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Early View

Research letter

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The effect of physical activity on asthma incidence over 10 years: population-based study

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Take home message

Although there are many health benefits from being active, there was no benefit observed in this study from vigorous physically activity in reducing the risk of asthma onset in middle aged adults Asthma remains a common disease around the world, with global estimates indicating that 4.3% of adults have doctor diagnosed asthma [1]. Physical activity has been found to improve asthma outcomes in adult with asthma [2, 3]. While it has been hypothesised that physical activity could also reduce asthma incidence through a variety of mechanisms, studies to date have provided mixed results. Some studies find that physical activity reduces the incidence of asthma [4, 5], yet others find no evidence for a reduction in risk [6, 7]. These inconsistent findings could be partly attributed to variation in the definition of incident asthma, which is mostly restricted to self-reported asthma outcomes. In this analysis, we investigated the association between (frequency and duration of) vigorous physical activity and asthma incidence over 10 years, using the European Community Respiratory Health Survey (ECRHS), considering multiple asthma related outcomes in an initially asthma-free population.

ECRHS is a multi-centre cohort involving 46 centres in 25 countries from Europe and Australia [8]. From a random sample in ECRHSI, participants (originally 20-44 years of age) completed questionnaires and a battery of tests twice more at 10-year intervals. The present analysis uses data from ECRHSII (42 to 57 years of age) and ECHRSIII (54 to 68 years of age) as physical activity data were not collected in ECRHSI. There were 10,217 participants in ECRHSII. Of these, we excluded participants who reported: (1) 'ever asthma' in ECRHSI or II (n=1895), (2) wheeze in the previous 12-months at ECRHS I or II (n=2328), or (3) an asthma attack prior to ECRHSI or ECHRSII (n=70). Additionally, 2421 participants were lost to follow-up, leaving 3503 participants for analysis. Ethics approval was gained by each center.

The ECRHSII and ECRHSIII questionnaires included items regarding vigorous physical activity during leisure time, in addition to questions regarding the diagnosis of respiratory diseases, respiratory symptoms, medications taken, occupation, smoking and other socio-demographic factors. The responses from the questions "How often do you usually exercise so much that you get out of breath or sweat?" and "How many hours a week do you usually exercise so much that you get out of breath or sweat?" were categorised by frequency (≤ once/month, one to three times/week, four or more times/week) and duration (zero to 30 mins, one hour to three hours, four or more hours per week) respectively. Participants reporting at least one hour of vigorous activity across 2-3 incidences per week were classified as 'vigorously active' and participants reporting less in either question were classified as 'not vigorously active' [9]. This classification was applied across ECRHSII and ECRHSIII data and used to create the categories of 'consistently vigorously active', 'becoming vigorously

inactive', 'becoming vigorously active', and 'consistently not vigorously active' as a 'change in vigorous activity status' variable.

Asthma incidence was assessed using several outcomes at ECRHSIII. Firstly, current asthma was deemed present if participants responded positively to the question 'Have you had wheezing or whistling in your chest at any time in the last 12-months' and/or 'Are you currently taking any medicines including inhalers, aerosols or tablets for asthma' [10]. Secondly, asthma-like symptoms were deemed present with more than three positive responses to questions regarding 12-month symptoms of: (1) wheeze, (2) wheeze with breathlessness, (3) wheeze without a cold, (4) nocturnal chest tightness, (5) nocturnal shortness of breath, (6) nocturnal attack of coughing (7) asthma attack, and (8) current asthma medications [11]. Bronchodilator reversibility was deemed present when there was an increase or decrease in FEV₁ of 12% and >200ml from baseline [12]. This change is accepted as being consistent with asthma in those with respiratory symptoms [12]. We also utilised ECRHSI data on sex, age, age at completion of education (<17, 17-20, \geq 21) years), ECRHS II data on occupation (categorised according to the International Standard Classification of Occupations-88 code [13]) and objectively measured weight and height, from which we derived body mass index (BMI). ECRHS II smoking data were collected across multiple questions and categorised as never, ex-smoker, current-smoker. Associations between the physical activity measurements (ECRHSII vigorous activity status, frequency and duration, change in vigorous activity status during follow-up) were examined for each asthma outcome (current asthma, asthma-like symptoms, bronchodilator reversibility) using modified Poisson regression [14]. Age, sex, age at the completion of education, BMI, smoking and occupation at ECRHSII were included as covariates, as they were identified as potential confounders a priori. Centre clustering was taken into account using robust standard errors and interactions between physical activity and age, sex, BMI and smoking were considered.

We conducted three sensitivity analyses: (1) to account for potential residual confounding we repeated analyses with adjustment for heart disease at ECRHS III, available in a subsample (n=2195); (2) to investigate the potential attenuating effects of asthma medications, we repeated the analyses with bronchodilator reversibility as the outcome excluding those taking asthma medications at ECRHSIII; (3) to investigate heterogeneity across regions, we conducted a random-effects meta-analysis. Stata ver16 (StataCorp, College Station, TX) was used.

