Study population

considerations for clinical trial design utilizing digital measurement of **nocturnal scratch**

NOCTURNAL SCRATCH

Digital Measures Development

www.dimesociety.org/tours-of-duty/digital-measures-nocturnal-scratch

A project by the DIGITAL MEDICINE SOCIETY

Atopic dermatitis population

What is atopic dermatitis?

- Atopic dermatitis (AD), also called atopic eczema, is a common chronic or recurrent inflammatory skin disease
- It is a condition that causes the skin to become itchy, dry, and cracked

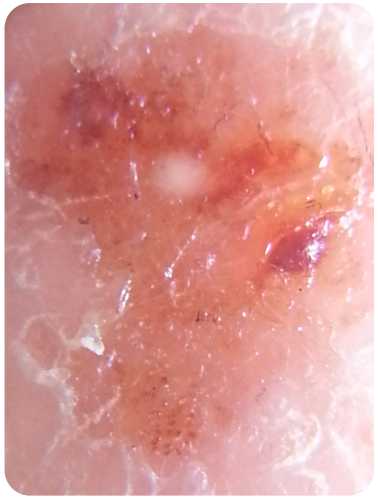


Image Source: https://commons.wikimedia.org/wiki/File:Atopic_dermatitis_close_up_ad.jpeg

Who are the affected patients?

- 15-20% of children worldwide
- 1-3% of adults worldwide[1]

[1]Nutten S: Atopic Dermatitis: Global Epidemiology and Risk Factors. Ann Nutr Metab 2015;66(suppl 1):8-16. doi: 10.1159/000370220

Digital measurement of nocturnal scratch in atopic dermatitis population

Two main sensor types used to assess nocturnal scratching are:

Contact sensors

Worn on a body part

- Placement of the sensor on the body determines the body area from which we are able to detect the movement to be processed by algorithms into resulting scratch measure
- This placement may be different for adults and children, and may also be subject to places known to be more frequently involved in disease activity
- Usually wrist and hand actigraphy sensor placement to capture scratching movements is well accepted in research
- Actigraphy sensors require placement on the body surface, which can be affected by eczema and thus requires careful consideration of aspects that may further irritate the skin or cause the device to not function properly

Non-contact sensors

Not worn on the body part

- Are able to detect scratch movements from the whole body, and it's important to assess the evaluating mechanism for optimal device function
- Videography remains a gold standard methodology for scratch assessment, despite inter-observer variability

Patient behaviors, preferences, & disease characteristics

> “It is important to look at the participants in research as whole persons with distinct behaviors and preferences rather than uniform pool of subjects.”

Skin interface

Consider the following aspects for sensors and devices interfacing the skin:

Is the device made of non-irritant materials to the skin?

- *Some materials, such as nickel, rubber, or silicone, may cause irritation of the skin*
- *Are the materials that come in contact with skin (e.g. bands, adhesives) breathable?*
- *Assess all parts of the device, including the bands, adhesives, or metal external parts of the device*

Does it need to be worn directly on the skin?

- *Will wearing it on the skin add additional measurements, such as heart rate, or can it be worn on top of wrap or cloth?*
- *Will use of lotions, moisturizers, or other treatments to the skin interfere with the measurement device function?*

Where in the body will it be worn?

- *Will it be worn on one place, or multiple places?*
- *Consider differences for adults and children, or wear on places known to be more frequently involved in disease activity*

Is it easy to put on and take off?

Does the device need to be cleaned frequently or washed daily?

- If yes, consider the cleansers that can also pose as skin irritants

Can any external part of the device enter the mouth?

- *Consider if using the measurement in children*

Is the device waterproof?

- *To assess need for removing before bath or shower for patient instructions*

Can it be worn for a long period of time without skin irritation?

- *To assess need for continuous vs. intermittent wear*

Will the device function be altered when worn by people with different skin colors?

Can the device be adjusted for both adults and children?

Patient behaviors, preferences, & disease characteristics

Consider following aspects for sensors and devices:

Sleep patterns

Bedtime routines

Individual baselines

Right sensor to the right patient

Technology literacy

Continuous monitoring vs. only at night

Consider following aspects that can **change sleep patterns**, resulting in changes in measurement of nocturnal scratching.

