PsA digital phenotyping and inflammation drivers study

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Primary objectives:To develop and internally validate a novel and interpretable machine learning model for detecting flare in PsA patients using integrated accelerometer data, keystroke dynamics and screen time metrics (i.e., digital biomarker) to...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Autoimmune disorders
Study type	Observational non invasive

Summary

ID

NL-OMON56256

Source
ToetsingOnline

Brief title
iPROLEPSIS-PDPID

Condition

- Autoimmune disorders
- Joint disorders

Synonym
"Psoriatic arthritis" and "Rheuma"

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: HORIZON-HLTH-2022-STAYHLTH-02-01 (Grant Agreement No. 101095697).

Intervention

Keyword: digital biomarker, flare, Inflammation, Psoriatic arthritis

Outcome measures

Primary outcome

Absence of flare in psoriatic arthritis evaluated every 3 months, defined as:

Patients

At this time, is your psoriatic arthritis in remission , if this means: you feel your disease is as good as gone? (for REM)

*At this time, are you in low disease activity, if this means: your disease is in low activity but it*s not as good as gone?* (for LDA).

Doctors

At this time, is the psoriatic arthritis in remission, if this means: the absence of clinical and laboratory evidence of significant inflammatory disease activity?

*At this time, is the psoriatic arthritis in low or minimal disease activity?**

*The study is powered on low or minimal disease activity as noted by the doctor.

Patient Acceptable Symptom State (PASS)

If you were to remain for the next few months as you were during the last 48 hours, would this be acceptable or unacceptable for you? yes/ no

Secondary outcome

Based on clinical evaluation and the patient reported outcomes the following composites will be calculated:

Minimal disease Activity (MDA)

Psoriatic Arthritis Disease Activity Score (PASDAS)

Disease Activity Psoriatic Arthritis (DAPSA)

Likert Scale questions on a daily basis from the Psoriatic Arthritis Impact of Disease (PSAID):

Severity of pain (PSAID 1). When in pain, follow-up question: *did you use painkillers or NSAIDs?*

Severity of fatigue (PSAID2)

Sleep (PSAID 7)

10 point Likert scale for Severity of stiffness (morning stiffness)

In addition the following flare questions will be asked at baseline, follow-up visits, and when patients experience disease flare in which they seek help from the rheumatologist:

Doctors

At this time, is the disease in flare (i.e., significantly worsened/more active compared to usual)? yes/no

Patients

*At this time, are you having a flare of your psoriatic arthritis, if this

means the symptoms are worse than usual?* yes/no

Other study parameters

Phone captured:

Keypad time-related data and metadata

Accelerometer and gyroscope sensor data

Screen time

Hand and feet photos

Hand, gesture and posture videos (no raw videos will be stored)

Smart watch captured:

Sleeping time and type

Accelerometer data

Screen time

Body battery / Stress levels

Heart rate and Beat-to-beat intervals

Motion intensity

Pulse Ox

Steps

Physical activity intensity and categories as captured by the device

Distance

The digital parameters will be provided as raw data from Garmin (e.g., heart

rate) or if they are calculated from other parameters (e.g., respiration rate) as determined by Garmin.

Clinical assessment

Medical history:

Age

Sex

Years of disease

Medication over the year of the study

Comorbidity

Care activities

Job title, shift work and frequent flying

Handedness and typing fingers

Onset of flare

Clinical evaluation:

66/68 joint count for swelling and tenderness

6 tendon count for enthesitis using Leeds Enthesitis Index (LEI)

Body Surface Area for skin

BMI

Abdominal circumference

CASPAR score calculation for the classification of PsA which include: (i) evidence of current psoriasis, or personal or family history of psoriasis, (ii) dactylitis, (iii) juxtaarticular new bone formation, (iv) nail dystrophy, and

(v) negative for rheumatoid factor.

Biological markers

Saliva:

DNA (selected genetic variants)

Stool:

Gut microbiome

Hair:

Hair cortisol levels

Blood (standard care):

Inflammatory blood marker CRP obtained from medical records as part of standard care

Questionnaires:

Demographics

VAS pain and patient global

HAQ to measure physical function

Psoriatic Arthritis Impact of Disease (PSAID)

36-item Short Form Survey (SF36) for general health assessment

EQ5d for general health assessment

Work Productivity and Activity Impairment (WPAI)

Patient Health Questionnaire (PHQ9) for depression assessment

Life events

Health care usage

Global Rating of Change Questionnaire (GRCQ) to evaluate disease activity change

Perceived Stress Scale (PSS)

Digital literacy

Questionnaire for stool analysis

Questionnaire for hair cortisol analysis

Environment:

Humidity

Temperature

Air Pollution (namely, NO, NO2, NOx, O3, PM10, PM25, SO2)

