GlucoseReady™ 2024 Galien Award Application - History

Clinical Ink has more than 10 years of experience developing a GCP compliant electronic data capture platform, BrainBaseline, that integrates eCOA with various sensors and digital biomarkers. This platform has been audited and validated by numerous large pharma and academic collaborators. It has been used to assess endpoints in neurodegeneration [Watch-PD, 2022], COVID-19 [Pfizer, 2021], and bleeding disorders [ApcinteX, 2021], incorporating a broad range of consumer devices like the iPhone and Apple Watch, and advanced APIs to passively detect disease symptoms [Erb, 2020; Ehlers, 2020].

The emergence of new FDA regulations in cardiometabolic disease and the rise in trials for weight loss, diabetes, and MASH/MASLD led to the development of GlucoseReady™ in April 2023. This platform leveraged the core code and validation of BrainBaseline and the expertise of the same product design and engineering team [Lee, 2012; Watch-PD, 2022; Pfizer, 2021; ApcinteX, 2021]. The mobile platform seamlessly integrates 'bring your own device' (BYOD) or provisioned device data collection from wearables and sensors supporting continuous passive data capture along with management of data derived from active tasks driven by the study protocol.

GlucoseReady's initial objectives were threefold: (1) establish a library of diabetes-specific eCOA on various devices; (2) offer sensor integration to capture data from continuous and standalone glucose monitoring devices; and (3) trigger eCOA for symptomatic and asymptomatic hypoglycemia [FDA, 2024b]. Collaboration with key sponsors revealed a broader demand, extending GlucoseReady's application to chronic weight management, obesity, and MASH/MASLD. Objectives expanded to include the development of disease-specific eCOA libraries, connected weight scales and actigraphy solutions, and the ability to trigger specific eCOA based on digital biomarker data.

The product's scope was developed with senior clinical and technology executives from leading drug developers. These experts emphasized the importance of the ability to predict, track, and prevent non-adherence. To address the known high dropout and low adherence rates in cardiometabolic trials, a digital behavior tool was required. Accordingly, Clinical ink has established an exclusive clinical trial partnership with Observia, a specialist provider of predictive behavioral digital tools and patient reported adherence measures (PRAMs) [Clinical ink, 2024]. This tool, SPUR™, has been integrated into the GlucoseReady™ suite to ensure seamless provision of a best-in-class solution for adherence and retention. Developed over a 13 year period, the SPUR™ tool has been validated in seven publications covering multiple chronic disorders including diabetes [de Bock, 2022a; de Bock, 2022b; Wells, 2021; Wells, 2022; Wells, 2023; Tugaut, 2021; Dolgin, 2020]. The SPUR™ tool has been validated across different demographics and is used by over 15 biopharma companies in 50 thousand patients and 20 different approved medications as an adherence tool.

Data science advancements have added numerous data transfer and visualization elements to GlucoseReady™. Figure 1a outlines several glycemia metrics (e.g. GMI, GV, GRI and time in/above/below ranges). Figure 1b presents a dynamic, navigable view of raw participant estimated glucose values from a CGM. Figure 1c presents an aggregated Median Ambulatory Glucose Profile for the selected study trial participant and timeframe.

