Clinical Researcher
September 2021
HOME STUDY TEST
Soft Skills and Hard Choices

Earn 2.0 Continuing Education Credits

Two articles from the September 2021 issue of *Clinical Researcher* have been selected as the basis for a Home Study test that contains 20 questions. For your convenience, the selected articles and test questions are combined and posted in the form of this printable PDF at **https://www.acrpnet.org/professional-development/training/home-study/**, where the test may be purchased. *The test will be active until September 30, 2022.* This activity is anticipated to take two hours. **Answers must be submitted using the electronic answer form online (members $30; non-members $50).** Those who answer 80% or more of the questions correctly will receive an electronic statement of credit by e-mail within 24 hours. Those who do not pass can retake the test for no additional fee.

The *Clinical Researcher* archive is at **https://www.acrpnet.org/resources/clinical-researcher/**.

CONTINUING EDUCATION INFORMATION

The Association of Clinical Research Professionals (ACRP) is an approved provider of clinical research continuing education credits.

Contact Hours

The Association of Clinical Research Professionals (ACRP) provides 2.0 contact hours for the completion of this educational activity. These contact hours can be used to meet the maintenance requirements for certification programs of the Academy of Clinical Research Professionals. (ACRP-2021-HMS-009)

ACRP DISCLOSURE STATEMENT

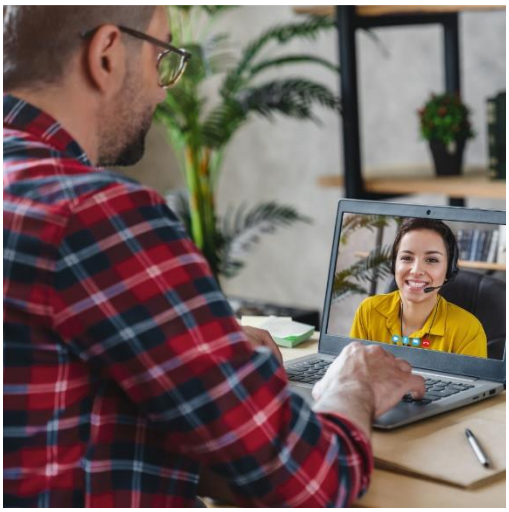
The Association of Clinical Research Professionals (ACRP) requires everyone who is in a position to control the planning of content of an education activity to disclose all relevant financial relationships with any commercial interest. Financial relationships in any amount, occurring within the past 12 months of the activity, including financial relationships of a spouse or life partner, that could create a conflict of interest are requested for disclosure. The intent of this policy is not to prevent individuals with relevant financial relationships from participating; it is intended that such relationships be identified openly so that the audience may form their own judgments about the presentation and the presence of commercial bias with full disclosure of the facts. It remains for the audience to determine whether an individual's outside interests may reflect a possible bias in either the exposition or the conclusions presented.

Clinical Researcher—September 2021 (Volume 35, Issue 7)

PEER REVIEWED

The Health and Productivity Effects of Remote Work on Clinical Research Associates

Sucheta Sachdeva; Tyler D. Green; Terry L. Oroszi



The COVID-19 pandemic has affected the health and productivity of employees in nearly every industry in the world. If companies were able to stay afloat and survive financial hardship, their leaders often had to make challenging and innovative decisions. Some companies required essential workers to report to work, while others had to furlough or lay off employees. Many companies turned to options for having some or all of their traditionally in-office employees transition to working remotely to remain functional.{1}

Although not uncommon before the pandemic, remote work gained tremendous popularity as a workaround option for many companies that could no longer safely allow employees to work in an office per local regulations. Remote working became a “new normal” practice almost overnight.{1,2}

Despite the recent increased prevalence of remote work, the clinical research industry is no stranger to the concept.{3} Larger companies tend to provide the option of remote work to a number of their employees. There are many positions associated with clinical research that can be completed in a remote fashion. Examples of these positions include, but are not limited to, project managers, data managers, safety managers, line managers, clinical research associates (CRAs), clinical trial assistants, and other similar positions.

Although this review could be applied to a variety of clinical research positions, the primary purpose of this paper is to focus on the health and productivity effects of remote work on CRAs, also known as monitors. A CRA "supervises, monitors, and supports the administration and progress of a clinical trial on behalf of a sponsor."{4}

Although many CRAs typically travel frequently in fulfillment of their job duties, there are also remote-working CRAs that are known by a variety of titles depending on the employer, including in-house CRAs (IHCRAs), site management associates (SMAs), site managers, etc.

The 2020 pandemic placed significant traveling restrictions on many CRAs.{5} To maintain oversight for studies, clinical research sponsors decided to push for remote source document verification methods to be implemented where possible.{6} As sites adjusted to new monitoring plans, CRAs found themselves working from home for extended periods and experiencing the benefits and shortcomings of such a lifestyle.