Study description

Background summary

The level of disease activity in Psoriatic Arthritis (PsA) and the perception thereof by the patients determines the actions the rheumatologist takes to optimize treatment outcomes among patients with this disease. Currently, disease activity is measured by a combination of clinical measures and patients* self-reported symptoms and functional ability. This requires the patients to visit the outpatient clinic at regular intervals, which during the Covid-19 pandemic was not always possible. The use of questionnaires to collect Patients* Reported Outcomes (PRO*s) is a feasible option for monitoring patients at a distance. However, from a long term perspective, survey fatigue is a known limiting factor of PRO*s. Currently, there is no valid alternative for unobtrusive remote disease activity monitoring.
The widespread use of smart devices by the general population, such as

smartphones or smartwatches, provides opportunities to develop and study possibilities for Unobtrusive Remote Disease activity monitoring (URD) using behavioural data captured by the sensors embedded within the smartphones/smartwatches. We hypothesize that a high level of disease activity in PsA will lead to changes in physical activity as registered by a patient*s smartphone and smart watch as compared to a low disease activity state. We also hypothesize that the information acquired by digital biomarkers will be comparable to the information received through clinical measures and PROs. Additionally, digital biomarkers are likely to provide information on other disease characteristics such as tiredness and sleep problems. Adding these will enhance the discriminative ability of our approach. Last but not least, we hypothesize that patients will see the use of smartphone data as a privacy-wise safe and fair deal in return for better insight in their disease. And in low disease activity the use of digital biomarkers could reduce the amount of follow-up appointments at the out-patient clinic.

Study objective

Primary objectives:
To develop and internally validate a novel and interpretable machine learning model for detecting flare in PsA patients using integrated accelerometer data, keystroke dynamics and screen time metrics (i.e., digital biomarker) to assess changes in their physical activity patterns against clinical defined flare by the rheumatologist. Accelerometer data is captured by both smartphone and smartwatch.
To develop and internally validate machine learning models that capitalize on sleep, fatigue, pain, stress, mechanical stress, composition of gut microbiome, genetic risk and environmental exposure for flare prediction (either clinically established or evaluated by the digital biomarker) in patients with PsA.

Secondary objectives:
To assess construct validity of the novel and interpretable machine learning model for detecting flare in PsA patients using integrated accelerometer data, keystroke dynamics and screen time metrics (digital biomarker) to assess changes in physical activity patterns against the continuous measure of clinical composite scores of disease activity and impact of disease used by the rheumatologist and impact of disease as reported by the patient
To develop and internally validate a novel and interpretable machine learning model for changes in joint and skin appearance that relates to flare in PsA patients using video analysis of hand, posture and gesture and photos of the hands and feet against clinically defined flare by the rheumatologist
To determine intraperson reliability of the AI-driven digital biomarker system
To determine clinically relevant changes in the AI-driven digital biomarker system
To determine minimal detectable difference in the AI-driven digital biomarker

system
To assess the intraperson variation of stress, mechanical stress and changes in gut microbiome on the occurrence of flare
To identify genetic contribution to disease activity and pain
To evaluate costs and effects of the digital biomarker of future care to current care
To evaluate the compliance and satisfaction of the users with the smartphone- and smartwatch-based measurement of disease activity and flare.

Study design

One year international multicenter prospective observational cohort

Study burden and risks

Patients with PsA experience difficulties in dealing with unpredictable disease activity which can have consequences on their daily living. With the introduction of smart devices, they could have better understanding on the disease influence on their physical activity patterns, stress levels, sleep, pain, stiffness and fatigue. During the study, patients will benefit from the features provided by the Garmin Smart watch Vivoactive 5 such as physical activity and heart rate.
Digital monitoring of patients will be performed continuously for a year using a smart watch that will be provided for patients to wear daily, and a data capturing application (app) that will be installed on their smartphone. The data capturing app will collect -unobtrusively- the keystroke dynamics and the accelerometer/gyroscope data of the smartphone. The levels of pain, fatigue and stiffness will be also monitored via questions provided by the app on these symptoms. These are very short questions that appear one time a day for the first 14 days, and are answerable within a few seconds. In addition, the app allows the patients to self-register a disease flare by pressing the flare button. Once patient registers a flare, these questions will appear again. When flare button is off, patients are inquired every two weeks if they are flare free. Besides, photos of hands and feet and videos of hands, posture and gesture will be collected at baseline, every 6 weeks and when patient experiences disease flare. Photos captured by the patient must contain only hands and feet, otherwise they will be discarded. Regarding the videos of hands, posture and gesture, only the time series of hand/body landmarks from the raw videos will be saved (no raw videos will be stored).
Patients will be assessed at baseline and followed-up every 3 months for a total duration of one year. Each study visit requires around 30 minutes. Patients are clinically assessed for disease activity at study center and are requested to fill questionnaires, at baseline and every 3 months. Saliva collection for DNA analysis is performed at baseline only, using a salivary collection kit at the study center or at home. For microbiome analysis, patients are provided with a home kit to collect stool at baseline and when

experiencing disease flare for which they seek help from rheumatologist. In the Netherlands, additional stool sample collection is requested from patients attending centers that are participating in DEPAR at months 6 and 12. Depending on the hospital facilities, patients can bring samples back during their hospital visit or send it to a central location via postal mail. To analyse cortisol from hair, 3cm of hair will be sampled at study center from posterior vertex at baseline and every 3 months.
Burden on patients include more outpatient clinical visits than standard care, response burden, continuous use of smartwatch and continuous monitoring of patient activity for 12 months, taking photos and videos, providing hair and stool samples, and providing saliva for DNA analysis.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

At least 18 years of age and competent
With PsA
Using s smartphone
Agree to use smartwatch
Good command of the local language

Exclusion criteria

Age less than 18 years
Incapacitated patients

Study design

Design

Study type: Observational non invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	04-09-2024
Enrollment:	150
Type:	Actual

Ethics review

Approved WMO

Date:	06-11-2023
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO Date:	08-01-2024
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	05-03-2024
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	13-06-2024
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	22-07-2024
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL84429.078.23