- It has been reported that adults with AD had higher probability of sleep disturbances, including shorter sleep duration, trouble falling asleep, and early morning awakenings[2]
- Changes between sleep on weekdays and weekends
- Working shifts
- Variable sleep patterns in infants (e.g. interruptions by frequent feeding, diaper change)
- Higher age-related changes in sleep patterns
- Being used to wear a watch at night or not
- Possible light or vibrations from the device that may interrupt sleep
- Taking naps during the day
- Starting new treatment for AD or other conditions (e.g. mental health)
- Illness, pregnancy, or other change in physiology
- Lifestyle changes (exercise, stress, social occasions, etc.)
- Environmental changes (temperature, humidity, etc.)

[2] Yu, Sherry H. BS, BA; Attarian, Hrayr MD; Zee, Phyllis MD; Silverberg, Jonathan I. MD, PhD, MPH Burden of Sleep and Fatigue in US Adults With Atopic Dermatitis, Dermatitis: March/April 2016 - Volume 27 - Issue 2 - p 50-58 doi: 10.1097/DER.0000000000000161

Patient behaviors, preferences, & disease characteristics

Consider following aspects for sensors and devices:

- Sleep patterns
- **Bedtime routines**
- Individual baselines
- Right sensor to the right patient
- Technology literacy
- Continuous monitoring vs only at night

Consider patients' **bedtime routines** & added stress from the new measurement

Bedtime routines may include:

- Baths
- Applying topical treatments
- Using lotions or moisturizers
- Spacing orally taken treatments
- Wraps
- Etc.

Patient behaviors, preferences, & disease characteristics

Consider following aspects for sensors and devices:

- Sleep patterns
- Bedtime routines
- **Individual baselines**
- Right sensor to the right patient
- Technology literacy
- Continuous monitoring vs only at night

Consider & measure **individual baselines**

- Every person may scratch differently, use different treatment or cognitive approaches to avoid scratching, even within the same disease severity group
- Moreover, symptoms (such as itch or scratching) may be variable over time
- Consider if a person is currently (or at the start of the measurement) experiencing a flare of eczema symptoms

Patient behaviors, preferences, & disease characteristics

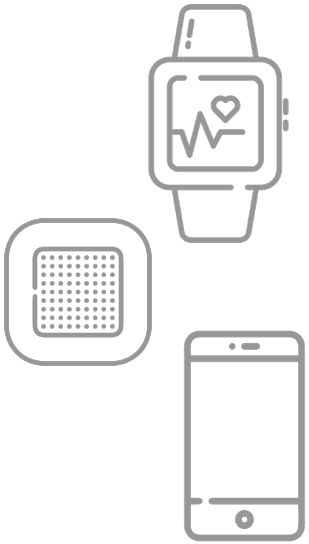
Consider following aspects for sensors and devices:

- Sleep patterns
- Bedtime routines
- Individual baselines
- **Right sensor to the right patient**
- Technology literacy
- Continuous monitoring vs only at night

Get the "**right sensor to the right patient**."

There may be individual preferences or access barriers that would make some sensors preferable over others.

- For example, some people may have eczema on their hands or wrists and may not tolerate wrist-worn sensors or patches
- Consider using a device that is ubiquitous (more familiarity with the device, less stigma associated with wearing or using the device)
- Is the device stand-alone or does it need an accompanying base-station (e.g. phone) - do these need to be close-by or charged, or require any additional interaction by participants?

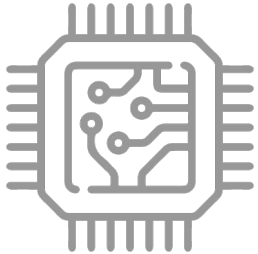


Patient behaviors, preferences, & disease characteristics

Consider following aspects for sensors and devices:

- Sleep patterns
- Bedtime routines
- Individual baselines
- Right sensor to the right patient
- **Technology literacy**
- Continuous monitoring vs only at night

Consider **technology literacy** of the patients or caregivers



Technology should be **easy** to:

- ✓ Set up
- ✓ Use
- ✓ Maintain

Patient behaviors, preferences, & disease characteristics

Consider following aspects for sensors and devices:

- Sleep patterns
- Bedtime routines
- Individual baselines
- Right sensor to the right patient
- Technology literacy
- **Continuous monitoring vs only at night**

Consider pros & cons of continuous use vs. use only at night

Continuous monitoring

Pros

+ Longitudinal data collection
+ Better compliance (patient does not have to remember to switch or put the device on/off)

Cons

- Long wear increases stress of skin irritation
- Battery life may be shorter than study duration, increasing risk of missing data

Use only at night

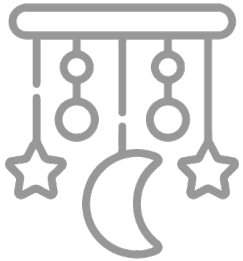
Pros

+ Lower risk of skin irritation
+ Device may charge or process data when not in use

Cons

- Risk of lowered compliance (forgetting to turn or put device on/off)
- Higher data variability (not monitoring for the same time period every night)

Use in pediatric population



Use of digital measurement devices in children requires unique considerations regarding the impacts of disease and measurements of movements and scratching

On top of the general considerations, consider the following specific aspects for sensors and devices used in pediatric populations:

- Is the device made of non-irritant materials to the skin?
  - Children may have more sensitive skin than adults
  - Be even more considerate to the used materials - some of the materials, such as nickel, rubber, or silicone, may cause irritation of the skin
  - Are the materials that come in contact with skin (e.g. bands, adhesives) breathable?
  - Does the device need to be cleaned frequently or washed daily?
    - If yes, be cautious that the cleansers can also be skin irritants
- Assess all parts of the device, including the bands, adhesives, or metal external parts of the device
- Can any external part of the device enter the mouth (e.g. for measurement in young children)?
- Is the device easy to put on and take off?
- The right fit is important for both compliance and correct data retrieval. Is the size of the device appropriate for use in children or infants?
  - Wearable device form factors must account for smaller size, developmental factors, and expected somatic growth in children
    - Is there a requirement to outsource a different band size?
- Consider social interactions of older children in school and with peers, friends, or family members
  - Allow pediatric patients to act and feel like kids, not patients under constant surveillance
  - Can the device be hidden underneath the clothing?
  - Will it interfere with social interactions of older children in school and with peers, friends, or family members?

Patient motivation

Various aspects can affect AD patients' motivation to join the study or to stay adherent to the required assessments in research

- Consider the possibility of **severity of the disease** affecting motivation of the patient to withstand more burdensome changes connected to measurement
  - Patients with more severe disease will be more likely to withstand more burdensome changes connected to measurement and be more adherent
  - However, ***even mild eczema is bothersome for patients and/or caregivers and thus motivating good adherence in a study***

Treat the patient as a **research partner**, rather than a subject

- Consider sharing collected data with the study participants if possible (view CTTI decision support tool for this activity)

Consider creating a community approach

- Experience in clinical trials may feel isolating for AD patients
- Connection to patients with similar experiences or hearing shared testimonials can be beneficial
- Consider added value in organized communities (such as patient advocacy organizations - GPER, NEA, etc.) for people in the same trial - as opposed to unrelated social media or online groups the patients may find for themselves

Determine usability and utility of the measurement device and method

- Put simply, *utility* is whether a product has the features that users need, and *usability* is how easy and pleasant those features are to use
- Use previously published data, or consider using *Patient usability form* resource from this toolkit

Be clear in support, education, and onboarding of the patient to the trial

- Find more in the *Optimizing patient experience* resource

Determining wear duration

For each study incorporating digital measurement, the design should aim for:

The smallest number of sensors that yield the necessary information

The shortest wearing times that provide stable quantification of key variables

Minimum required wear time can be calculated from the previous studies where the participants had complete wear time compliance by simulating the effect of having only a portion of the data available (*Here's how*)

Additional Relevant Resources

- The Playbook: How do we get patient input so we can select the right digital sensing product?
- FDA Guidance: Patient-Focused Drug Development: Collecting Comprehensive and Representative Input
- FDA Guidance: Digital Health Technologies for Remote Data Acquisition in Clinical Investigations
- CTTI: CTTI decision support tool on real time data sharing to patients
- CIOMS: Ethical framework for biomedical research
- UK Biobank study to estimate wear time for physical activity trackers

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National Eczema Association

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