Numerous terms are used to describe remote work, such as work from home (WFH), virtual work, telework, telecommuting, and e-work.{7} Unfortunately, finding an agreed-on definition for each term is still a challenge.{8} For this paper, remote work is defined as work completed with technology outside the office setting, most commonly in the employee's residence.

General Positive Attributes of Remote Work for Employers

There are several potential cost and productivity advantages to allowing CRAs to work remotely. It can be argued that remote work can save companies on their bottom line,{9} in part because they would not need to lease office space and maintain it for employees.{10} The idea of cost-savings can be further applied to employers of CRAs. Although the employer may cover the cost of internet and home office equipment (e.g., desk, chair, printer, supplies), for remote CRAs, employees are typically expected to cover most, if not, all utilities.

Travel savings are yet another benefit to remote work that would be especially applicable to the CRA position. In the case of traveling CRAs who transition to a fully remote position, the company would save costs on flights, food, per diems, hotel stays, car rentals, transportation, travel time, and any other travel-related expenses.

Another benefit of remote work would be a decrease in employee absenteeism. Employees are less likely to call off work or be late if they work remotely.{11} There would be no need to commute to work and potentially be caught in traffic. Employees would likely work remotely despite minor illnesses or childcare trouble, as they could potentially adjust their environment and workday to accommodate such challenges.{7} IHCRAs/SMAs could take advantage of this flexibility to work later in the day to make up for any time lost during typical business hours. In the end, less company time would be lost, and more work could potentially be completed for the employer.

Increasing productivity by completing a greater amount of work, in general, is another positive attribute of remote work. Remote employees tend to work with fewer distractions than would be found in the office. Productivity findings could also be applied to clinical research. Typical CRA positions require travel during most weekdays. These former traveling CRAs would replace trip time with more frequent general communication with sites and possibly more frequent official remote monitoring visits, thus transitioning more into the IHCRA/SMA role.

More communication with sites could result in issues being resolved quickly, fewer study issues arising in general, protocol deviations being minimized, safety concerns being reported in a timely fashion, and/or growth of confidence between site staff and CRAs in their work on studies.

In 2013, the U.S. Food and Drug Administration (FDA) released guidance on the subject of centralized (remote) monitoring that encouraged it to be used more frequently than onsite monitoring. Centralized monitoring was especially suggested to reduce costs of clinical trials, improve data quality, identify data trends, and increase efficiency.{12}

The confidence in remote work for CRAs has gained momentum as a forefront option to continue clinical trials during the COVID-19 pandemic. The FDA released further guidance during this pandemic, recommending that sponsors “evaluate alternative methods” to in-person monitoring and giving phone contacts and virtual visits through remote monitoring as examples.{13}

Overview of Benefits and Shortcomings of WFH for CRAs	
Pros	**Cons**
Cost savings for employers and CRAs	Prone to overworking (dependent on individual and employer expectations)
Decrease in employee absenteeism	Health risks from extended sedentary work
Increased productivity	Overwork can lead to burnout
Fewer distractions	Burnout can lead to turnover
Less time spent travelling	
More time spent identifying/resolving site issues	
Increased efficiency	

General Negative Attributes of Remote Work for Employers

Some research disputes the findings on the potential benefits of remote work, citing conflicting information and difficulty measuring the amount of work being completed for specific remote versus in-person roles as obstacles to accurate assessment.{14} Employee accountability is a concern for employers, as it can be challenging to verify that a remote employee is at a workstation and working during business hours. However, the concerns for accountability may be a moot point for CRAs; the traveling CRA position already requires a degree of autonomy to complete most assignments remotely, due to travel to sites for monitoring responsibilities.

Similarly, IHCRAs/SMAs are required to complete remote contacts and visits with their sites. Accountability can easily be verified by contacting the site staff with whom the CRAs complete their visits. Additionally, nearly all CRAs must write reports regarding their visits and provide updates about their sites. Being accountable for their work is engrained into CRAs, as many other team members and the sponsor rely on their updates. Thus, the negative stance of remote work held by some employers may not apply to this position.

Still, depending on the CRA's personality and work/life balance skills, working from home could turn from being a more relaxed option to one where the work appears never to end. If the

CRA has difficulty drawing a clear line between work and personal life, he or she may experience more intense stress due to never being “off” work. These individual coping styles were discussed and helped to postulate a person-centered boundary management theory.{15}

CRAs may feel pressured to work beyond typical business hours to feel “justified” for not traveling. They may think that it is important to be available to site staff and clients at all times, since they appear to be more accessible due to being off the road.

The full responsibility for overwork cannot fall squarely on the employee. Recent meta-analyses for physician and other healthcare employee burnout suggests that organizational interventions would have more effect on the well-being of said employees than ones directed by the employees individually.{16} A prudent clinical research employer would state they support their employees’ health and well-being and provide the necessary tools, incentives, and opportunities for remote employees to live healthier lives.

