

# Physical activity is important for cardiovascular health and cardiorespiratory fitness in patients with psoriasis

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## Summary

**Background.** Patients with psoriasis have a level of physical activity below that recommended for cardiovascular health, which is significantly limited by disease severity and other psoriasis-specific barriers. We hypothesized that physical activity is important for cardiovascular health in patients with psoriasis and that its objective measurement could have clinical utility.

**Aim.** To explore whether physical activity influences the risk of cardiovascular disease (CVD) in patients with psoriasis.

**Methods.** In total, 242 patients with chronic plaque psoriasis were recruited. History, examination and physical activity were assessed and arteriography, the noninvasive measurement of arterial function, was performed for each participant.

**Results.** We observed a significant relationship between volume of physical activity and the likelihood of future CVD as measured by pulse wave velocity (PWV;  $P < 0.02$ ). We identified a significant relationship between the diastolic reflection area (DRA) and health-promoting levels of physical activity ( $P < 0.001$ ), in addition to a significant correlation between DRA and the likelihood of future CVD ( $P < 0.001$ ). The DRA is a complex, dimensionless variable that describes the intensity of diastolic wave reflection and the duration of diastole, which are key determinants of the blood supply to the left ventricle. Our data suggest that DRA may represent a surrogate marker for cardiorespiratory fitness.

**Conclusion.** Our study describes a significant relationship between exercise, cardiorespiratory fitness and PWV, a preclinical indicator of future CVD risk, in patients with psoriasis. The DRA offers a noninvasive, objective measurement of exercise adherence, which could have clinical utility in the future.

## Introduction

Psoriasis has serious systemic associations, including an increased risk of cardiovascular disease (CVD).<sup>1</sup> Traditional risk factors for CVD such as obesity, hypertension and insulin resistance are highly prevalent in the psoriasis population, and their detrimental

effect on cardiac health may be compounded by psychological distress and lifestyle choices made by patients.<sup>2</sup>

Guidelines for physical activity in the UK are similar to those from the American Heart Association (AHA), who recommend that healthy adults, aged 18–65 years, should expend  $\geq 500$ –1000 metabolic equivalent-minutes (MET-min)/week, computed from the energy requirements for an activity (MET), weighted by duration (min/week).<sup>3</sup> Physical activity promotes healthy body mass index (BMI), lowers blood pressure, improves self-confidence and reduces stress.<sup>4</sup>

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However, the health-promoting levels of exercise for patients with psoriasis are significantly limited by a number of psoriasis-specific barriers including severity, treatments, skin sensitivity, clothing choice and participation in social/leisure activities; potentially augmenting the increased risk of CVD in patients with psoriasis.<sup>5</sup>

Pulse wave velocity (PWV), a measure of arterial stiffness with a prospectively validated relationship to CVD risk,<sup>6</sup> can be significantly improved through aerobic activity.<sup>7</sup> Studies suggest that moderate to severe chronic plaque psoriasis may be independently associated with increased arterial stiffness,<sup>8</sup> although the effect of physical activity on arterial stiffness in psoriasis is not known. Arterial stiffness increases the velocity of the aortic pulse wave in both forward and reflected components. Increased arterial stiffness promotes early arrival of the reflected wave in systole instead of diastole, resulting in increased systolic arterial pressure, reduced diastolic aortic pressure,<sup>9</sup> and mismatched myocardial oxygen requirement and perfusion.<sup>10</sup> Diastolic reflection area (DRA), a complex dimensionless variable, describes these key determinants of left ventricular function, with higher DRA indicating better coronary perfusion.<sup>11</sup> DRA is significantly higher in people who exercise, suggesting that it may objectively quantify volume of physical activity undertaken.<sup>12</sup>

The aim of this study was to explore whether physical activity influences CVD risk in patients with psoriasis. We hypothesized that physical activity is important for cardiovascular health in patients with psoriasis, and that objective measurement of activity has clinical utility.

## Methods

The study was approved by the local research ethics committee (11/NW/0654, 12/NW/0239, 10/H1003/10) and was conducted in accordance with the Declaration of Helsinki principles. Written informed consent was obtained from all participants.

### Study population

Participants with chronic plaque psoriasis (aged  $\geq 18$  years) were recruited from a regional psoriasis clinic in northwest England and from primary care centres with the same geographical footprint.

