

*Data Tells the Story*

# Wearables in Pulmonary Hypertension

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# Disclosures

Grant funding from NIH/NHLBI and United Therapeutics

Both commercial and research-grade actigraphy devices will be discussed. I use research-grade devices in my work. I do not receive funding from any actigraphy companies.

# Wearables in Pediatric Cardiology

- Exercise intolerance is common
- Standard exercise testing has limitations
- Actigraphy: non-invasive technique used to assess cycles of activity and rest over several days to several weeks
- Near continuous monitoring in the home setting – more accurate “picture” of our patients’ functional capacity?
- Activity, sleep, heart rate variability, skin temperature, oxygen saturation, and more...
- Field is moving away from proprietary sensors and software to raw sensor data and open-source algorithms
- Potential targets for interventions and clinical trials

# Factors contributing to exercise intolerance in PH

## Cardiac factors

- ↓ RV stroke volume
- ↑ RV afterload
- RV dyssynchrony
- Impaired RV adaptation
- RV ischaemia
- Tricuspid regurgitation
- ↓ LV preload
- R-L PFO flow
- Chronotropic incompetence

## Skeletal muscle dysfunction

- ↓ Oxidative enzymes
- ↑ Anaerobic enzymes
- ↑ Metabolic acidosis
- ↓ Type I muscle fibres
- ↓ Muscle CSA
- ↓ Strength
- Capillary rarefaction
- Altered metaboreflex



## Pulmonary factors

- ↓ Pulmonary distensibility
- ↑ Arterial stiffness
- Pulmonary endothelial dysfunction
- Rapid transit time
- ↓ Perfusion
- R-L shunting → ↓ systemic O<sub>2</sub>
- Ventilatory inefficiency
- Increased dead space
- Respiratory muscle dysfunction

## Other factors

- Iron deficiency/anaemia
- Systemic endothelial dysfunction
- ↑ Inflammation
- ↑ Oxidative stress
- ↑ Sympathetic activity
- ↓ Physical activity levels

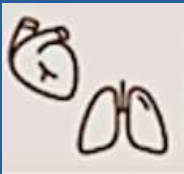
Exercise performance



Physical activity



Cardiopulmonary status



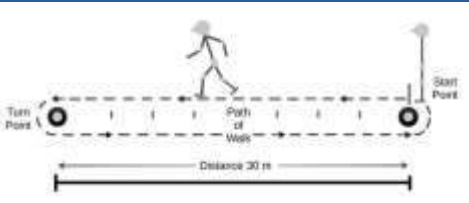
Functional status



Quality of life



Clinical trial targets



# Commercial vs. Research Grade

Commercial devices with proprietary algorithms  
\*\*Children's Online Privacy Protection Act (COPPA)



FitBit



Apple



Garmin

Research-grade device with activity intensity cutpoints applied to raw data



Geneactiv

Research-grade devices with activity intensity cutpoints applied in vendor software



ActiGraph  
GT9X Link



CentrePoint  
Insight Watch



ActiGraph  
LEAP

Open-source algorithms applied to raw data from multi-sensor research-grade devices in real time



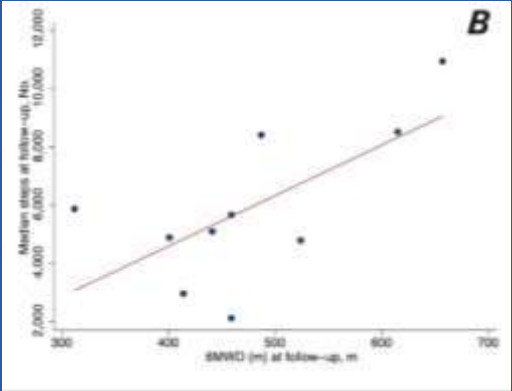
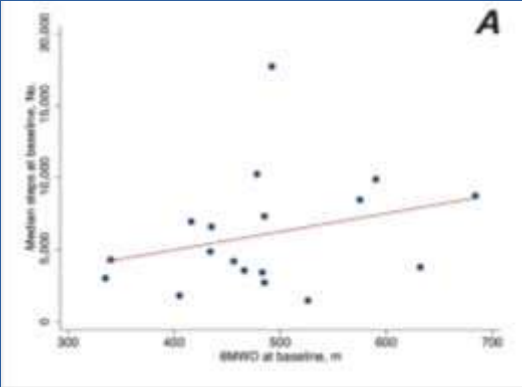
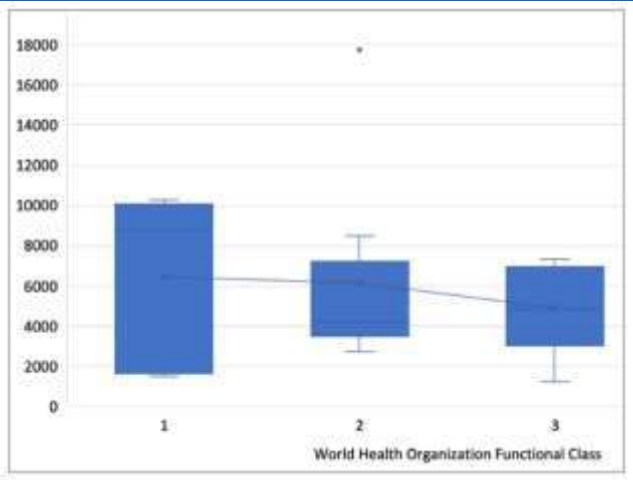
# Efficacy of a Commercial Physical Activity Monitor in Longitudinal Tracking of Patients With Pulmonary Hypertension: A Pilot Study