The risks of prolonged sitting can especially be applied to remote CRAs who need to complete source document verification (SDV) with sites during remote monitoring visits that can last many hours. If employers implement changes to decrease sedentary work time for CRAs, it would demonstrate the idea that clinical research employers complete clinical trials and embrace research results to ensure that not just patients of clinical trials, but also their employees, are living healthier lives.

Productivity and Efficiency Tools

Several communication and exercise tools can help remote employees stay healthy and still productively complete their jobs. Many full-time remote employees receive their home office furniture and supplies from the employer. Employers can incentivize a healthy lifestyle for employees by to providing convertible sitting-standing or, preferably, treadmill desks, so employees are encouraged to stand and/or walk while working. Studies have shown potential benefits from combining standing desks with taking active breaks involving movement as the best option for a healthier and less sedentary work lifestyle.{17,18}

For those who make numerous calls, such as IHCRAs, employers can provide high-quality wireless headsets that allow the employee to stand and walk hands-free during meetings and calls. Mild exercise, such as walking, could improve the IHCRA's mood and allow for a refreshing change of pace from sitting through calls. Employers could also proactively provide employees with options for ergonomic computer hardware (mouse, keyboard, etc.) to allow for a more comfortable experience while sitting and typing for long hours. A comfortable and supportive chair could also prevent body aches and sores for employees when forced to sit for many hours due to heavy workload assignments.

These are just a few examples to potentially demonstrate to employees that their employer cares about their well-being and is well aware of the benefits of using such tools to better their health.

Fatigue, Burnout, and Employee Turnover

A study by Helfrich, et al. conducted with primary care providers, nurse care managers, licensed practical nurses, and administrative clerks found that understaffing, turnover, and patient panel overcapacity all largely contributed to burnout within the team, regardless of a specific occupation. The study observed burnout as 30.1% lower for fully staffed teams with no turnover and within the capacity panel of patients.{19} Since these results were the same regardless of profession, they could be applied to the CRA.

Remote employees may feel unheard and exhausted if overworked, which can lead to higher turnover. Burnout can be significantly amplified if the employer does not actively encourage work/life balance, adding to the employee's stress of always being "on the clock." Many organizations impede their employees' time by expecting them to remain in touch with work using remote-based technology, like smartphones, outside business hours.{7}

Moreover, finding replacement employees can take much time, which leads to overburdening of current employees. Overwork due to turnover may especially be evident in the contract research organization setting, where revenue usually depends on new study awards, billable hours worked, and the number of completed monitoring visits.

If CRAs are already working remotely, employers often encourage them to work longer hours and take on more work, especially if their coworkers leave the company. Since the process of finding and replacing employees is costly and time-consuming, delays may lead to never replacing empty positions on certain studies, eventually making it the norm for the covering CRA to become overworked. The vicious cycle may continue to take its toll, leading to CRAs exhibiting symptoms of burnout and further increasing the chances for turnover. One option to break the cycle is to have the employer change tactics for hiring qualified replacements quickly.

Employee Retention

Although the bottom line is important, there is a shared responsibility for companies and employees to implement working limits in consideration of the well-being of employees. The employer should try to be respectful of the employee's time by assigning appropriate workload and ceasing the push for work to be completed outside business hours.

Along with the employer, employees can be trained to manage their time and tasks better so that working past business hours is rarely necessary. Remote employees would also need to work on individual traits to learn to separate work time from off time at home.

One suggestion for remote CRAs is to not forward their work e-mails to their personal phones and to turn off their computers at the end of the business day, effectively "cutting the leash" to the habit of checking work e-mails or walking back to the home office computer to address issues that could wait until the next business day. Having this discipline would be dependent on the individual's dedication to maintaining a pleasant work/life balance.

Conclusion

Although accountability and oversight may initially be a concern, by hiring remote CRAs, employers would enjoy cost savings, fewer employee absentee days, and increases in productivity, among other benefits listed in the table earlier in this article. The CRA, meanwhile, may have several advantages in working remotely, including feeling less distracted, having less stress due to no travelling, increased job satisfaction, and a more manageable work/life balance.

Conversely, if overworked, the remote CRA position would adversely affect mental health, especially if the CRA cannot draw clear boundaries between work and home life.

Overall, both the employer and remote employee are responsible for the success of the business and the health of the remote employee. Although this paper attempts to apply known research regarding remote work to the CRA position, more research needs to be collected and documented, focusing on feedback and data collection regarding remote work from traveling CRAs and remote CRAs directly.

The clinical research industry has had remote working positions for years. Still, it will be interesting to see if employers will have the prescience to amplify the benefits and tackle the challenges involved with the remote CRA position and simultaneously retain employees for the long term.

