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The GH-Method

Applying the Distributional Data Analysis Tool of Biomarker Density with the Collected Daily Data of 5 Biomarkers Over 7.5 Years from a Patient with Chronic Diseases to Investigate his Overall Health Conditions Based on GH-Method: Math-Physical Medicine (No. 516)

Gerald C. Hsu*

eclaireMD Foundation, USA

Abstract

Recently, the author conducted a series of medical research projects by applying a distributional data density analysis tool on his weight, glucose, blood pressure (BP), and heart conditions, while using his collected big data regarding certain biomarker's density distribution for the selected years. In this article, he consolidated five selected biomarkers, weight, finger piercing estimated average glucose (eAG), heart rate (HR), systolic blood pressure (SBP), and diastolic blood pressure (DBP), within a longer time span of 7.5 years (4/1/2014-9/13/2021). The reason he omitted his continuous glucose monitoring (CGM) sensor eAG, sensor fasting plasma glucose (FPG), and sensor postprandial plasma glucose (PPG) is due to their relatively shorter data availability timeframe of 3.5 years (5/8/2018-9/13/2021). With the personal data, he can interpret the results and explore additional information since he is most familiar with his own health conditions. Of course, these findings regarding his own body are also applicable to other patients with chronic diseases. The main purpose of writing this series of research articles is to further demonstrate the applicability and power of using this specific distributional data density analysis tool. In the past, when he researched certain biomarkers and their relationship with other influential factors, he generally used the average values of those biomarkers. However, we know that most biomarkers, including body weight, glucose, and BP would fluctuate along the time scale in the form of a wave. Each wave has its unique amplitude and a specific measuring unit that is associated with this particular biomarker. There are two other key factors, frequency and wavelength, which need to be considered as well. Particularly, the frequency component is associated with energy and excessive energy causes damage to the internal organs. Therefore, without focusing on the waveform of a biomarker and depending only on its mean value, we would lose many vital, interesting, and useful hidden information. These types of mean values, such as HbA1C, or sparsely collected finger-pierced glucose, or quarterly available lab-tested blood lipid results, can provide partial views of the overall health conditions. Those biomarkers still have some missing information that carries hidden internal turmoil or vital signs, e.g., biomarker variation or its severe stimulation due to all types of external and/or internal stimulators. By applying this basic knowledge of distributional data analysis by defining a new term known as the general biomarker density or bio-density% (BMD%), he can explore additional, different, deeper, and useful hidden information from the collected biomarker data and their associated waveforms. The term biomarker density percentage (BMD%) is defined as the occurrence frequency at a specific person's biomarker value. In this way, he can then calculate and examine each biomarker's occurrence rate within a certain range over his selected timespan. This selected timespan is dependent on the study which is suitable to specific patients (in this case, himself). As of 1/1/2012 he started to track his daily weight and daily finger glucose and began collecting his BP and HR on 4/1/2014. By examining the changes of the peak biomarker value with their associated BMD% from year to year, he can easily and clearly observe his biomarker's moving trend and understand his actual health problems or necessary health improvement effort. The above description provides the reason he keeps searching for applicable tools to analyze the collected big data of any biomarker. If this type of biomarker examination method is accepted by the medical community, it can be an extremely beneficial tool for doctors to quickly study the health conditions of their patients. Furthermore, the author programmed this algorithm into an iPhone app software. Through the combination of his

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*Corresponding author: Gerald C. Hsu, eclaireMD Foundation, USA