Eliana Rosenzweig, BS<sup>1</sup>; Gerson Antonio Valencia Villeda, MD<sup>1,3</sup>; Sarah Crook, PhD<sup>2</sup>; Fatima Koli, MS<sup>2</sup>; Erika B. Rosenzweig, MD<sup>1</sup>; Usha S. Krishnan, MD<sup>1</sup>



Commercial device with proprietary algorithms

FitBit Charge



Lower average daily step count trended lower with worsening WHO FC in 21 PAH patients

Daily step count positively correlated with 6MWD at 3-4 month follow-up ( $r=0.72$ ,  $p=0.03$ )

# Physical Activity in Pediatric Pulmonary Arterial Hypertension

## Measured by Accelerometry

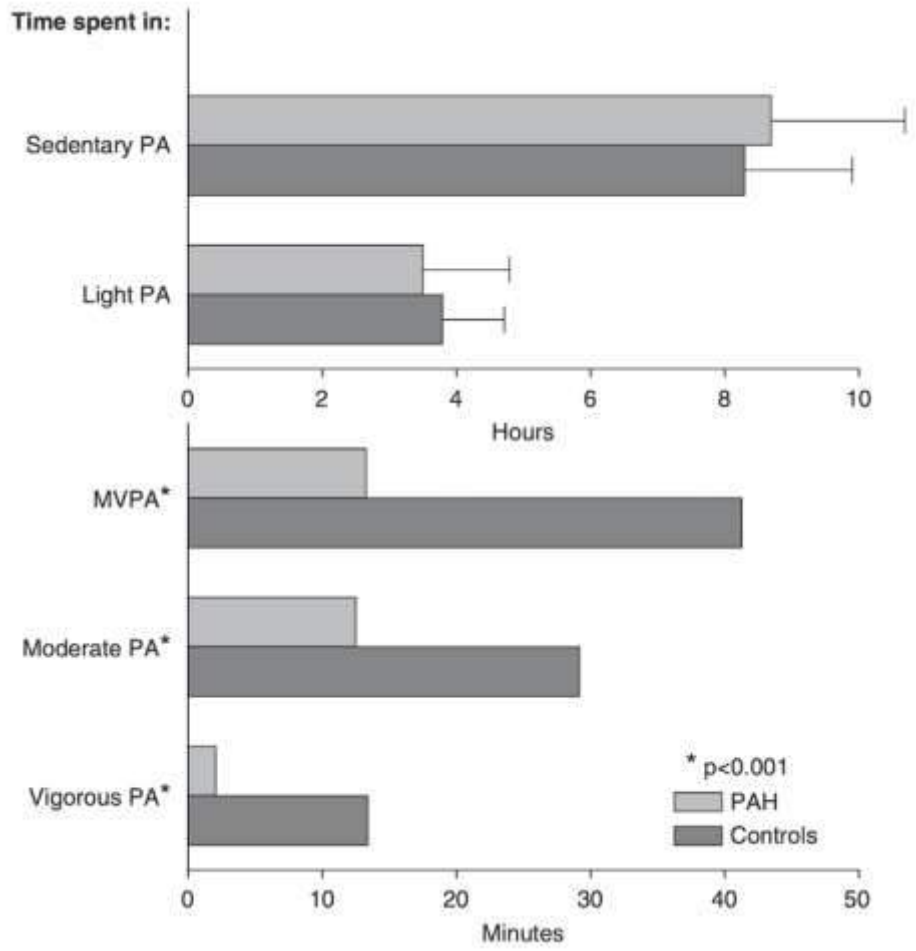
### A Candidate Clinical Endpoint

Willemijn M. H. Zijlstra<sup>1</sup>, Mark-Jan Ploegstra<sup>1</sup>, Theresia Vissia-Kazemier<sup>1</sup>, Marcus T. R. Roothoof<sup>1</sup>, Gideon du Marchie Sarvaas<sup>1</sup>, Beatrijs Bartelds<sup>1</sup>, Annette Rackowitz<sup>1</sup>, Freek van den Heuvel<sup>1</sup>, Hans L. Hilleg<sup>2</sup>, Guy Plasqui<sup>3</sup>, and Rolf M. F. Berger<sup>1</sup>

<sup>1</sup>Center for Congenital Heart Diseases, Beatrix Children's Hospital, and <sup>2</sup>Department of Epidemiology, University Medical Center Groningen, University of Groningen, Groningen, the Netherlands; and <sup>3</sup>Maastricht University Medical Center, University of Maastricht, Maastricht, the Netherlands



- Research grade accelerometer, vendor software, cut points applied
- Less MVPA in 29 PAH compared with 60 controls
- MVPA inversely correlated with FC
- Moderate PA positively correlated with 6MWD



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## Measurement of Physical Activity by Actigraphy in Infants and Young Children with Pulmonary Arterial Hypertension