References

1. Kniffin KM, Narayanan J, Anseel F, Antonakis J, Ashford SP, Bakker AB, Bamberger P, Bapuji H, Bhave DP, Choi VK, Creary SJ, Demerouti E, Flynn FJ, Gelfand MJ, Greer LL, Johns G, Kesebir S, Klein PG, Lee SY, . . . Vugt M. 2021. COVID-19 and the Workplace: Implications, Issues, and Insights for Future Research and Action. *American Psychologist* 76(1): 63–77. https://doi.org/10.1037/amp0000716
2. Wang B, Liu Y, Qian J, Parker SK. 2020. Achieving Effective Remote Working During the COVID-19 Pandemic: A Work Design Perspective. *Applied Psychology* 70(1):16–59. https://doi.org/10.1111/apps.12290
3. Apostolaros M, Babaian D, Corneli A, Forrest A, Hamre G, Hewett J, Podolsky L, Popat V, Randall P. 2019. Legal, Regulatory, and Practical Issues to Consider When Adopting Decentralized Clinical Trials: Recommendations from the Clinical Trials Transformation Initiative. *Therapeutic Innovation & Regulatory Science* 54(4):779–87. https://doi.org/10.1007/s43441-019-00006-4
4. The Association of Clinical Research Professionals. https://acrpnet.org/certifications/cra-certification/
5. Sathian B, Asim M, Banerjee I, Pizarro AB, Roy B, Van Teijlingen ER, Nascimento IJ, Alhamad HK. 2020. Impact of COVID-19 on Clinical Trials and Clinical Research: A Systematic Review. *Nepal Journal of Epidemiology* 10(3):878–87. https://doi.org/10.3126/nje.v10i3.31622

6. Izmailova ES, Ellis R, Benko C. 2020. Remote Monitoring in Clinical Trials During the COVID-19 Pandemic. *Clinical & Translational Science* 13(5):838–41. https://doi.org/10.1111/cts.12834
7. Grant CA, Wallace LM, Spurgeon PC. 2013. An Exploration of the Psychological Factors Affecting Remote e-Worker's Job Effectiveness, Well-Being and Work-Life Balance. *Employee Relations* 35(5):527–46. https://doi.org/10.1108/er-08-2012-0059
8. Sullivan Cath 2003. What's in a Name? Definitions and Conceptualizations of Teleworking and Homeworking. *New Technology, Work & Employment* 18(3):158–65. https://doi.org/10.1111/1468-005x.00118
9. Rapoport R, Lewis S, Bailyn L, Gambles R. 2005. Globalization and the Integration of Work with Personal Life. In: Poelmans SAY (ed.), Work and Family: An International Research Perspective. Mahwah, N.J.: Lawrence Erlbaum Associates. https://www.routledge.com/Work-and-Family-An-International-Research-Perspective/Poelmans/p/book/9780805848823
10. Lewis S, Cooper CL. 2005. Work-Life Integration: Case Studies of Organizational Change. John Wiley and Sons Ltd. https://www.wiley.com/en-us/Work+Life+Integration%3A+Case+Studies+of+Organisational+Change-p-9780470853436
11. Noonan MC, Glass JL. 2012. The Hard Truth about Telecommuting. *Monthly Labor Review* 135(6):38–45. https://search-ebscohost-com.ezproxy.libraries.wright.edu/login.aspx?direct=true&db=ehh&AN=78045555&site=ehost-live
12. U.S. Food and Drug Administration. 2013. Oversight of clinical investigations — A risk-based approach to monitoring. https://www.fda.gov/media/116754/download
13. U.S. Food and Drug Administration. 2021. Conduct of clinical trials of medical products during the COVID-19 public health emergency. https://www.fda.gov/media/136238/download
14. Mintz-Binder R, Allen P. 2019. Exploring the Perspectives of Telecommuting Nursing Faculty. *Journal of Nursing Education* 58(3):152–9. https://doi.org/10.3928/01484834-20190221-05
15. Kossek EE, Ruderman MN, Braddy PW, Hannum KM. 2012. Work–Nonwork Boundary Management Profiles: A Person-Centered Approach. *Journal of Vocational Behavior* 81(1):112–28. https://doi.org/10.1016/j.jvb.2012.04.003
16. Panagioti M, Panagopoulou E, Bower P, Lewith G, Kontopantelis E, Chew-Graham C, Dawson S, van Marwijk H, Geraghty K, Esmail A. 2017. Controlled Interventions to Reduce Burnout in Physicians. *JAMA Internal Medicine* 177(2):195–205. https://doi.org/10.1001/jamainternmed.2016.7674
17. Edwardson CL, Yates T, Biddle SJ, Davies MJ, Dunstan DW, Esliger DW, Gray LJ, et al. 2018. Effectiveness of the Stand More AT (SMArT) Work Intervention: Cluster Randomized Controlled Trial. *British Medical Journal* 363. https://doi.org/10.1136/bmj.k3870
18. Finch LE, Tomiyama AJ, Ward A. 2017. Taking a Stand: The Effects of Standing Desks on Task Performance and Engagement. *International Journal of Environmental Research and Public Health* 14(8):939. https://doi.org/10.3390/ijerph14080939

19. Helfrich CD, Simonetti JA, Clinton WL, Wood GB, Taylor L, Schectman G, Stark R, Rubenstein LV, Fihn SD, Nelson KM. 2017. The Association of Team-Specific Workload and Staffing with Odds of Burnout Among VA Primary Care Team Members. *Journal of General Internal Medicine* 32(7):760–6. https://doi.org/10.1007/s11606-017-4011-4

Sucheta Sachdeva (ssachde@rockets.utoledo.edu) is a Pharmacology and Toxicology graduate student in the Boonshoft School of Medicine at Wright State University in Dayton, Ohio, and a remote Clinical Research Associate/Site Management Associate with more than 10 years of experience in the clinical research field.