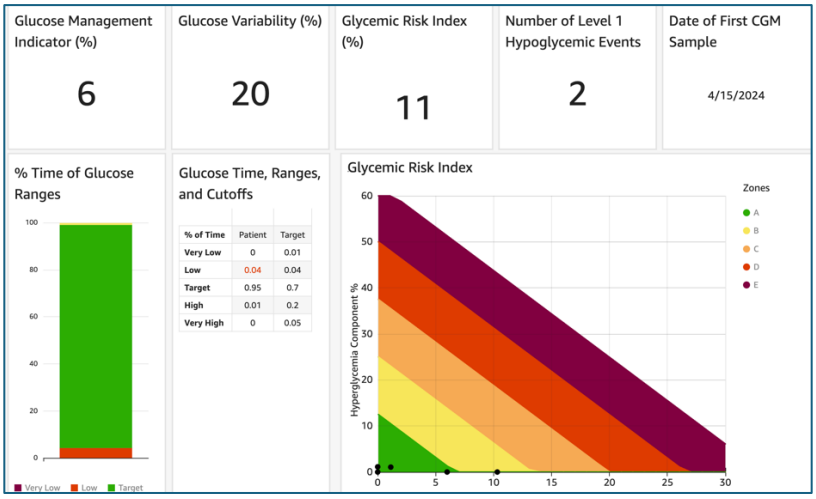

Figure 1a – GlucoseReady™ Glycemia Metrics

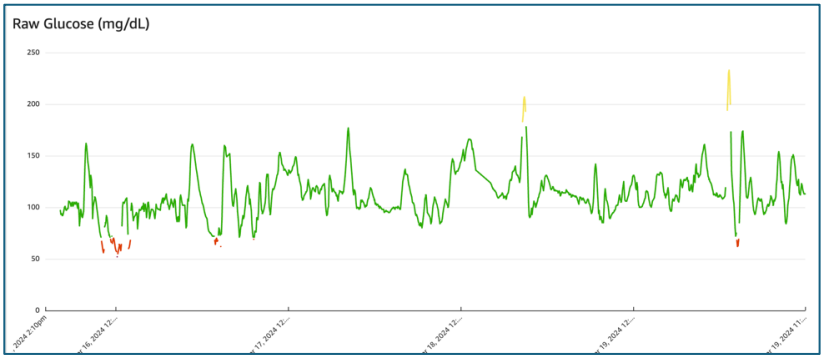

Figure 1b – GlucoseReady™ Raw Estimated Glucose Values (EGV)

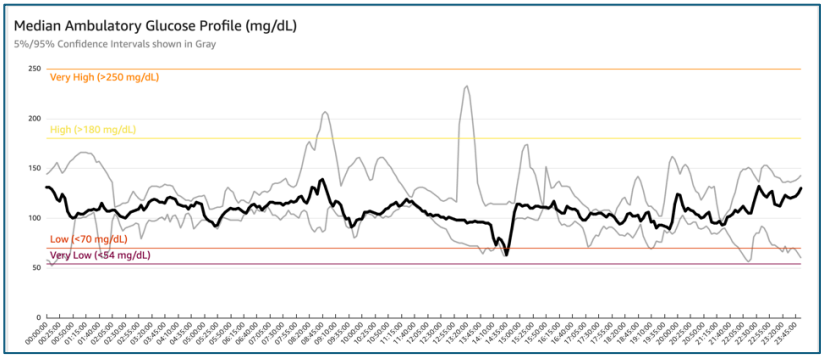

Figure 1c – Median Ambulatory Glucose Profile

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Using an API, GlucoseReady™ also leverages Cyntegrity's SOC 2 (Type II) Compliant Risk-Based Quality Management (RBQM) solution to identify protocol non-compliance, provide study site-to-site comparisons, create action lists for sponsor companies or CROs, and provide insights into key risk indicators (KRIs) (See Figures 2a-2d). These issue streams are audited and tracked within the embedded ticketing system.

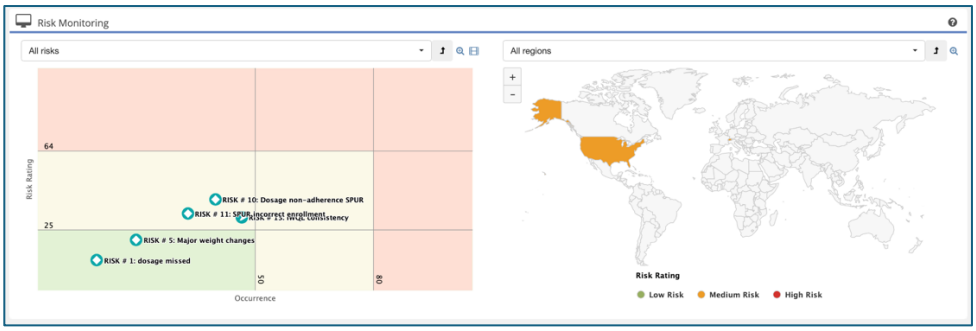

Figure 2a – Visualizing regional risk ratings

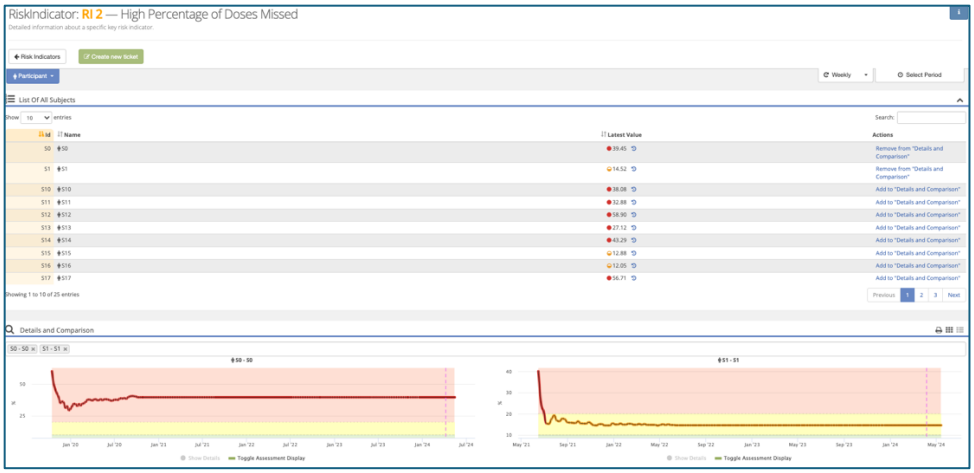

Figure 2b - Participant level adherence with multi-panel visualizations for comparison