Catherine M. Avitabile, MD<sup>1</sup>, Delphine Yung, MD<sup>2</sup>, Stephanie Handler, MD<sup>3</sup>, Rachel K. Hopper, MD<sup>4</sup>, Jeff Fineman, MD<sup>5</sup>, Grace Freire, MD<sup>6</sup>, Nidhi Varghese, MD<sup>7</sup>, Mary P. Mullen, MD, PhD<sup>8</sup>, Usha S. Krishnan, MD<sup>9</sup>, Eric Austin, MD<sup>10</sup>, Lori Silveira, PhD<sup>11</sup>, and D. Dunbar Ivy, MD<sup>11</sup>



FitBit Inspire



wGT3X-BT

- 47 (18 PAH, 29 control) participants ages 0-6 years
- FitBit Inspire (>1 yo) and ActiGraph wGT3X-BT (all pts)
- Both commercial with proprietary software & research-grade with cut points applied
- Obtained complete ActiGraph data in 81% and FitBit data in 72%
- PAH: fewer steps, lower vector magnitude counts per minute, more sedentary activity, less intense physical activity at all levels c/w controls
- Fewer steps by ActiGraph compared with FitBit in control patients, not PAH
- Measurement of physical activity by wearables is feasible in young PAH patients
- Future studies to explore relationships with disease severity

# Kids ModPAH Trial

- Ongoing Phase III multicenter RCT testing upfront monotherapy (sildenafil) vs. combination therapy (sildenafil + bosentan) in patients ages 3 months to 18 years with treatment naïve PAH or PH and FC II or III at 12 North American centers
- Primary outcome is WHO FC at 12 months
- Actigraphy measurement of physical activity is an exploratory secondary outcome
- Research-grade devices with vendor software/cut points
- Syncing to vendor platform via mobile app
- Transfer of aggregate data to a REDCap database via an application programming interface (API)