Tyler D. Green, DNP, APRN, PMHNP-BC, is a Clinical Instructor in the College of Nursing & Health teaching at Wright State University and a mental health nurse practitioner for a private practice in Dayton, Ohio.

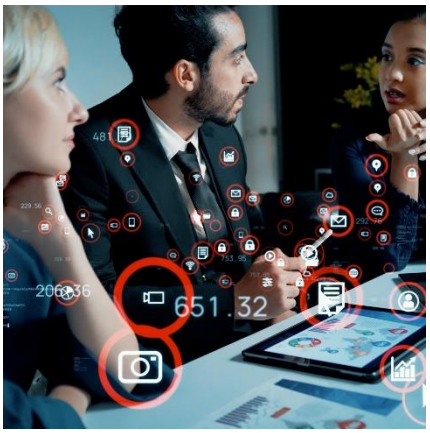
Terry L. Oroszi, MS, EdD, is a specialist in healthcare and homeland security and an Associate Professor and Vice Chair of Pharmacology and Toxicology in the Boonshoft School of Medicine at Wright State University.

Clinical Researcher—September 2021 (Volume 35, Issue 7)

PRESCRIPTIONS FOR BUSINESS

Streamlining Adoption of Digital Technology in Clinical Trials Through Use of Open-Source Algorithms

Geoffrey Gill, MS



Clinical trials have become both increasingly expensive and less reliable as the focus of therapy development has shifted to managing chronic illnesses. Wearables and other digital technologies have the potential to transform clinical trials by allowing investigators to transition from using occasional—often subjective—measures of health, such as patient-reported outcomes, to continuous, objective measures, such as the patient's level of activity or quality of sleep as measured by a wearable device. These metrics have the potential to be highly targeted and precise.

For example, stride velocity 95th centile measured at the ankle with a wearable device was recently accepted as a secondary endpoint for ambulant Duchenne muscular dystrophy patients by the European Medicines Agency.{1} Recognizing the potential of digital endpoints, the Clinical Trials Transformation Initiative (CTTI) released a series of recommendations, including a detailed flowchart showing how to develop endpoints, in June 2017.{2} These recommendations provide a clear path to developing digital endpoints.

The Quest for Qualification and Validation

Despite the potential benefit of digital endpoints and clear guidance on how to qualify them, getting even one endpoint accepted by regulators still requires significant work. The challenge comes from the fact that there are literally thousands of potential digital endpoints and more than 100 types of digital sensors, each with its own algorithms and outputs. Even different versions of the same device will often have different algorithms that generate different results.

There is also a need to validate endpoints on the patient population of interest, as validation on one patient group might not necessarily mean an endpoint will provide accurate outputs for another patient group. Therefore, it is very unlikely that a study team will find a prepackaged solution with a validated endpoint and sensor combination for a pathology of interest. In practice, this means that clinical trials study teams are faced with the choice of going through the entire validation process for their particular patient, sensor, and endpoint combination; capturing just an exploratory endpoint; or abandoning the effort altogether. Further, unless the sensor they use provides the raw data and the algorithm is available, teams will be tied to that particular sensor if they choose the exploratory endpoint alternative and want to use it in later trials.

Fortunately, using open-source algorithms can dramatically streamline this process. By using the V3 validation framework published by members of the Digital Medicine Society,{3} the validation process can be broken into three logically distinct steps:

1. **Verification** – verifying that the sensor provides the right data.
2. **Analytical Validation** – proving the algorithm converts the sensor data into a physical phenomenon, like steps, accurately.
3. **Clinical Validation** – ensuring the physical phenomenon is a relevant clinical measure.

The first step, verification, depends only on the sensor. It should be performed by the manufacturer and should only need to be done once. Assuming verified data, both analytical and clinical validation depend on the algorithm. By using open-source algorithms, researchers can effectively share algorithm validation—no matter what sensor was used to generate the data—if the sensor went through the verification step.

The power of this approach can be demonstrated using atopic dermatitis (eczema) as an example. There are many potential endpoints of interest with this condition that could be measured using wearable sensors,{4} including:

- Scratching events per hour
- Number of scratching events
- Scratching duration per hour
- Total sleep time
- Wake after sleep onset
- Sleep efficiency

There are already open-source algorithms that address these endpoints. For example, Pfizer has developed software called Scratch.PY that calculates all these endpoints for nocturnal scratching, based on data from a wrist-worn accelerometer.{5} Pfizer has performed significant validation studies on this algorithm, and it is free for anyone to use. Researchers that employ Scratch.PY can build on this significant validation effort. Furthermore, if they publish their research, that strengthens the foundation for future researchers looking to validate endpoints for their studies.