The participants included in this analysis were similar to those eligible, in regard to age, sex, physical activity and BMI. However, those included were less likely to be current smokers (21% versus 27%) and more likely to have completed their education \geq 21 years of age (48% versus 41%) at ECRHSII than those lost to follow-up (40% of the ECRHS II cohort). The average age at of the 3503 participants at ECRHSII was 43 years (standard deviation [SD] 7.0), 52% were female and average BMI 25.1 (SD 3.9) kg/m². The majority were never smokers (48%) with 31% ex-smokers and 21% current smokers. Over half (52%) completed their education by 21 years of age and 37% were working in management/professional fields. The majority of participants were classified as not vigorously active (63%) at ECRHSII. Almost half of participants (43%) were not- vigorously active at both time points. At ECRHSIII, 9% of participants had current asthma, 2% reported more than three asthma-like symptoms and 2% had a positive bronchodilator response.

There was little association between the vigorous physical activity measures and asthma outcomes (Table 1). No differences were observed in the sensitivity analyses, and no interactions were found with the potential effect modifiers investigated (results not shown). In this population of initially asthma-free middle-aged adults, we found little association between vigorous physical activity and the onset of asthma measures over a 10-year period. These results are consistent with some previous research investigating the effect of physical activity on asthma incidence [6, 7]. Of the two studies that found a beneficial effect of physical activity on asthma incidence, one appeared to not adjust for relevant confounders, such as age and smoking [4], and the other study used lighter physical activity as the exposure [5]. The lack of observable beneficial associations from physical activity in our study may be because of insufficient statistical power, that only less vigorous physical activity in regard to asthma incidence.

The strengths of this study were the long-term follow-up, reduction in asthma misclassification by combining self-report with objective measurements, and inclusion of several sensitivity analyses to minimise other potential biases. Study weaknesses include loss to follow-up and the utilization of self-reported (instead of objective) physical activity measures; self-report of physical activity can impact validity due to individual's propensity to overestimate physical activity levels. Additionally, bronchodilator reversibility, although a measure of asthma, can also be present with other respiratory diseases [15]. In conclusion, although multiple health benefits from physical activity are known, we did not find evidence

that participating in vigorous physical activity during leisure time reduced the risk of asthma developing in adults.

 Table 1. Association between ECRHSII vigorous activity status, frequency and duration, change in vigorous activity status

 and ECRHSIII current asthma, asthma-like symptoms and bronchodilator reversibility in middle aged adults.

	Current asthma at ECRHS III (%) (n≥3129)	Risk of current asthma, adjusted analyses (95% CI) [#] (n≥2757)	More than three asthma-like symptoms at ECRHS III (%) (n≥3057)	Risk of asthma- like symptoms, adjusted (95% CI) [#] (n≥2695)	Bronchodilator reversibilty present at ECRHS III (%) (n≥2451)	Risk of bronchodilator reversibility, adjusted analyses (95% CI) [#] (n≥2148)
Activity status						
Not vigorously	182 (8.9)	1.00	54 (2.8)	1.00	38 (2.5)	1.00
active						
Vigorously active	102 (8.4)	0.96 (0.75, 1.23)	22 (1.9)	0.71 (0.42, 1.18)	21 (2.2)	0.82 (0.46, 1.47)
Frequency of vigo	orous activity					
\leq 1 times/month	120 (9.1)	1.00	36 (2.8)	1.00	25 (2.6)	1.00
1-3 times/week	120 (7.7)	0.94 (0.73, 1.22)	31 (2.1)	0.78 (0.48, 1.28)	29 (2.4)	0.86 (0.49, 1.50)
4+ times/week	45 (10.7)	1.14 (0.82, 1.63)	10 (2.5)	0.93 (0.45, 1.93)	6 (1.9)	0.67 (0.25, 1.76)
Amount of vigoro	us activity					
0 - 30 mins/week	132 (9.8)	1.00	39 (3.0)	1.00	28 (2.8)	1.00
1-3 hours/week	105 (7.4)	0.82 (0.63, 1.07)	30 (2.2)	0.79 (0.48, 1.30)	24 (2.2)	0.74 (0.42, 1.31)

4+ hours/week	47 (9.5)	1.00 (0.71, 1.42)	7 (1.5)	0.49 (0.21, 1.17)	7 (1.8)	0.66 (0.27, 1.61)					
Change in vigorous activity from ECRHSII to ECRHSIII											
Consistently not	123 (9.1)	1.00	43 (3.2)	1.00	29 (2.8)	1.00					
vigorously active											
Becoming	54 (8.7)	1.00 (0.70, 1.43)	11 (1.9)	0.83 (0.34, 1.35)	9 (1.9)	0.96 (0.44, 2.08)					
vigorously											
inactive											
Becoming	41 (9.1)	1.11 (0.80, 1.54)	11 (2.4)	0.68 (0.42, 1.61)	10 (2.8)	0.83 (0.39, 1.78)					
vigorously active											
Consistently not	60 (8.5)	1.01 (0.73, 1.41)	11 (1.6)	0.50 (0.24, 1.03)	11 (1.9)	0.64 (0.29, 1.42)					
vigorously active											
at a											

CI: Confidence Interval, FEV₁: Forced Expiratory Volume in one second

[#] Adjusted for sex, ECRHSII age, smoking status, occupation, education and BMI

References

1. To T, Stanojevic S, Moores G, Gershon AS, Bateman ED, Cruz AA, Boulet LP. Global asthma prevalence in adults: findings from the cross-sectional world health survey. *BMC Public Health* 2012: 12: 204.