published papers and medical books along with a widely distributed app for patient's use in the future, he believes that worldwide patients with chronic diseases can benefit from his research work. Hopefully, his research papers would not be limited within the scope of a "descriptive style using 26 alphabets" but instead as a "quantitative style using 10 digits". Numbers do not lie as long as we don't use fake, unorganized, and/or uncleaned data. Statistics is a tricky tool to use for any research work because it has the obvious characteristics of garbage in and garbage out (GIGO). It is also important to know that using statistics with different selected time-windows for certain studies will result in varying conclusions. In summary, the author has chosen to perform his research work using the tools of BMD% with his collected 5 daily biomarker data over the same period of 7.5 years (4/1/2014-9/13/2021). Each one of these 5 selected biomarkers has its unique biomarker data range and specifically defined biomarker's normal conditions. As a result, this makes the combined study and data presentation quite difficult. For example, his target weight is 170 lbs. (equal to BMI 25 for his case), target glucose is 120 mg/dL, target HR is 60-100 bpm (but chose 60 bpm), target SBP is 120 mmHg, and target DBP is 80 mmHg. In order to combine these 5 biomarkers into one single diagram, he must redefine a common general-scale for the data range from 1 to 250 with equal intervals of 1. With this new numbering system, he can then align these 5 different normal conditions or target values at #70. Now, he is able to plot all 5 density% curves into a combined single diagram with their relative positions indicating their relative biomedical meanings. Through a closer examination of this combined diagram, he can provide the following three conclusive statements: (1) Since all 5 biomarkers have been rearranged according to a common scale (from #1 to #250 with #70 as the normal condition), he can then use an eyeball-viewing method to examine these biomarker curves. Other than the weight curve, all the other 4 biomarkers have their majority of data being distributed below #70 which means that most of these 4 biomarkers, glucose, SBP, DBP, and HR, are within their normal range. (2) The peaks of finger glucose and HR are located around #67 while the peaks of SBP and DBP are located around #55. All of them are below #70 which indicates being in a healthy range. (3) The weight density distribution curve appears different from the other 4 biomarker curves. From the time-domain analysis, his body weight decreased from 180 lbs. in 2014 to below 170 lbs. during 2020-2021. Therefore, in this density-domain analysis, the majority of his weight density% are located within the range of #80 (171 lbs.) to #150 (178 lbs.). This fact indicates that during the majority of the 7.5 years, his body weight was in the overweight category. By combining the two different analysis methods, the traditional time-domain analysis and the newly defined density-domain analysis, he can then explore additional insights on the five biomarkers.

Keywords: Blood pressure; Heart rate; Biomarker density; Systolic blood pressure; Diastolic blood pressure; Type 2 diabetes; Fasting plasma glucose

Abbreviations: BP: blood pressure; eAG: estimated average glucose; HR: heart rate; SBP: systolic blood pressure; DBP: diastolic blood pressure; CGM: continuous glucose monitoring; FPG: fasting plasma glucose; PPG: postprandial plasma glucose; BMD%: biomarker density percentage; MPM: math-physical medicine; HbA1C: hemoglobin A1C

1. INTRODUCTION

Recently, the author conducted a series of medical research projects by applying a distributional data density analysis tool on his weight, glucose, blood pressure (BP), and heart conditions, while using his collected big data regarding certain biomarker's density distribution for the selected years.

In this article, he consolidated five selected biomarkers, weight, finger piercing estimated average glucose (eAG), heart rate (HR), systolic blood pressure (SBP), and diastolic blood pressure (DBP), within a longer time span of 7.5 years (4/1/2014-9/13/2021). The reason he omitted his continuous glucose monitoring (CGM) sensor eAG, sensor fasting plasma glucose (FPG), and sensor postprandial plasma glucose (PPG) is due to their relatively shorter data availability timeframe of 3.5 years (5/8/2018-9/13/2021).

With the personal data, he can interpret the results and explore additional information since he is most familiar with his own health conditions. Of course, these findings regarding his own body are also applicable to other patients with chronic diseases. The main purpose of writing this series of research articles is to further demonstrate the applicability and power of using this specific distributional data density analysis tool.