A great example of how a validation foundation can be built steadily over time is provided by an open-source package called GGIR, which generates a wide variety of activity and sleep endpoints from wrist-worn accelerometer data. More than 300 peer-reviewed papers have used GGIR, including more than 90 published in just the past year.{6} Hundreds of thousands of participants have been studied in a wide variety of therapeutic areas. Table 1 summarizes a small selection of the studies performed using GGIR to process the data.{7} No single organization could match this level and rate of research.

Table 1:

STUDIES PERFORMED USING GGIR DATA PROCESSING.

Therapeutic area	Patient Cohort	Number of Patients (n)
Cardiovascular	Heart surgery patients [44]	80
	Stroke [15]	41
	Cardiovascular Disease [16]	23,742
	Coronary Artery Disease [17]	58
Central Nervous System	Muscular Dystrophy [18]	128
	Dementia [19]	26
Musculoskeletal	Idiopathic inflammatory myopathy [20]	55
	Muscular Dystrophy [18]	128
	Sarcopenia [21]	131
Mental Health	Depression [22]	359
	Bipolar Disorder [23]	46
	Post-Partum Depression [24]	21
Diabetes	Gestational Diabetes [25]	697
	Type II Diabetes Mellitus [26]	635
	Type II Diabetes [27]	246
Rehabilitation and recovery	Pulmonary rehab patients [28]	79
	Bariatric surgery patients [29]	22
Pulmonary	Cystic Fibrosis [30]	9
	Idiopathic Pulmonary Fibrosis [31]	35
Aging	Older adults [32]	1,451
	Post-menopausal women [33]	1,316
Lifestyle	Sedentary adults [34]	191
	Obesity [35]	1,986
	Smoking [36]	3,063
	General population [37]	85,388
Children	Obese / overweight [38]	208
	Adolescents [39]	2,526
	Children [40]	2,636
Pregnant Women	Pregnant women [41]	2,317
	Pregnant and overweight [42]	257

What's more, all this validation material is available for any sensor that provides accurate accelerometry data. The GGIR research has used many different types of wrist-based accelerometers. By using open-source code, researchers are no longer tied to a single device and can leverage validation and user studies from a wide group of researchers.

The work that has been done to date is just a start for GGIR to achieve approval as a validated endpoint for a clinical trial.{6} However, once approval has been granted, any organization can potentially use that approval as evidence for its own trial—even if it uses a different device. Furthermore, the availability of a large amount of evidence from different therapeutic areas should make extending the validation to those applications significantly easier. Finally, consolidating around a de facto standard like GGIR will start to provide a consistent measurement to be integrated into medical practice.

The Consistency Conundrum

One cannot overstate how important consistent measurements across devices are to using digital medicine to help treat patients. It would be impossible for doctors to treat patients if every blood pressure monitor or thermometer relied on its own metrics for measuring these symptoms. Doctors need to establish consistent normal ranges and thresholds to know how to treat their patients.

Of course, it is relatively easy for different manufacturers to make their blood pressure monitors and thermometers comply to the standards without common algorithms, because they only measure one or two metrics taken at a single time. That is essentially the same as the verification step for digital sensors. Achieving consistency in digital measures without using a common algorithm, on the other hand, is far more difficult.

A major value of digital measurements is that they can monitor continuously over a long period of time to measure subtle changes in health in the real world. This facility is vital to accurately measure the progression of chronic diseases, which affect more than 50% of the U.S. population and represent more than 86% of the country's healthcare costs.{8} However, this means that rather than measuring a single value at a point in time, huge amounts of data must be aggregated, consolidated, evaluated, and summarized.

Without common algorithms, achieving consistent results is effectively impossible. By embedding these algorithms in open-source software, it is possible to ensure consistent results from the start.

The Challenges

Although the benefits of using open-source algorithms appear quite clear, not all stakeholders in the industry support them. Some companies believe that they will be able to get their proprietary algorithms adopted and achieve monopoly profits as a result.

This approach faces immense barriers, not only because of the huge effort required to validate algorithms and the need for consistency across devices, but also because customers, regulatory bodies, and healthcare providers all want levels of transparency which are not generally available with proprietary algorithms. While some companies may succeed at keeping their algorithms to themselves, the majority of applications being developed by various firms will likely adopt common algorithms, if not open source.

Moving Forward

Clinical trial sponsors and regulators are starting to play a major role in this movement toward adopting open-source algorithms. Many of the leading pharmaceutical companies and other industry organizations are participating in the Open Wearables Initiative (www.OWEAR.org), which promotes and facilitates the use of open-source algorithms for clinical endpoints. OWEAR is also working on CTTI's Novel Endpoints Project. In Europe, Mobilise-D is a major collaborative program involving industry, academia, and government to develop open-source algorithms for gait measurement.

