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An Interactive Web Application for the Statistical Analysis of Continuous Glucose Monitoring Data in Epidemiological Studies

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Abstract

Motivation: Continuous glucose monitoring (CGM) systems are an essential part of novel technology in diabetes management and care. CGM studies have become increasingly popular among researchers, healthcare professionals, and people with diabetes due to the large amount of useful information that can be collected using CGM systems. The analysis of the data from these studies for research purposes, however, remains a challenge due to the characteristics and large volume of the data.

Results: Currently, there are no publicly available interactive software applications that can perform statistical analyses and visualization of data from CGM studies. With the rapidly increasing popularity of CGM studies, such an application is becoming necessary for anyone who works with these large CGM datasets, in particular for those with little background in programming or statistics. CGMStatsAnalyser is a publicly available, user-friendly, web-based application, which can be used to interactively visualize, summarize, and statistically analyze voluminous and complex CGM datasets together with the subject characteristics with ease.

Keywords
continuous glucose monitoring, statistical analysis, visualization, software

Introduction

Self blood glucose monitoring is an important part of diabetes management.[1] Continuous glucose monitoring (CGM) sensors are modern technological wearable devices that measure glucose in interstitial fluid at frequent intervals usually every one to five minutes, and these have become an essential part of clinical practice in diabetes and a vital part of many research studies.[2]

Beyond the ease and comfort of wearable technology compared to conventional finger-prick testing, the CGM systems have revolutionized the availability of data for diabetes research. However, the volume and complexity of the CGM datasets make the statistical analysis of these data a challenging task. Despite the increase in the number of research studies using CGM, the development of software for handling and analyzing multiple datasets has not progressed adequately.

In recent times, three R packages have been designed for the analysis of CGM data.[3,4] Both these packages require the manual installation and direct use of R software.[5] While both packages allow for visualization of CGM data and calculation of summary statistics, Zhang et al[3] in addition allow for comparison of CGM indices between groups of patients. The R package "iglu" provides a comprehensive list of functions for outputting relevant metrics for data collected from CGM.[6]

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Currently, to the best of our knowledge, there are no publicly available, interactive, web-based software applications that can perform statistical analysis of CGM data, allowing between-group comparisons. An interactive and user-friendly application is particularly needed by clinicians and researchers with little background in programming or statistics. To fill this gap, we have developed CGMStatsAnalyser as a publicly available, user-friendly, interactive web-based application. The package can be used to (i) visualize the time-series blood glucose level from each person, (ii) calculate CGM summary indices for each person, (iii) visualize these summary indices according to a specified grouping variable, (iv) measure and visualize the strength of association between different metrics, and (iv) statistically compare the summary metrics between groups of subjects.

Details

Requirements

Users can access CGMStatsAnalyser at https://baker-biostats.shinyapps.io/CGMStatsAnalyser/

It is a stand-alone application that does not require installation of any external software.

Reading Data

Uploading the CGM data files. A simple "generic" format is available for CGM data upload. This generic format is similar to the format that is being used by R packages such as "iglu."[6] Under this generic format, users need to provide comma-seperated values (CSV) files with two columns named "time" and "gl." The first is a factor or a character string column with the date and time stamp (using dd/mm/yyyy hh:mm:ss format) and the second is a numeric column with the glucose measurements in mmol/L. This generic format is further illustrated in the User Guide using the second example dataset. In addition, the software can import raw data files that are directly downloaded from ipro2 as illustrated in the User Guide using the first example dataset (ipro2 v.1.0.1). Multiple such CGM data files can be read into the software using the button "Upload data files here" as illustrated in the User Guide. The type of the data file ("generic" or "ipro2") need to be specified using the button "Device type" under the heading "Files Upload."

Uploading the subject characteristic file. In order to use the "Statistical Analysis" module of the apps to compare CGM indices between groups of subjects, a subject characteristic file must be uploaded. This file must be uploaded in CSV format and its first column should contain the filenames (without the .csv extension) of the raw data files. This file must contain at least one variable as a factor/character string in addition to the filename column. The first example dataset provided includes a subject characteristics file and the use of this file is illustrated with step-by-step instructions in the User Guide.

Visualizations of CGM Data and Key CGM Indices

The CGM data from a specific file can be visualized using Glucose profile (see top right panel of Figure 1). For each file, six of the commonly used CGM indices[7] are computed using the CGMStatsAnalyser. These are the (i) mean blood glucose (MBG), (ii) mean amplitude of glycemic excursion (MAGE),[8] (iii) J-index,[9] (iv) standard deviation of the glucose profile (SD), (v) continuous overall net glycemic action (CONGA for the indicated *n* hours),[10] and the (vi) area under the curve (AUC). The first five of these indices are shown as *Main CGM indices*, and the AUC is elaborated as *Secondary CGM indices*. In addition to these indices, the users are able to calculate the following *Other CGM indices* [11]: (i) primary glycemic variability (coefficient of variation), (ii) percentage of time in level 2 hypoglycemic range, (iii) percentage of time in level 1 hypoglycemic range, (iv) percentage of time in target range, (v) percentage of time in level 1 hyperglycemic range, (vi) percentage of time in level 2 hyperglycemic range, (vii) estimated HbA1c (eA1C), (viii) high blood glucose index (HBGI), and (ix) low blood glucose index (LBGI). Supplementary Tables 1 and 2 show the values of the overlapping metrics that can be obtained from our software and that from "iglu"[6] using the second example dataset. These overlapping metrics are consistent with the exception of MAGE, because our algorithm calculated MAGE based on the adjacent infliction points (zenith and nadir points) of the CGM data, as suggested by Hill et al.[12]

The desired index can be selected using *Select Indices*, optionally stratified *By variable*, as specified in the column names of the *Subject Characteristics File*, and visualized interactively using violin plots. Static figures of these interactive plots are shown in Figure 1. While the view of the plots can be interactively altered, publication-quality static figures can be immediately saved by clicking on the "*camera*" icon.