### Questionnaires

A clinical history was taken from each participant and assessments of Psoriasis Area and Severity Index

(PASI) (scale 0–72 points) and Dermatology Life Quality Index (DLQI) (0–30 points)<sup>13</sup> were documented. The short version of the International Physical Activity Questionnaire (IPAQ) questionnaire (scale 0–18 900 MET-min/week)<sup>14</sup> was completed, generating categorical scores for activity (low, moderate or high levels) and continuous scores for intensity [walking (slow), moderate (brisk walking, doubles tennis) and vigorous activity (hiking, jogging, fast cycling, singles tennis) in MET-min/week] (Table 1).<sup>3,14</sup>

### Arterial function assessment

Participants underwent noninvasive measurement of arterial function (Arteriograph; Colson Medical Ltd, Budapest, Hungary), which uses brachial artery oscillometry to calculate PWV (normal range 7–9.7 m/s) and DRA (normal  $> 40$ ).<sup>9,15</sup> Briefly, the jugulum–symphysis distance was measured and entered into the device. The arteriograph cuff was placed on the patient's upper arm and inflated. Pressure variations

**Table 1** Methodology used for the computation of the continuous and categorical activity scores using the short-version International Physical Activity Questionnaire.

Computations of scores	
<i>Continuous activity score, MET-min/week</i>	
Intensity of activity <sup>a</sup>	
Walking <sup>b</sup>	$3.3 \times \text{min walking} \times \text{days walking}$
Moderate <sup>c</sup>	$4.0 \times \text{min moderate activity} \times \text{days of moderate activity}$
Vigorous <sup>d</sup>	$8.0 \times \text{min vigorous activity} \times \text{days of vigorous activity}$
Total IPAQ	Walking + moderate + vigorous scores
<i>Categorical activity score</i>	
Level of activity	
Low	Individuals who do not meet the criteria for moderate or vigorous levels of physical activity
Moderate	$\geq 3$ days of vigorous-intensity activity, $\geq 20$ min/day or $\geq 5$ days of moderate-intensity activity and/or walking, $\geq 30$ min/day or $\geq 5$ days of any combination of walking, moderate- or vigorous-intensity activities, achieving $\geq 600$ MET-min/week
High	Vigorous-intensity activity $\geq 3$ days/week, achieving $\geq 1500$ MET-min/week OR $\geq 7$ days of any combination of walking, moderate- or vigorous-intensity activities, achieving $\geq 3000$ MET-min/week

IPAQ, International Physical Activity Questionnaire; MET, metabolic equivalent. <sup>a</sup>Examples; <sup>b</sup>walking slowly; <sup>c</sup>walking briskly, doubles tennis; <sup>d</sup>hiking, jogging, fast cycling, singles tennis.

in the cuff were processed by the system software to produce the arterial function report.

### Statistical analysis

Data were recorded and missing observations coded. Descriptive statistics summarized variables [median and interquartile range (IQR) for non-normal continuous variables and percentages for categorical variables]. Participants who achieved a total energy expenditure of  $\geq 500$  MET-min/week through moderate-intensity and/or vigorous-intensity activity were considered to have met AHA guidelines.<sup>7</sup>

Spearman correlation determined relationships between IPAQ and PWV and between IPAQ and DRA. Kruskal–Wallis test was used to determine differences in PWV and DRA across categorical levels of activity. Dunn–Bonferroni testing was used in *post hoc* analyses. Mann–Whitney *U*-test was used to assess differences in DRA between those who adhered (or not) to AHA guidelines. Spearman correlation examined relationships between sedentary behaviour and DRA and between PWV and DRA. SPSS Statistics software (V27; IBM SPSS, Armonk, NY, USA) was used for analyses and  $P < 0.05$  was considered significant.

Hierarchical multiple regression analysis investigated relationships between cardiovascular health, measured by PWV, as the dependent (continuous) variable (Model 1), with the independent (continuous) variables of self-reported physical activity (IPAQ) and age. Sex, history of myocardial infarction (MI)/angina/transient ischaemic attack (TIA) and treatment for hypertension were included as binary independent variables. Independent variables were entered sequentially in three blocks: Block 1, age and sex; Block 2, history of MI/angina/TIA and treatment for hypertension; and Block 3, physical activity. A second hierarchical multiple regression analysis investigated the relationship between DRA [dependent (continuous) variable (Model 2)] with the same independent variables used in Model 1. Participants with missing values were excluded.

