GlyCulator 3.0: A Fast, Easy-to-Use Analytical Tool for CGM Data Analysis, Aggregation, Center Benchmarking, and Data Sharing

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Continuous glucose monitoring (CGM) has become the target standard of care for people with diabetes and an abundant source of health care data (1). However, downloading those data is difficult (especially for large numbers of patients or long records) and researchers have to rely on manufacturer or commercial software for analysis. An increasing number of public domain tools strive to bridge this gap, but they vary substantially in their capabilities and ease of use. GlyCulator (2), developed by our team, was one of the first such tools and has been updated several times along with the advancement of sensor technology and analysis guidelines. In this article, we present GlyCulator 3.0, a free open-access online platform that facilitates large-scale consensus-compliant analyses of CGM files and enables data storage and sharing. This solution allows for easy integration between various CGM files and downstream analysis using more specialized tools. It is available freely from https://glyculator.btm.umed.pl after account creation. The current version allows users to upload CGM files downloaded from all popular CGM systems without preprocessing. While GlyCulator 3.0 cannot directly access CGM manufacturer databases yet and requires raw data files downloaded from the proprietary software, the upload and file processing were made as easy as possible. CGM technology and file format are automatically detected—the software is compatible with most current or past CGM sensors—or may be defined by the user on upload. The tool also provides an option to integrate multiple files from a single CGM user into a single standard file; this is especially useful for Medtronic CGM users, as those files are typically limited to storing only 90 days of data.

Following file upload, all files from one analysis are converted into a uniform format (GlyQ) and an analysis template is created for further editing. Conversion removes embedded personal or clinical data and allows manufacturer-agnostic analysis as long as the same sampling frequency, 288 or 96 measurements/day, is constant. The GlyQ format was created to facilitate downstream analysis of raw CGM records and can be used with external software solutions with no or few modifications required. CGM records in GlyCulator 3.0 may be parsed for a predefined date frame that allows for center benchmarking, clinical outcome evaluation or monitoring an individual patient over time. After upload of full-length CGM records, the user specifies the start and end dates, thus creating the desired window of analysis for all files or selecting specific ones using a graphical interface or manual date entry. The next step is quality check and filtration, which allows the user to review data completeness through visual representation and adjust the chosen time frame before proceeding. Afterward, the user may enable missing data imputation or skip this step and proceed directly to analysis. The analytical stage calculates glycemic variability indices (GVIs) compliant with the 2019 international consensus (1) for the chosen periods for all files in the analysis. Postanalysis, the user may access separate file-specific reports (including record configuration, standard ambulatory glucose profile, and GVIs), a summary detailing metadata and GVIs for all files (presented visually), and raw glucose data used for calculations. The summary report and aggregated CGM data in GlyQ format can also be downloaded for further processing with use of more specialized or custom-made analytical tools as well as external statistical software.

At each step, the users may share their results or processed files with other researchers and users of our tool. Finally, the anonymized CGM data are also securely backed up by the host institution and can potentially be used as a reference for further joint analyses or reproducibility evaluations. The users may save, delete, access, or revisit their analyses at any time, allowing for rapid reanalysis or exploration of different analytical scenarios or variants of data imputation or filtering. We hope that

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Table 1—Functionality comparison of popular free CGM analysis software