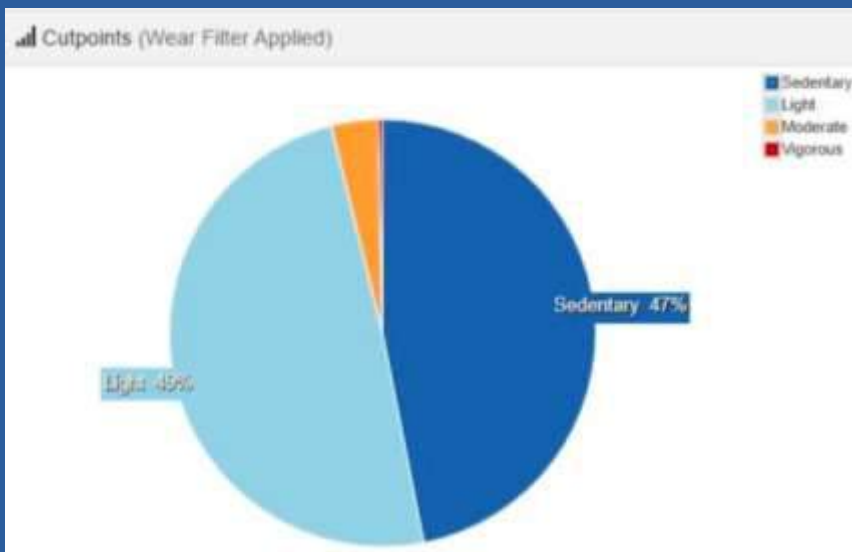


wGT3X-BT



ActiGraph CPIW

# Kids ModPAH Trial



Daily Activity (Wear Filter Applied)

Show 100 entries

Day	Steps	Axis X Counts	Axis Y Counts	Axis Z Counts
7/25/2023	447	36,995	32,598	34,065
7/26/2023	50	8,582	8,208	12,503
7/27/2023	512	24,052	20,526	33,627
7/28/2023	490	36,618	43,617	44,232
7/29/2023	17	2,452	2,534	2,287
7/30/2023	2,285	56,704	66,853	101,308
7/31/2023	4,780	155,474	122,153	194,991
8/1/2023	4,467	143,495	108,060	143,561



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# Physical activity, muscle mass and quality, and functional status

	PH N=19	Healthy N=17	p
<b>MVPA, minutes</b>	5 (1, 10)	18 (10, 42)	<0.01
<b>6MWD, m</b>	601 (495, 635)	675 (607, 730)	0.04
<b>LLMZ</b>	-1.41 (-1.80, -0.32)	-0.61 (-0.88, -0.09)	0.02
<b>D-HGZ</b>	-0.95 (-2.74, -0.55)	-0.43 (-1.11, 0.16)	0.02

	MVPA		PH status	
	Est. (SE)	p	Est. (SE)	p
<b>6MWD</b>	2.70 (1.06)	0.01	-28.42 (38.05)	0.46
<b>LLMZ</b>	0.00 (0.01)	0.85	-0.76 (0.32)	0.02
<b>D-HGZ</b>	-0.02 (0.01)	0.22	-1.41 (0.48)	<0.01



Geneactiv

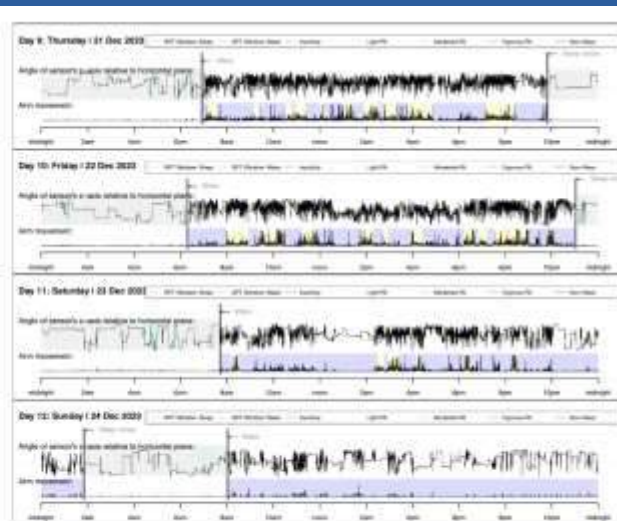
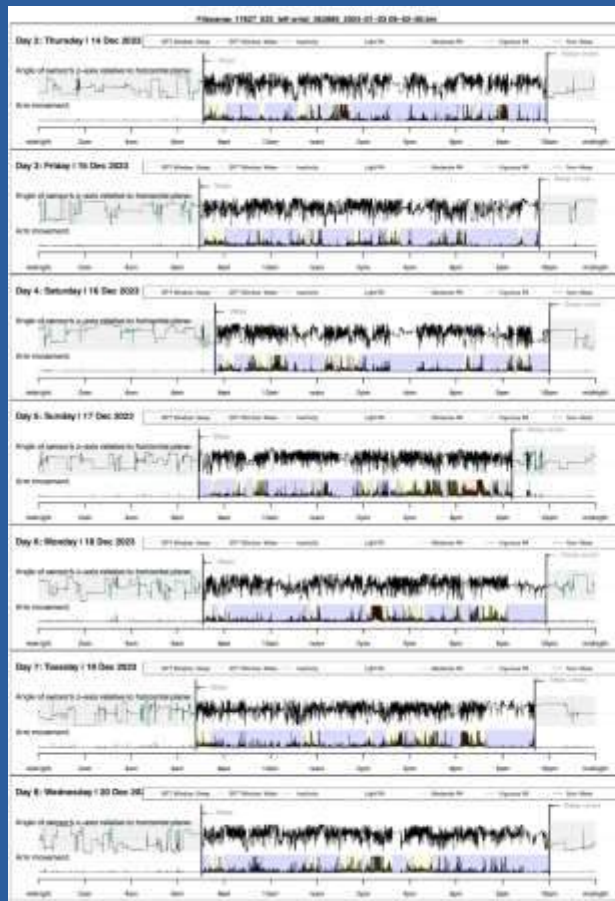
Funded by: 1K23HL150337-01