## Results

### Participants

In total, 242 patients (124 men, and 118 women) with psoriasis were enrolled (Table 2), of whom 23% had psoriatic arthritis, 21% had PWV levels indicating arterial stiffness and 27% had DRA results suggesting impaired coronary circulation.

**Table 2** Characteristics of the study participants ( $n = 242$ ).

Parameter	Results
Sex (M/F), % <sup>a</sup>	51/49
Recruitment from primary care/secondary care, % <sup>a</sup>	52/48
Age, years; median (IQR) <sup>a</sup>	49 (38–59)
Age of psoriasis onset, years; median (IQR) <sup>d</sup>	21 (14–35)
Family history of psoriasis, % <sup>e</sup>	58.9
Comorbidities, %	
Psoriatic arthritis <sup>c</sup>	23.0
Myocardial infarction <sup>a</sup>	3.7
Angina <sup>a</sup>	4.5
Atrial fibrillation <sup>a</sup>	5.4
TIA <sup>a</sup>	0.8
Stroke <sup>a</sup>	0
Treatment for hypertension <sup>l</sup>	32.5
Measures; median (IQR)	
PASI <sup>a</sup>	2.7 (0.9–6.0)
DLQI <sup>b</sup>	4 (1–8)
PWV, m/s <sup>i</sup>	8.2 (6.9–9.6)
DRA <sup>g</sup>	46 (38.4–54.7)
Exercise, MET-min/week; median (IQR)	
Intensity	
Walking <sup>j</sup>	924 (330–2079)
Moderate <sup>g</sup>	0 (0–720)
Vigorous <sup>f</sup>	0 (0–1200)
Total IPAQ <sup>k</sup>	1957.5 (694.8–4135.5)
Exercise within AHA guidelines (Yes/No), % <sup>h</sup>	48.9/51.1
Level	
Low <sup>j</sup>	23.4
Moderate <sup>j</sup>	36.2
High <sup>j</sup>	40.4

AHA, American Heart Association; DRA, diastolic reflection area; IPAQ, International Physical Activity Questionnaire; IQR, interquartile range; PASI, Psoriasis Area and Severity Index; PWV, pulse wave velocity. Missing values: <sup>a</sup>none; <sup>b</sup>0.4%; <sup>c</sup>1.2%; <sup>d</sup>1.65%; <sup>e</sup>2.5%; <sup>f</sup>4.5%; <sup>g</sup>7%; <sup>h</sup>8.7%; <sup>i</sup>9.5%; <sup>j</sup>9.9%; <sup>k</sup>15.7%; <sup>l</sup>32.6%.

### Relationship between physical activity and cardiovascular health in patients with psoriasis

There was a significant ( $P < 0.01$ ) negative correlation between PWV and vigorous-intensity activity, with PWV decreasing as the quantity of vigorous-intensity activity increased indicating a reduced likelihood of CVD. This relationship was stronger in patients aged  $< 65$  years, and a significant ( $P < 0.001$ ) negative correlation was found between PWV and the amount of vigorous-intensity activity reported. Analysis by sex and age  $> 65$  years did not reveal any significant relationships between PWV and physical activity.

Participants undertaking high levels of physical activity had significantly reduced PWV compared with

those undertaking moderate and low levels of activity ( $P < 0.02$ ). *Post hoc* analysis identified significant difference between those participating in high and moderate levels of activity (adjusted  $P < 0.03$ ). Those relationships were replicated in those patients aged  $< 65$  years ( $P = 0.01$ , *post hoc* analysis adjusted  $P < 0.02$ ). There were no significant differences in patients aged  $> 65$  years.

#### Relationship between physical activity and markers of cardiorespiratory fitness in patients with psoriasis

We observed a statistically significant ( $P = 0.02$ ) correlation between DRA and total IPAQ scores, indicating that as participation in exercise (of all intensities) increased, DRA also increased. Similarly, we observed significant correlation between vigorous-intensity ( $P < 0.01$ ) and moderate-intensity activity ( $P < 0.01$ ) and DRA.