More can be done. Sponsors and regulators should strongly encourage the use of open-source algorithms. Sponsors should share validation material and pre-competitive data more broadly. Regulators should encourage and facilitate this sharing as much as possible. Through collaboration, we can accelerate the adoption of these vital tools significantly and help patients live healthier lives.

References

1. https://www.ema.europa.eu/en/documents/scientific-guideline/qualification-opinion-stride-velocity-95th-centile-secondary-endpoint-duchenne-muscular-dystrophy_en.pdf
2. https://ctti-clinicaltrials.org/wp-content/uploads/2021/06/CTTI_Novel_Endpoints_Detailed_Steps.pdf
3. Goldsack JC, Coravos A, Bakker JP, Bent B, Dowling AV, Fitzer-Attas C, Godfrey A, et al. 2020. Verification, analytical validation, and clinical validation (V3): the foundation of determining fit-for-purpose for Biometric Monitoring Technologies (BioMeTs). *npj Digital Medicine* 3 (article number 55). https://doi.org/10.1038/s41746-020-0260-4
4. This example borrows heavily from work presented by Janssen's DEEP initiative at several conferences. It is an illustrative example. It is not meant to be comprehensive and has not been validated.
5. Mahadevan N, Christakis Y, Di J, et al. 2021. Development of digital measures for nighttime scratch and sleep using wrist-worn wearable devices. *npj Digital Medicine* 4 (article number 42). https://doi.org/10.1038/s41746-021-00402-x
6. A partial list of GGIR references can be found at https://github.com/wadpac/GGIR/wiki/Publication-list.
7. Gill G, Patterson MR. 2021. Verisense Validation According to the V3 Validation Framework. https://verisense.net/validation-v3-framework
8. Chapel JM, Ritchey MD, Zhang D, Wang G. 2017. Prevalence and Medical Costs of Chronic Diseases Among Adult Medicaid Beneficiaries. *American Journal of Preventive Medicine* 53(6) Supplement 2:143–54. https://www.ajpmonline.org/article/S0749-3797(17)30426-9/fulltext

Geoffrey Gill, MS, is President of Shimmer Americas, leading the U.S. operations and the commercial efforts for North and South America for Shimmer Research, a designer and manufacturer of medical grade wearables.

ACRP HOME STUDY
CLINICAL RESEARCHER—SEPTEMBER 2021 (VOLUME 35, ISSUE 7)
Soft Skills and Hard Choices

Article #1: **The Health and Productivity Effects of Remote Work on Clinical Research Associates**

LEARNING OBJECTIVES
After reading this article, the participant should be able to summarize the factors behind current conditions for clinical research associates working remotely, address employer- and employee-driven mitigations to the challenges of remote work, and describe expected trends in the practice.

DISCLOSURES
Sucheta Sachdeva; Tyler D. Green, DNP, APRN, PMHNP-BC; Terry L. Oroszi, MS, EdD: *Nothing to disclose*

1. Prior to the COVID-19 pandemic, how common was remote work in the clinical research industry?
a. Remote work was strictly prohibited by nearly all sponsors and study sites.
b. Small companies often allowed remote work, but large companies discouraged it.
c. Larger companies tended to provide remote work options to some employees.
d. Remote work was nearly universally utilized among sponsors and study sites.

2. What clinical research associate (CRA) practice was pushed by sponsors due to pandemic-generated travel restrictions?
a. Remote source document verification
b. Waiver of informed consent requirements
c. Expedited institutional review board decisions
d. Elimination of protocol amendments

3. Which of the following is noted as a potential cost advantage to having CRAs work remotely?
a. No company dress code
b. Decreased health benefits
c. Lower insurance rates
d. Travel savings

4. During the pandemic, the U.S. Food and Drug Administration released guidance recommending that sponsors do which of the following regarding in-person monitoring of studies?
a. Continue live visits whenever possible
b. Hire temporary employees for visits
c. Evaluate alternative methods
d. Only visit non-COVID-19 study sites

5. What do the authors say about concerns over employee accountability regarding CRAs under pandemic conditions?

a. Traveling CRAs are often considered to be ungovernable due to being held to low levels of accountability.

b. Such concerns are minimal because traveling CRAs were already held to high levels of accountability.

c. Autonomous CRAs may conspire with study site personnel to hide how well monitoring visits were conducted.

d. Sponsors have greatly relaxed their standards for CRA accountability in order to keep more of them willing to work.

6. What do the authors recommend regarding clinical research employers' role in remote employee burnout?

a. Employers should provide tools, incentives, and opportunities for employees to live healthier lives.

b. Employers have no legal responsibilities tied to the health and well-being of their remote employees.

c. Employers should recommend that dissatisfied remote employees return to in-person study site visits.

d. Employers need to immediately reassign remote CRAs in crisis to duties at the sponsor's central offices.