Statistical Analysis

The most commonly encountered research question in CGM studies is the comparison of the CGM indices between groups of patients with different characteristics. Our *Statistical Test* module caters to this need. An appropriate statistical test can be specified using *Choose test* for an index selected using *Index to test* and by variable chosen using *By variable*. For comparing variables with two categories, the user is able to choose either a t test or a Wilcoxon test, while

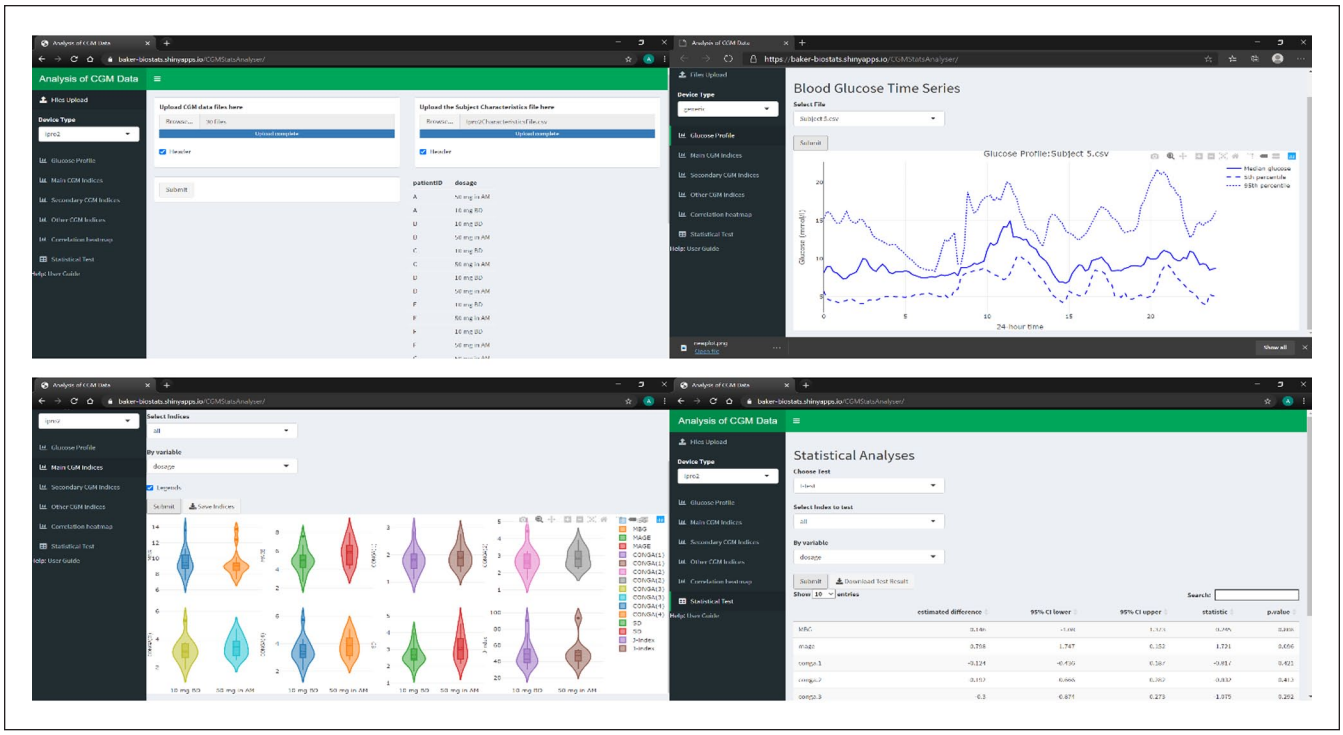

Figure 1. Top left: A screenshot of the CGMStatsAnalyser application. Top right: CGM profile of an individual over multiple days. Bottom left: Violin plots of the main CGM indices. Bottom right: Example results from a statistical analysis. CGM: continuous glucose monitoring.

for variables with more than two categories either an ANOVA or a Kruskal-Wallis test is available. A summary of the test results is displayed and can be downloaded as a CSV file.

Conclusion

The CGMStatsAnalyser is a publicly available, user-friendly, interactive web-based application that can be used to suitably visualize, summarize, and statistically analyze data from CGM studies. In comparison with the existing software, CGMStatsAnalyser has the ability to interactively visualize and analyze voluminous and complex CGM datasets with ease as a web-based standalone application. The software can also be easily extended to accommodate additional CGM indices and statistical capabilities.

Abbreviations

CGM, continuous glucose monitoring.

Declaration of Conflicting Interests

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Data Availability

Freely available on the web https://baker-biostats.shinyapps.io/CGMStatsAnalyser/

Supplemental Material

Supplemental material for this article is available online.

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