There was a significant correlation between DRA and total IPAQ score ( $P < 0.01$ ), vigorous-intensity activity ( $P < 0.01$ ) and moderate-intensity activity ( $P = 0.001$ ) in patients aged 18–65 years. Analysis by sex revealed a significant correlation between DRA and total IPAQ scores ( $P < 0.02$ ) for men aged 18–65 years, and between DRA and both vigorous-intensity activity ( $P < 0.01$ ) and moderate-intensity activity ( $P < 0.03$ ) for women aged 18–65 years.

We identified significant difference in DRA across the three categories of physical activity ( $P < 0.05$ ). *Post hoc* testing identified significant differences in DRA between low and high levels of activity (adjusted  $P < 0.05$ ). This was replicated in patients aged  $< 65$  years who had significant differences in DRA and levels of activity ( $P = 0.03$ ). *Post hoc* testing identified significant (adjusted  $P = 0.04$ ) differences in DRA between low and high levels of activity.

There was a significant difference between DRA in patients who met the AHA guidelines and those who did not, both for the overall group ( $P < 0.001$ ) and for patients aged 18–65 years ( $P = 0.001$ ). We identified similar relationships between DRA and adherence to AHA guidelines for women in the overall group ( $P < 0.01$ ) and women aged 18–65 years ( $P = 0.01$ ).

We observed significant negative correlations between DRA and sitting time, meaning that as sedentary behaviour increased, DRA decreased, and this was seen both for the overall group of patients aged 18–65 years ( $P < 0.04$ ) and for women aged 18–65 years ( $P < 0.04$ ).

#### Relationship between cardiovascular health and cardiorespiratory fitness in patients with psoriasis

We observed a significant negative correlation between DRA and PWV, meaning that as DRA increased, PWV decreased, indicating a reduced likelihood of CVD; this was seen both for the overall group ( $P < 0.001$ ) and for participants aged 18–65 years ( $P < 0.001$ ).

There was also a significant negative correlation between DRA and PWV for both men ( $P < 0.02$ ) and women ( $P < 0.01$ ) in the overall group, which was also observed in the 18–65-year group for women ( $P < 0.01$ ) but not for men.

#### Factors predicting cardiovascular health and cardiorespiratory fitness in patients with psoriasis

Having found significant relationships between both patient-reported physical activity and PWV, and between patient-reported physical activity and DRA, we investigated whether self-reported physical activity (IPAQ) was a significant predictor of either variable after controlling for confounding factors by performing a hierarchical regression analysis.

Our first model (Fig. 1) explained 36% of the variance in PWV ( $P < 0.001$ ). After adjustment for sex, history of MI/angina/TIA, treatment for hypertension and IPAQ, we found that age was a significant predictor of PWV, which increased by 0.06 m/s ( $P < 0.001$ ) for each year of life. Similarly, after adjustment for age, sex, history of MI/angina/TIA and IPAQ, we found that treatment for hypertension was also a significant predictor of PWV, which increased by 1.35 m/s ( $P = 0.001$ ) for those receiving treatment for hypertension. Self-reported vigorous-intensity activity explained 0.1% of the variation in PWV, which was not significant.

Our second model (Fig. 2) explained 32.1% of the variance in DRA ( $P < 0.001$ ). After adjustment for sex, history of MI/angina/TIA, treatment for hypertension and IPAQ, age was found to be a significant ( $P < 0.001$ ) predictor of DRA, with a significant ( $P < 0.001$ ) reduction of 0.59 in DRA for each year of life.

These data suggest that self-reported activity is not a significant predictor of PWA or DRA. The characteristics of cases omitted due to missing data were similar to those of the whole group.

## Discussion

We found a significant relationship between volume of physical activity in patients with psoriasis and the

