortality, particularly with life threatening infections. In fact, other UK studies show an overall 10% decrease in child mortality and 51% decrease in infection related child mortality during the first year of the covid-19 pandemic.[6]

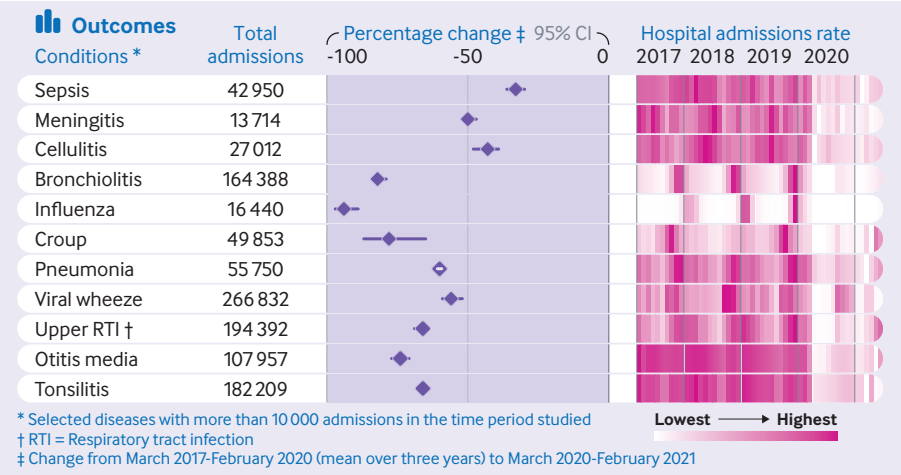
Early in the pandemic, healthcare avoidance and limitations on access probably led to a decrease in the diagnosis of certain infections, but convincing evidence now suggests that the apparent decreases shown here and elsewhere reflect true decreases in the incidence of infectious diseases.

These gains are likely to be temporary. Seasonally circulating viruses rely on growth in the size of the susceptible population caused by waning protective immunity in previously exposed people and the introduction of unexposed infants to that population. This might explain an unexpected outbreak of respiratory syncytial virus in the northern hemisphere during summer 2021, including in the UK,[7] because children and infants had almost no exposure to respiratory syncytial virus due to lockdown measures in the preceding 15 months. As measures such as lockdowns, mask mandates, and social distancing ease, there will probably be an increase in the incidence of primarily, but not exclusively, viral infections.

Economists often referred to a pent-up demand for goods and services as lockdown

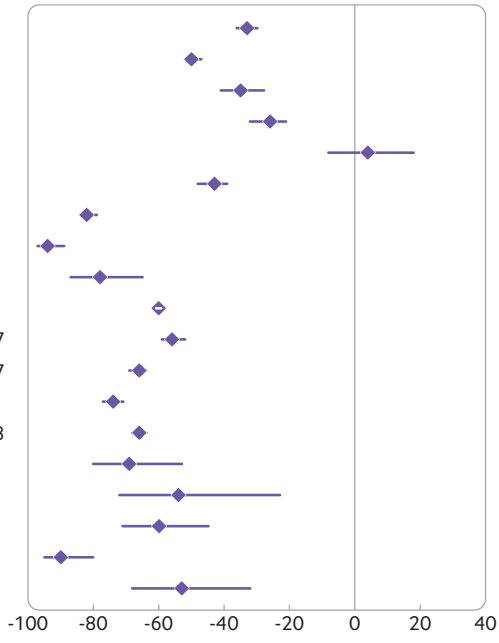
who died within 60 days increased (age-sex adjusted odds ratio 1.71, 95% confidence interval 1.43 to 2.05). More recent data indicate that some respiratory infections increased to higher levels than usual after May 2021. The study did not cover patients who were managed solely in primary care, at home, or in emergency department and outpatient settings.

What this study adds Substantial overall reductions in hospital admissions were found for respiratory, severe invasive, and vaccine preventable infections in children during the covid-19 pandemic in England. Corresponding decreases were also found for absolute numbers of deaths within 60 days of hospital admission.