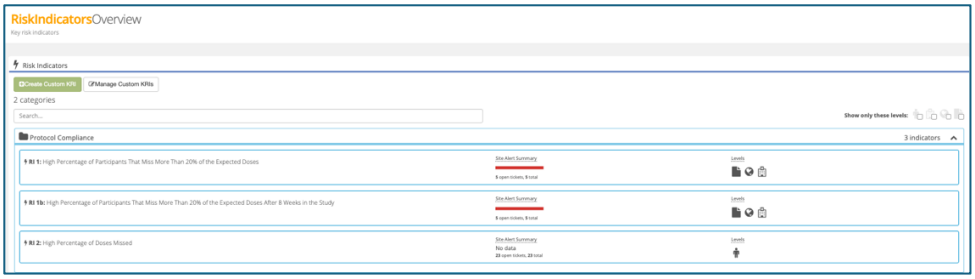

Figure 2c - Key Risk Indicators at the participant, site, and study level

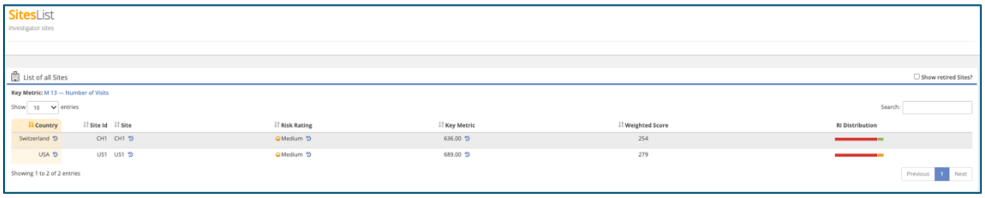

Figure 2d - Overall risk rating for each site

As of May 2024, GlucoseReady™ has been audited, validated, released, and contracted with several sponsors, initially focusing on type 2 diabetes and weight management. To date, 8 GLP-1 biopharma companies have requested RFI/RFPs and 68 have requested information.

Please provide appropriate references (PubMed, Abstract, Website)

- [Abdelmalek, 2024] Abdelmalek, Manal F., Stephen A. Harrison, and Arun J. Sanyal. "The role of glucagon-like peptide-1 receptor agonists in metabolic dysfunction-associated steatohepatitis." *Diabetes, Obesity and Metabolism* 26, no. 6 (2024): 2001-2016.
- [Anderson et al, 2024] Anderson, D., Polyak, S., Merickel, M., Severson, B., Best, A., Djurhuus, C., & Goldman, J. (2024). GlucoseReady: Technical validation of a novel GxP platform for real-time CGM capture. To be presented at the 84th annual meeting of the American Diabetes Association, Orlando, FL.
- [ApcinteX, 2021] ApcinteX Ltd. The Efficacy and Safety of SerpinPC in Participants with Severe Hemophilia A or Moderately Severe to Severe Hemophilia B (PRESent-2). ClinicalTrials.gov; 03/29/2023; Trial ID: NCT05789524
- [Burgess, 2017] Burgess, Emily, Peter Hassmén, and Kate L. Pumpa. "Determinants of adherence to lifestyle intervention in adults with obesity: a systematic review." *Clinical obesity* 7, no. 3 (2017): 123-135.
- [Clinical ink, 2024] Clinical ink. “Clinical ink Expands Patient Engagement Solutions with Behavioral Diagnostic Tool SPUR”. Public Press Release. 2024. https://www.clinicalink.com/clinical-ink-expands-patient-engagement-solutions-with-behavioral-diagnostic-tool-spur/
- [de Bock, 2022a] de Bock E, Dolgin K, Kombargi L, Arnould B, Vilcot T, Hubert G, Laporte ME, Nabec L, Reach G. Finalization and Validation of Questionnaire and Algorithm of SPUR, a New Adherence Profiling Tool. *Patient Prefer Adherence*. 2022;16:1213-1231 https://doi.org/10.2147/PPA.S354705
- [de Bock, 2022b] Elodie de Bock, Kevin Dolgin, Benoit Arnould, Guillaume Hubert, Aaron Lee & John D. Piette (2022). The SPUR adherence profiling tool: preliminary results of algorithm development, Current Medical Research and Opinion, 38:2, 171-179, DOI: 10.1080/03007995.2021.2010437
- [Dolgin, 2020] Dolgin K. The SPUR Model: A Framework for Considering Patient Behavior. *Patient Prefer Adherence*. 2020;14:97-105 https://doi.org/10.2147/PPA.S237778
- [Ehlers, 2020] Ehlers, Diane K., Jason Fanning, Alexis Sunderlage, Joan Severson, Arthur F. Kramer, and Edward McAuley. "Influence of sitting behaviors on sleep disturbance and memory impairment in breast cancer survivors." *Cancer medicine* 9, no. 10 (2020): 3417-3424.
- [Erb, 2020] Erb, M. Kelley, Daniel R. Karlin, Bryan K. Ho, Kevin C. Thomas, Federico Parisi, Gloria P. Vergara-Diaz, Jean-Francois Daneault et al. "mHealth and wearable technology should replace motor diaries to track motor fluctuations in Parkinson’s disease." *NPJ digital medicine* 3, no. 1 (2020): 6.