Dependent variable PWV						
Predictor variables	Unstandardized B-coefficient	95% CI of the (unstandardized) B-coefficient	P value	R <sup>2</sup>	R <sup>2</sup> change	Significance of model
<b>BLOCK 1</b>				<b>0.307</b>	<b>0.307</b>	<b>1.194 x10<sup>-11</sup></b>
Age	<b>0.08</b>	<b>0.062 : 0.105</b>	<b>2.5 x10<sup>-12</sup></b>			
Sex	0.40	-0.204 : 1.001	0.19			
<b>BLOCK 2</b>				<b>0.355</b>	<b>0.048</b>	<b>6.397 x10<sup>-11</sup></b>
Age	<b>0.06</b>	<b>0.037 : 0.088</b>	<b>0.000004</b>			
Sex	0.36	-0.238 : 0.950	0.24			
History of MI	-0.34	-2.068 : 1.388	0.70			
History of angina	-0.20	-1.773 : 1.379	0.80			
History of TIA	-0.43	-3.739 : 2.879	0.80			
Treatment for hypertension	<b>1.25</b>	<b>0.462 : 2.030</b>	<b>0.002</b>			
<b>BLOCK 3</b>				<b>0.360</b>	<b>0.005</b>	<b>1.5 x10<sup>-10</sup></b>
Age	<b>0.06</b>	<b>0.034 : 0.086</b>	<b>0.000011</b>			
Sex	0.41	-0.192 : 1.018	0.18			
History of MI	-0.33	-2.061 : 1.395	0.70			
History of angina	-0.11	-1.723 : 1.436	0.86			
History of TIA	-0.35	-3.661 : 2.965	0.84			
Treatment for hypertension	<b>1.35</b>	<b>0.536 : 2.155</b>	<b>0.001</b>			
Self-reported exercise (IPAQ)	0.000045	-0.000045 : 0.000134	0.32			

**Figure 1** The relationship between the dependent variable (pulse wave velocity; PWV) and predictor variables including chronological age, sex, comorbidities and self-reported physical activity; results from the hierarchical regression analysis ( $n = 219$ ; missing data 9.5%). Statistically significant values are highlighted in bold. IPAQ, International Physical Activity Questionnaire; MI, myocardial infarction; TIA, transient ischaemic attack.

likelihood of future CVD as measured by PWV. There was a significant relationship between DRA and physical activity or adherence to AHA guidelines, and also a significant correlation between DRA and the likelihood of future CVD. Our data suggest that DRA may quantify cardiorespiratory fitness and that increased levels of physical activity could increase fitness and reduce CVD risk in patients with psoriasis.

An inverse association has been described between intensity of physical activity and the risk of developing coronary heart disease, independent of the total volume of activity, in large cohort studies of healthy men.<sup>16,17</sup> However, individuals with psoriasis have higher heart rates and systolic blood pressure during exercise, together with lower heart rate recovery than healthy individuals.<sup>18</sup> Psoriasis plaques limit normal sweating and heat dissipation, which may reduce tolerability of higher exercise intensities in patients,<sup>19</sup> suggesting that a tailored approach to engagement with exercise in the psoriasis population may be required.

Decreased expression of the inflammatory markers C-reactive protein and interleukin (IL)-6 following moderate-intensity to vigorous-intensity activities in healthy adults has been observed previously,<sup>20,21</sup> and recent investigations concluded that downregulation of inflammation is greatest in those exercising at higher intensities.<sup>22</sup> Other groups have reported significant reduction of key inflammatory cytokines such as tumour necrosis factor- $\alpha$ , IL-6 and interferon- $\gamma$  in patients with metabolic syndrome following 12-week exercise interventions.<sup>23,24</sup> It is possible that exercise may ameliorate a proinflammatory phenotype in patients with psoriasis; evidence has shown that median skin involvement is 5% among regular exercisers compared with 10% among nonexercisers.<sup>25</sup>

Measurement of physical activity is important when evaluating health behaviours and assessing the effectiveness of exercise interventions within a population. Self-report questionnaires involve a degree of subjectivity, while objective measures such as accelerometry or calorimetry can be time-/cost-intensive and require