7. Which of the following are mentioned by the authors as examples of productivity and efficiency tools for remote employees?

a. Yard care and laundry pick-up services

b. "Staycations" and home schooling

c. Meal delivery services and chauffeurs

d. Standing desks and wireless headsets

8. What do the authors say about situations in which organizations expect employees to stay in touch outside business hours using remote-based technology?

a. It is critical that study sponsors always know they can reach employees to do work at any time of the day.

b. Remote employees should not have to expect to be in touch on any regular schedule set by the sponsor.

c. Always being "on the clock" is an impediment on employees' time which can lead to higher turnover.

d. Remote employees should take comfort in having frequent contact with the corporate office even on days off.

9. What do the authors recommend employers do to forestall CRA burnout and turnover during times of short-staffing conditions?

a. Change tactics for hiring qualified replacements quickly.
b. Increase remaining CRAs' salaries by at least 50%.
c. Decrease the number of studies each CRA monitors.
d. Refuse to provide good references for departing CRAs.

10. How do the authors say remote CRAs can "cut the leash" to work duties at the end of the business day to preserve their work/life balance?

a. Fill up their evenings with non-work activities so that being online is impossible.
b. Stop forwarding e-mails to personal phones and turn off their computers.
c. Arrange a contractual agreement with their employers to never work after 5 p.m.
d. Take on a second job so that after-hours work as a CRA becomes untenable.

Article #2: **Streamlining Adoption of Digital Technology in Clinical Trials Through Use of Open-Source Algorithms**

LEARNING OBJECTIVES

After reading this article, the participant should be able to outline the function and advantages of open-source algorithms in relation to the use of digital endpoints in clinical trials, highlight several challenges to their adoption, and cite several examples of organizations/initiatives promoting their use.

DISCLOSURE

Geoffrey Gill, MS: *Nothing to disclose*

11. Which of the following are cited by the author as being potentially useful for enabling clinical trial investigators to switch from subjective to objective measures of health?

a. Trial master files and electronic informed consents
b. Wearables and other digital technologies
c. Medication adherence policies and trackers
d. Video monitoring of patients at home and onsite

12. Recommendations for developing digital endpoints were released by which organization in 2017?

a. Alliance for Clinical Research Excellence and Safety
b. Multi-Regional Clinical Trials Center
c. Clinical Trials Transformation Initiative
d. Public Responsibility in Medicine and Research

13. Which of the following is mentioned by the author as a challenge to validating digital endpoints?

a. The same endpoint may not provide accurate outputs across different patient groups.
b. The U.S. Food and Drug Administration (FDA) does not recognize the validity of digital endpoints.
c. Institutional review boards are reluctant to approve research into digital endpoint validation.
d. Study sites often fail to follow sponsor instructions for collecting desired digital endpoints.

14. Which of the following forms the basis of the sensor/digital endpoint combination validation framework promoted by the Digital Medicine Society?

a. A regulatory approval pathway for use in non-U.S.-based studies.
b. A patient-centric approach for choosing endpoints.
c. A cost analysis justification for using digital endpoints.
d. A process broken into three logically distinct steps.

15. Who should verify that a sensor provides the right data?

a. The principal investigator
b. Regulatory authorities
c. The manufacturer
d. Study sponsors

16. What is the nature of the GGIR package cited by the author?

a. Open-source algorithms for generating digital endpoints
b. Freely available online digital endpoint training sessions
c. Regulatory review software for validating digital endpoints
d. Case studies on digital endpoints that failed to be validated

17. What does the author note about different organizations using the same validated endpoints?

a. Sponsors are universally in favor of using only their own proprietary endpoints.
b. Participants in studies by different sponsors must sign separate consents on digital endpoints.
c. Validated endpoints can be used as evidence in other trials using different devices.
d. Institutional review boards will demand revalidation of any digital endpoints to be used.

18. What does the author cite as a major value of digital measurements in terms of studying chronic diseases?

a. Costs associated with using them do not depend on study length.
b. They can monitor continuously over a long period of time.
c. Less data must be aggregated and evaluated using this method.
d. Clinical study coordinators do not have to be involved.

19. What does the author cite as a barrier to companies that wish to have their proprietary algorithms adopted for use in studies?

a. Device technology is changing too quickly for proprietary algorithms to remain valid across a long-term study.

b. Such algorithms will still have to be described in great detail when studies are registered on ClinicalTrials.gov.

c. The FDA and European Medicines Agency may both soon outlaw use of proprietary algorithms in clinical trials.

d. The desire of other stakeholders for transparency from use of common or open-source algorithms.

20. Which of the following is noted as promoting the use of open-source algorithms for clinical endpoints?

a. The Open Wearables Initiative

b. The Clinical Data Interchange Standards Consortium

c. The Collaborative Institutional Training Initiative

d. The Decentralized Trials and Research Alliance