Geneactiv

Research-grade  
device with analysis  
of raw data in GGIR  
R studio package

Cut points still  
needed



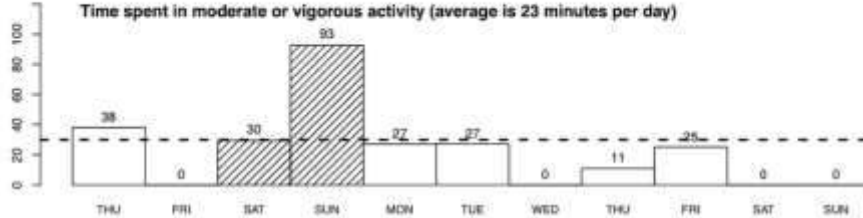


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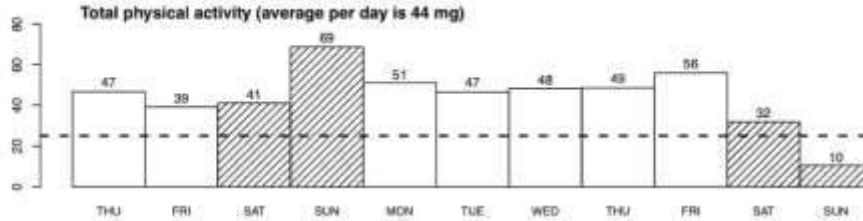
Research-grade device  
with analysis of raw data in  
GGIR R studio package

Activity and sleep report:17827\_023\_left wrist\_062889\_2024-01-03 09-52-50.bin

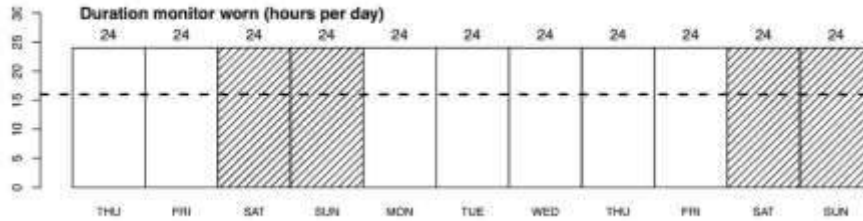
Time spent in moderate or vigorous activity (average is 23 minutes per day)



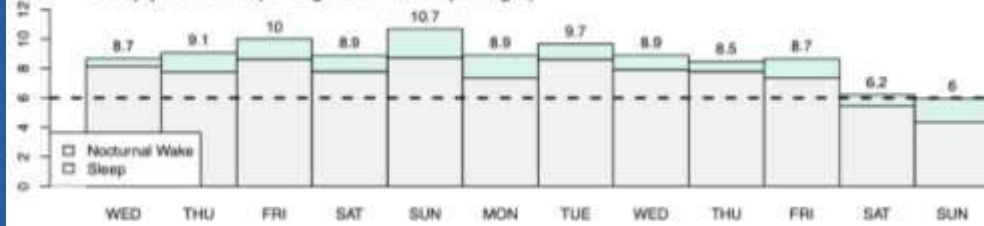
Total physical activity (average per day is 44 mg)