Dependent variable DRA						
Predictor variables	Unstandardized B-coefficient	95% CI of the (unstandardized) B-coefficient	P value	R <sup>2</sup>	R <sup>2</sup> change	Significance of model
<b>BLOCK 1</b>				<b>0.308</b>	<b>0.308</b>	<b>1.104 x10<sup>-11</sup></b>
Age	<b>-0.58</b>	<b>-0.74 : -0.43</b>	<b>4.607 x10<sup>-12</sup></b>			
Sex	-4.15	-8.42 : 0.13	0.06			
<b>BLOCK 2</b>				<b>0.317</b>	<b>0.009</b>	<b>2.308 x10<sup>-9</sup></b>
Age	<b>-0.58</b>	<b>-0.76 : -0.39</b>	<b>1.37 x10<sup>-8</sup></b>			
Sex	-4.11	-8.44 : 0.23	0.06			
History of MI	4.98	-7.63 : 17.58	0.44			
History of angina	3.03	-8.47 : 14.53	0.60			
History of TIA	7.98	-16.16 : 32.12	0.51			
Treatment for hypertension	-2.30	-8.02 : 3.43	0.43			
<b>BLOCK 3</b>				<b>0.321</b>	<b>0.004</b>	<b>5.745 x10<sup>-9</sup></b>
Age	<b>-0.59</b>	<b>-0.78 : -0.40</b>	<b>1.1053 x10<sup>-8</sup></b>			
Sex	-3.76	-8.18 : 0.66	0.10			
History of MI	5.02	-7.61 : 17.64	0.43			
History of angina	3.35	-8.19 : 14.89	0.57			
History of TIA	8.48	-15.72 : 32.68	0.49			
Treatment for hypertension	-1.69	-7.60 : 4.22	0.57			
Self-reported exercise (IPAQ)	0.00027	-0.00038 : 0.001	0.41			

**Figure 2** The relationship between the dependent variable (diastolic reflection area; DRA) and predictor variables including chronological age, sex, comorbidities and self-reported physical activity; results from the hierarchical regression analysis ( $n = 224$ ; missing data 7.4%). Statistically significant values are highlighted in bold. IPAQ, International Physical Activity Questionnaire; MI, myocardial infarction; TIA, transient ischaemic attack.

specialist training. Although further calibration is required (including comparison with accessible proxies of cardiorespiratory fitness such as waist circumference and blood pressure), our data suggest that DRA could offer a bedside measurement of physical activity with high clinical utility and greater objectivity than self-report instruments.

This study had some limitations. First, the short-version IPAQ does not quantify occupational activity and therefore the influence of this on cardiovascular health/fitness was beyond the scope of our study.<sup>14</sup> Second, our study was based in northwest England, an area with high levels of socioeconomic deprivation, which may influence exercise adherence and CVD. To mitigate this, participants were recruited from both affluent and deprived areas. Third, we did not formally assess mood (a risk factor for CVD) or collect data on treatment for psoriasis, which may have anti-inflammatory/anti-atherosclerotic activity and may differ between community-based cohorts (such as ours) and secondary-care cohorts. In

addition, we did not collect data on BMI, diet or ethnic background, which are factors that can affect cardiovascular health and may represent important confounders. Fourth, we were unable to make a comparison with healthy controls, and it remains unclear whether physical activity advice for patients with psoriasis should be different to that of the general population. Finally, participants with missing values were excluded from the analyses; however, the characteristics of those omitted were similar to those of the whole group and were therefore unlikely to have biased the results.

## Conclusion

Our study describes significant relationships between exercise, cardiorespiratory fitness and PWV, a preclinical indicator of future CVD risk, in patients with psoriasis. A tailored approach to increasing physical activity in the psoriasis population could help diminish CVD risk. We also propose use of DRA, as a non

invasive clinical tool to objectively quantify the amount of physical activity undertaken, in further investigations.

### Conflict of interest

HSY has acted as a scientific consultant or has received research funding (outside the submitted work) from Aspire Pharma, Almirall, Celgene, Janssen, Johnson and Johnson, LEO Pharma, Novartis and UCB Pharma. CEMG has received honoraria and/or research grants from AbbVie, Almirall, Amgen, BMS, Boehringer-Ingelheim, LEO Pharma, Lilly, Janssen, Novartis and UCB Pharma.

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#### What's already known about this topic?

- Traditional risk factors for CVD are highly prevalent in the psoriasis population.
- Owing to a number of psoriasis-specific barriers, patients with psoriasis have levels of physical activity below those recommended for cardiovascular health.

#### What does this study add?

- We report a significant relationship between volume of physical activity in patients with psoriasis and the likelihood of future CVD.
- DRA demonstrates significant correlation with the likelihood of future CVD.
- DRA may represent a surrogate marker for cardiorespiratory fitness and have clinical utility as a noninvasive method to objectively quantify the amount of physical activity undertaken.
- A tailored approach to increasing physical activity in the psoriasis population could diminish their CVD risk.

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