2. Garcia-Aymerich J, Varraso R, Anto JM, Camargo CA. Prospective Study of Physical Activity and Risk of Asthma Exacerbations in Older Women. *Am J Resp Crit Care Med* 2009: 179(11): 999-1003.

3. Franca-Pinto A, Mendes FA, de Carvalho-Pinto RM, Agondi RC, Cukier A, Stelmach R, Saraiva-Romanholo BM, Kalil J, Martins MA, Giavina-Bianchi P, Carvalho CR. Aerobic training decreases bronchial hyperresponsiveness and systemic inflammation in patients with moderate or severe asthma: a randomised controlled trial. *Thorax* 2015: 70(8): 732-739.

4. Lucke J, Waters B, Hockey R, Spallek M, Gibson R, Byles J, Dobson A. Trends in women's risk factors and chronic conditions: findings from the Australian Longitudinal Study on Women's Health. *Women's Health* 2007: 3(4): 423-432.

5. Russell MA, Janson C, Real FG, Johannessen A, Waatevik M, Benediktsdottir B, Holm M, Lindberg E, Schlunssen V, Raza W, Dharmage SC, Svanes C. Physical activity and asthma: A longitudinal and multi-country study. *J Asthma* 2017: 54(9): 938-945.

6. Benet M, Varraso R, Kauffmann F, Romieu I, Anto JM, Clavel-Chapelon F, Garcia-Aymerich J. The effects of regular physical activity on adult-onset asthma incidence in women. *Resp Med* 2011: 105(7): 1104-1107.

7. Brumpton BM, Langhammer A, Ferreira MA, Chen Y, Mai XM. Physical activity and incident asthma in adults: the HUNT Study, Norway. *BMJ Open* 2016: 6(11): e013856.

8. Burney PGJ, Luczynska C, Chinn S, Jarvis D. The European Community Respiratory Health Survey. *Eur Resp J* 1994: 7(5): 954-960.

9. Fuertes E, Carsin AE, Anto JM, Bono R, Corsico AG, Demoly P, Gislason T, Gullon JA, Janson C, Jarvis D, Heinrich J, Holm M, Leynaert B, Marcon A, Martinez-Moratalla J, Nowak D, Pascual Erquicia S, Probst-Hensch NM, Raherison C, Raza W, Gomez Real F, Russell M, Sanchez-Ramos JL, Weyler J, Garcia Aymerich J. Leisure-time vigorous physical activity is associated with better lung function: the prospective ECRHS study. *Thorax* 2018: 73(4): 376-384.

10. Cassim R, Milanzi E, Koplin JJ, Dharmage SC, Russell MA. Physical activity and asthma: cause or consequence? A bidirectional longitudinal analysis. *J Epidemiol Community Health* 2018: 72(9): 770-775.

11. Jarvis D, Newson R, Janson C, Corsico A, Heinrich J, Anto JM, Abramson MJ, Kirsten AM, Zock JP, Bono R, Demoly P, Leynaert B, Raherison C, Pin I, Gislason T, Jogi R, Schlunssen V, Svanes C, Watkins J, Weyler J, Pereira-Vega A, Urrutia I, Gullon JA, Forsberg B, Probst-Hensch N, Boezen HM, Martinez-Moratalla Rovira J, Accordini S, de Marco R, Burney P. Prevalence of asthma-like symptoms with ageing. *Thorax* 2018: 73(1): 37-48.

Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention; 2019.
 The ISCO Team Department of Statistics. ISCO International Standard Classification of

Occupations,. 9 June 2010 [cited; Available from:

http://www.ilo.org/public/english/bureau/stat/isco/

14. Zou GY, Donner A. Extension of the modified Poisson regression model to prospective studies with correlated binary data. *Stat Methods Med Res* 2013: 22(6): 661-670.

15. Janson C, Malinovschi A, Amaral AFS, Accordini S, Bousquet J, Buist AS, Canonica GW, Dahlen B, Garcia-Aymerich J, Gnatiuc L, Kowalski ML, Patel J, Tan W, Toren K, Zuberbier T, Burney P, Jarvis D. Bronchodilator reversibility in asthma and COPD: findings from three large population studies. *Eur Respir J* 2019: 54(3).