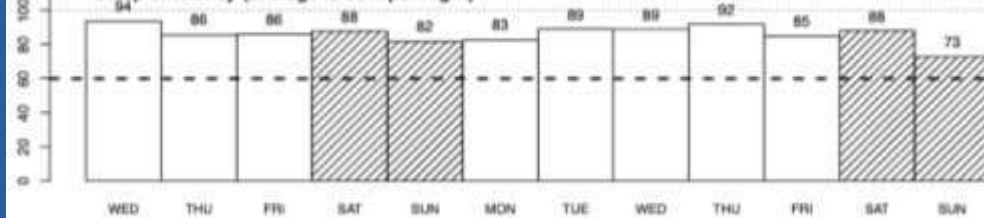
Duration monitor worn (hours per day)



Sleep period time (average is 8.7 hours per night)



Sleep efficiency (average is 86% per night)



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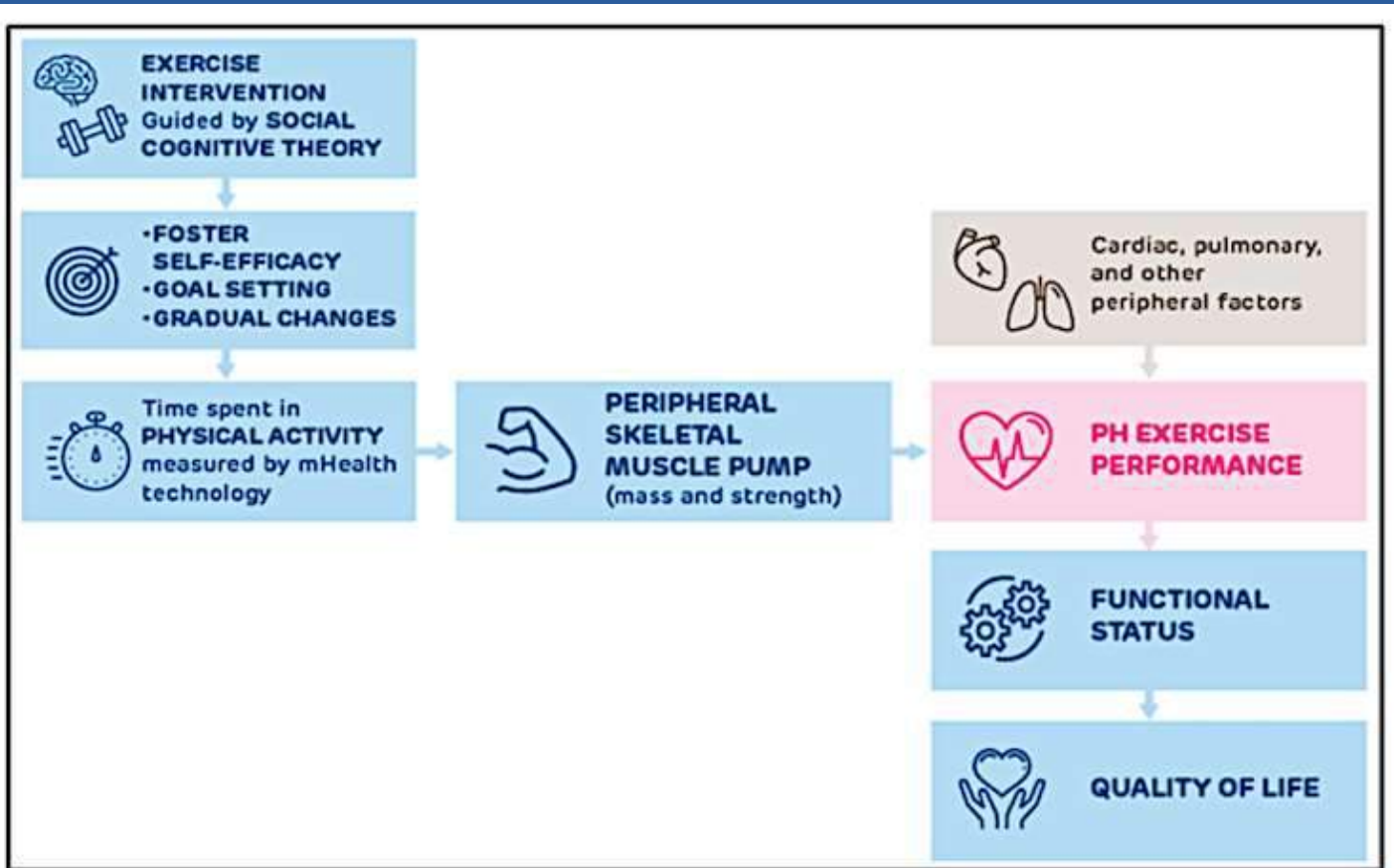
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# Novel Clinical Trial Design in PH