Funding, competing interests, and data sharing Funded by Public Health England, Health Data Research UK, and National Institute for Health Research Oxford Biomedical Research Centre.
Competing interests given on bmj.com.
The dataset can be obtained by applying to NHS Digital. Updated analyses available online (https://www.ctsu.ox.ac.uk/research/indirect-effects-of-the-covid-19-pandemic-on-childhood-infection-in-england).

Condition	Mean no 2017-20	Total no 2020-21	Percentage change (95% CI) 2017-20 to 2020-21
Sepsis	11 717	7798	-33 (-36 to -30)
Meningitis	3917	1964	-50 (-52 to -47)
Septic arthritis	849	554	-35 (-41 to -28)
Osteomyelitis	2017	1483	-26 (-32 to -21)
Pyelonephritis	317	331	4 (-8 to 18)
Cellulitis	7574	4290	-43 (-48 to -39)
Bronchiolitis	51 655	9423	-82 (-84 to -79)
Influenza	5379	304	-94 (-97 to -89)
Croup	15 500	3352	-78 (-87 to -65)
Pneumonia	16 403	6540	-60 (-61 to -59)
Viral wheeze	77 488	34 367	-56 (-59 to -52)
Upper RTI	58 238	19 677	-66 (-69 to -64)
Otitis media	33 103	8649	-74 (-77 to -71)
Tonsilitis	54 604	18 398	-66 (-68 to -64)
Neisseria meningitidis	618	191	-69 (-80 to -53)
Haemophilus influenzae	47	22	-54 (-72 to -23)
Streptococcus pneumoniae	270	108	-60 (-71 to -45)
Measles	149	15	-90 (-95 to -80)
Mumps	103	48	-53 (-68 to -32)



Number of hospital admissions and percentage change from March 2017-February 2020 (mean over three years) to March 2020-February 2021. RTI=respiratory tract infection

measures eased in Europe and North America during mid-2021. We might also see a similar catching up of common viral and bacterial infections, exacerbated by pandemic induced disruption of routine immunisation programmes,[8] resulting in a continued and unpredictable strain on healthcare systems.

Kadambari and colleagues' study and others show that societies have greater control over the incidence of a wide range of infectious diseases than previously appreciated. Interventions that once seemed far-fetched—universal mask wearing, protracted school and childcare closures, and travel restrictions—were implemented during the covid-19 pandemic.

Understanding which mitigation strategies were most effective is key to reopening safely. As many mitigation measures are relaxed globally, controlled epidemiological studies to determine which interventions provide the greatest benefit for a wide range of infectious diseases should be a research priority.

Cite this as: *BMJ* 2022;376:n3093

Find the full version with references at http://dx.doi.org/10.1136/bmj.n3093

Vitamin D and marine omega 3 fatty acid supplementation and incident autoimmune disease

Hahn J, Cook NR, Alexander EK, et al

Cite this as: *BMJ* 2022;376:e066452
Find this at doi: 10.1136/bmj-2021-066452

Study question Do vitamin D and marine derived long chain omega 3 fatty acids reduce the risk of autoimmune disease?

Methods This nationwide, randomised controlled trial in the United States (vitamin D and omega 3 trial: VITAL) enrolled 12 786 men who were at least 50 years old and 13 085 women who were at least 55 years old. Participants were given vitamin D (2000 IU/day) or matched placebo, and omega 3 fatty acids (1000 mg/day) or matched placebo. Participants self-reported new onset rheumatoid arthritis, polymyalgia rheumatica, autoimmune thyroid disease, psoriasis, and all other autoimmune diseases from baseline to a median of 5.3 years of follow-up; these diseases were confirmed by medical record review. Cox proportional hazard models tested the effects of vitamin D and omega 3 fatty acid supplementation on autoimmune disease incidence.

Study answer and limitations For the vitamin D arm, 123 participants in the treatment group and 155 in the placebo group had a confirmed autoimmune disease (hazard ratio 0.78, 95% confidence interval 0.61 to 0.99, P=0.05). In the omega 3 fatty acids arm, 130 participants in the treatment group and 148 in the placebo group had a confirmed autoimmune disease (0.85, 0.67 to 1.08, P=0.19). Compared with the reference arm (vitamin D placebo and omega 3 fatty acid placebo; 88 with confirmed autoimmune disease), 63 participants who received vitamin D and omega 3 fatty acids (0.69, 0.49 to 0.96), 60 who received only vitamin D (0.68, 0.48 to 0.94), and 67 who received only omega 3 fatty acids (0.74, 0.54 to 1.03) had confirmed autoimmune disease. The relatively low number of participants with definite autoimmune disease limited statistical power to detect an effect on individual disease outcomes.