	GlyCulator	iglu	cgm-analysis	CGDA	rGV	cgm-quantify	CGM-Stats-Analyzer	CGM-Shiny	GLU	CGM-analyzer	CGMTSA	GVAP	EasyGV
Glycemic variability													
Number of days CGM worn	X	X	X	X					X				
Active time %	X	X	X	X				X					
Mean glucose	X	X	X	X	X	X	X	X		X		X	X
Glucose management indicator	X	X	X	X	X	X							
Glycemic variability (%CV)	X	X	X	X	X	X	X						
Time above/in/below range	X	X	X	X	X			X					
Ambulatory glucose profile	X	X											
Day and night	X	X	X					X					
File upload													
Medtronic CareLink Pro/Personal	X	X	X				X		X	X	X		
Abbott Libre/LibreView/CoPilot	X	X	X	X					X	X	X		
Dexcom Studio/Clarity; diasend	X	X	X						X	X	X		
Roche Accu-Check Smart Pix (Eversense/Ascensia)	X	X											
User defined	X	X			X			X				X	
Software defined			X	X		X	X			X		X	X
File preparation													
Period selection for analysis	X												
Date–time format detection	X	X					X						
Quality control	X												
Missing data imputation	X		X	X				X	X	X	X		X
Multiple file processing	X	X	X	X			X	X	X	X			X
Many-to-single file merge	X												
Sharing and access													
Data anonymization and storage	X												
Analysis sharing	X												
Graphical user interface	X	X			X			X				X	
Online platform	X	X			X		X						
Programmatic access	Python	R	R	R	R	R/Python			R	R	R	MATLAB	
Source publication/code repository	This article	10.1371/journal.pone.0248560	10.1371/journal.pone.0216851	10.1177/19322968211070293	10.1177/19322968211028909	10.1109/OJEMB.2021.3105816	10.1177/1932296820985570	https://github.com/rolandhangelbroek/cgmshiny	10.1093/ije/dyaa004	10.1093/bioinformatics/btx826	10.1101/2020.07.06.174748	10.1186/s12938-015-0035-3	10.1089/dia.2010.0247

Xs represent functionalities implemented. Exact workings of specific functions may differ, but if a specific function was present in any extent we marked it as present. The following tools were omitted because of lack of continued support, inaccessibility through links/websites of original publications, or restricted or paid access: CGM-GUIDE, wiseCGM, hamsamilton/cgms.analysis, Glooko. URLs for the evaluated tools for which an online platform is provided and maintained (accessed 29 August 2022): GlyCulator (https://glyculator.btm.umed.pl/); rGV (https://shiny.biostat.umn.edu/GV/); iglu (https://irinagain.shinyapps.io/shiny_iglu/); CGMStatsAnalyser (https://baker-biostats.shinyapps.io/CGMStatsAnalyser/). CGDA, Continuous Glucose Data Analysis; CV, coefficient of variation; GVAP, Glycemic Variability Analyzer Program.

by providing external data storage and analysis capabilities, we will facilitate research independent of in-house hardware limitations.

Detailed instructions are provided on the tool's website: https://glyculator.btm.umed.pl/user_manual.

The list of features of GlyCulator 3.0 and their comparison with other popular community-based solutions are presented in Table 1. Our intention is not to replace the existing solutions but, rather, to allow for interoperability with outside software, which provides additional functionalities, such as nonstandard GVIs, additional data imputation algorithms, and alternative data visualizations. GlyCulator 3.0 was designed to provide an easy way to assess large amounts of data for benchmarking purposes. As an example, we performed such a study on 1,244 CGM users treated in the pediatric diabetology reference center for Lodzkie Voivodeship. Its detailed description, results, and a step-by-step manual for results reproduction, including all required anonymized patient files, are provided on the software's website (https://glyculator.btm.umed.pl/). Such benchmarks provide essential insight into diabetes care quality and may help with identification of areas that need improvement (3,4).

The possible applications of GlyCulator 3.0 exceed those provided in the example study. First, investigators can use it to process data from an increasing number of clinical trials using CGM (5) and (should raw files be stored) cross-reference those data between trials. Secondly, the data-sharing option might promote nationwide or international analyses, which could be a critical and invaluable asset for public health policy and future guidelines development. Finally, an application programming interface could be set up on request to enable high-throughput automated analyses for independent research networks. Overall, we believe that GlyCulator 3.0 is an accessible, comprehensive, and open resource for clinicians and researchers interested in CGM regardless of their statistical or programming experience.

Duality of Interest. No potential conflicts of interest relevant to this article were reported.
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