- [FDA, 2024a] U.S. Food and Drug Administration, FDA Approves First Treatment to Reduce Risk of Serious Heart Problems Specifically in Adults with Obesity or Overweight, March 08, 2024. https://www.fda.gov/news-events/press-announcements/fda-approves-first-treatment-reduce-risk-serious-heart-problems-specifically-adults-obesity-or
- [FDA, 2024b] U.S. Food and Drug Administration. Diabetes Mellitus: Efficacy Endpoints for Clinical Trials Investigating Antidiabetic Drugs and Biological Products. Guidance for Industry. May 2023.
- [Gomes, 2024] Gomes, D.A., Presume, J., de Araújo Gonçalves, P. *et al.* Association Between the Magnitude of Glycemic Control and Body Weight Loss With GLP-1 Receptor Agonists and Risk of Atherosclerotic Cardiovascular Disease: A Systematic Review and Meta-analyses of Randomized Diabetes Cardiovascular Outcomes Trials. *Cardiovasc Drugs Ther* (2024). https://doi.org/10.1007/s10557-024-07547-3
- [Lee, 2012] Lee, Hyunkyu, Pauline L. Baniqued, Joshua Cosman, Sean Mullen, Edward McAuley, Joan Severson, and Arthur F. Kramer. "Examining cognitive function across the lifespan using a mobile application." *Computers in Human Behavior* 28, no. 5 (2012): 1934-1946.
- [Pfizer, 2021] Pfizer. Acute Respiratory Illness Surveillance (AcRIS) With Mobile Application in a Low-Interventional Decentralized Study. ClinicalTrials.gov; 05/02/2021; Trial ID: NCT04748445
- [Tugaut, 2022] Tugaut, B., Shah, S., Dolgin, K. *et al.* Development of the SPUR tool: a profiling instrument for patient treatment behavior. *J Patient Rep Outcomes* **6,** 61 (2022). https://doi.org/10.1186/s41687-022-00470-x
- [Watch-PD, 2022] D. Anderson, M. Merickel, B. Severson, D. Amato, T. Kangarloo, J. Edgerton, R. Dorsey, J., Adams, S. Jezewski, A. Keil, S. Johnson, M. Kantartjis, S. Polyak, J. Severson, J. Cosman, 2022, June. WATCH-PD: Detecting Early-Stage PD Status using Feature Engineering and Machine Learning in Remote Sensor-Based Assessments. In MOVEMENT DISORDERS (Vol. 37, pp. S3-S3). 111 RIVER ST, HOBOKEN 07030-5774, NJ USA: WILEY.
- [Wells, 2021] J Wells, A El-Husseini, A Jaffar, K Dolgin, G Hubert, R Kayyali, A cross-sectional study to evaluate the validity of a novel patient-reported outcome measure of medication adherence in Type 2 Diabetes, *International Journal of Pharmacy Practice*, Volume 29, Issue Supplement_1, April 2021, Page i30, https://doi.org/10.1093/ijpp/riab015.036
- [Wells, 2022] Wells JS, El Husseini A, Okoh S, et al. SPUR: psychometric properties of a patient-reported outcome measure of medication adherence in type 2 diabetes. BMJ Open 2022;12:e058467. doi: 10.1136/bmjopen-2021-058467
- [Wells, 2023] Wells J, Wang C, Dolgin K, Kayyali R. SPUR: A Patient-Reported Medication Adherence Model as a Predictor of Admission and Early Readmission in Patients Living with Type 2 Diabetes. Patient Prefer Adherence. 2023 Feb 19;17:441-455. https://doi.org/10.2147/ppa.s397424
- Websites
    - https://www.clinicalink.com/technology/glucoseready/
    - https://www.clinicalink.com/clinical-ink-announces-new-continuous-glucose-monitoring-solution/
    - https://www.clinicalink.com/clinical-ink-expands-patient-engagement-solutions-with-behavioral-diagnostic-tool-spur/
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