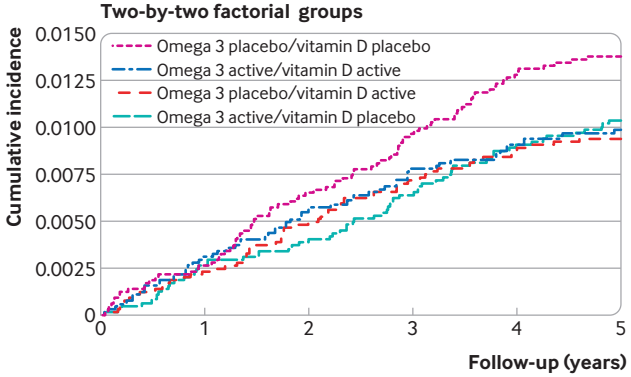
What this study adds Vitamin D supplementation for five years with or without omega 3 fatty acids was associated with a reduction in autoimmune disease by 22%, whereas omega 3 fatty acids with or without vitamin D were associated with a reduction in autoimmune disease by 15% (not statistically significant).

Funding, competing interests, and data sharing
Funded by National Institutes of Health grants R01AR059086, U01CA138962, and R01CA138962. No competing interests declared. Data might be released with appropriate institutional review board approval and publication clearances.

Study registration ClinicalTrials.gov NCT01351805, NCT01169259.

All incident confirmed autoimmune diseases

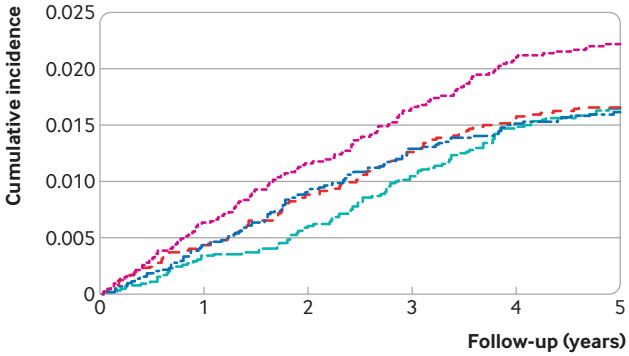
Two-by-two factorial groups



Omega 3 placebo/vitamin D placebo: reference
Omega 3 active/vitamin D active: hazard ratio 0.69 (95% CI 0.49 to 0.96)
Omega 3 placebo/vitamin D active: hazard ratio 0.68 (95% CI 0.48 to 0.94)
Omega 3 active/vitamin D placebo: hazard ratio 0.74 (95% CI 0.54 to 1.03)

Omega 3 placebo/vitamin D placebo					
	6441	6379	6301	6224	6157
Omega 3 active/vitamin D active					
	6420	6362	6300	6240	6167
Omega 3 placebo/vitamin D active					
	6431	6374	6315	6243	6169
Omega 3 active/vitamin D placebo					
	6432	6384	6325	6251	6182

All incident confirmed and probable autoimmune diseases



Omega 3 placebo/vitamin D placebo: reference
Omega 3 active/vitamin D active: hazard ratio 0.71 (95% CI 0.55 to 0.92)
Omega 3 placebo/vitamin D active: hazard ratio 0.76 (95% CI 0.59 to 0.99)
Omega 3 active/vitamin D placebo: hazard ratio 0.74 (95% CI 0.57 to 0.96)

Omega 3 placebo/vitamin D placebo					
	6417	6346	6257	6172	6104
Omega 3 active/vitamin D active					
	6411	6340	6267	6202	6127
Omega 3 placebo/vitamin D active					
	6418	6349	6280	6199	6125
Omega 3 active/vitamin D placebo					
	6429	6371	6301	6215	6145

Cumulative incidence rates of total autoimmune diseases in the VITAL (vitamin D and omega 3) trial. Hazard ratios are from Cox models controlled for age, sex, race, and randomization group in the opposite arm of the trial