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# Novel Clinical Trial Design in PH

- ✓ Wearable actigraphy device to measure activity and heart rate
- ✓ Continuous/real time measurement
- ✓ Feedback/alerts between study team and participant
- ✓ Survey capability
- ✓ On-demand access to study team with problems or symptoms

# The iTONE Trial



Bluetooth



Data transfer via  
API connection



DataHub with home  
ethernet connection



Cutpoints applied

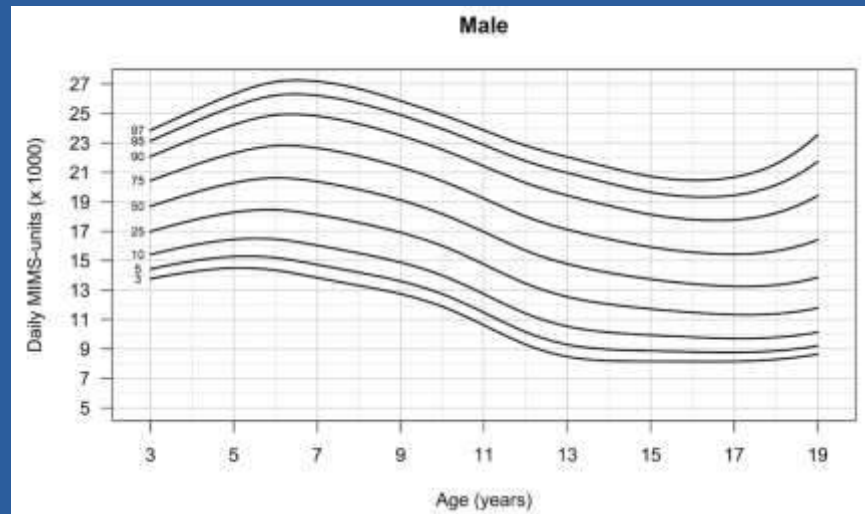
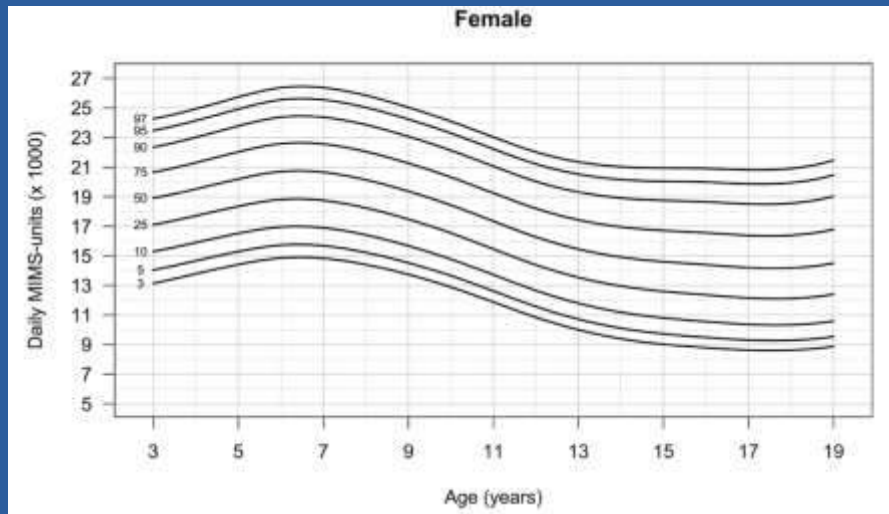


Messaging via Twilio  
communication



ChatBot for  
communication with team

# MIMS Units and Percentiles



Activity percentile curves derived from NHANES data  
Open-source algorithms applied to raw data from multi-sensor research-grade devices in real time

Belcher BR, et al. Med Sci Sports Exerc, 2021.

# Take Home

- Measurement of activity by wearable sensors is feasible in pediatric PH
- Field is shifting from commercial devices toward research-grade sensors
- Current practice is to apply published activity intensity cut points
- Next step is to analyze raw data with open-source algorithms to calculate activity percentiles
- Future studies are needed to study the relationships between activity, disease severity, and disease progression
- These approaches can be applied in other cardiac populations as well!

# Thank you

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# Thank you



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