In the past, when he researched certain biomarkers and their relationship with other influential factors, he generally used the average values of those biomarkers. However, we know that most biomarkers, including body weight, glucose, and BP would fluctuate along the time scale in the form of a wave. Each wave has its unique amplitude and a specific measuring unit that is associated with this particular biomarker. There are two other key factors, frequency and wavelength, which need to be considered as well. Particularly, the frequency component is associated with energy and excessive energy causes damage to the internal organs. Therefore, without focusing on the waveform of a biomarker and depending only on its mean value, we would lose many vital, interesting, and useful hidden information. These types of mean values, such as HbA1C, or sparsely collected finger-pierced glucose, or quarterly available lab-tested blood lipid results, can provide partial views of the overall health conditions. Those biomarkers still have some missing information that carries hidden internal turmoil or vital signs, e.g., biomarker variation or its severe stimulation due to all types of external and/or internal stimulators. By applying this basic knowledge of distributional data analysis[1] by defining a new term known as the general biomarker density or bio-density% (BMD%), he can explore additional, different, deeper, and useful hidden information from the collected biomarker data and their associated waveforms.

The term biomarker density percentage (BMD%) is defined as the occurrence frequency at a specific person's biomarker value. In this way, he can then calculate and examine each biomarker's occurrence rate within a certain range over his selected timespan. This selected timespan is dependent on the study which is suitable to specific patients (in this case, himself). As of 1/1/2012 he started to track his daily weight and daily finger glucose and began collecting his BP and HR on 4/1/2014. By examining the changes of the peak biomarker value with their associated BMD% from year to year, he can easily and clearly observe his biomarker's moving trend and understand his actual health problems or necessary health improvement effort.

The above description provides the reason he keeps searching for applicable tools to analyze the collected big data of any biomarker. If this type of biomarker examination method is accepted by the medical community, it can be an extremely beneficial tool for doctors to quickly study the health conditions of their patients. Furthermore, the author programmed this algorithm into an iPhone app software. Through the combination of his published papers and medical books along with a widely distributed app for patient's use in the future, he believes that worldwide patients with chronic diseases can benefit from his research work. Hopefully, his research papers would not be limited within the scope of a "descriptive style using 26 alphabets" but instead as a "quantitative style using 10 digits". Numbers do not lie as long as we don't

use fake, unorganized, and/or uncleaned data. Statistics is a tricky tool to use for any research work because it has the obvious characteristics of garbage in and garbage out (GIGO). It is also important to know that using statistics with different selected time-windows for certain studies will result in varying conclusions.

2. METHODS

2.1 MPM background

To learn more about his developed GH-Method: Math-Physical Medicine (MPM) methodology, readers can read the following three papers selected from his ~500 published medical papers.

The first paper, No. 386, describes his MPM methodology in a general conceptual format. The second paper, No. 387, outlines the history of his personalized diabetes research, various application tools, and the differences between the biochemical medicine (BCM) approach vs. the MPM approach. The third paper, No. 397, depicts a general flow diagram containing ~10 key MPM research methods and different tools.

In particular, his paper No. 453 illustrates his GH-Method: MPM in great detail, "Using Topology Concept of Mathematics and Finite Element Method of Engineering to Develop a Mathematical Model of Metabolism in Medicine in Order to Control Various Chronic Diseases and their Complications via Overall Health Conditions Improvement".

2.2 The author's case of diabetes and complications

The author has been a severe type 2 diabetes (T2D) patient since 1996. He weighed 220 lbs. (100 kg, BMI 32.5) at that time. By 2010, he still weighed 198 lbs. (BMI 29.2) with average daily glucose of 250 mg/dL (HbA1C of 10%). During that year, his triglycerides reached to 1161 (diabetic retinopathy or DR) and the albumin-creatinine ratio (ACR) at 116 (chronic kidney disease or CKD). He also suffered from five cardiac episodes within a decade. In 2010, three independent physicians warned him regarding his need for kidney dialysis treatment and future high risk of dying from severe diabetic complications. Other than the cerebrovascular disease (stroke), he has suffered most of the known diabetic complications, including both macro-vascular and micro-vascular complications.

In 2010, he decided to launch his self-study on endocrinology, diabetes, and food nutrition in order to save his own life. During 2015 and 2016, he developed four prediction models related to diabetes condition: weight, PPG, FPG, and A1C. As a result, from using his developed mathematical metabolism index (MI) model in 2014 and the four prediction tools, by end of 2016, his weight was reduced from 220 lbs. (100 kg, BMI 32.5) to 176 lbs. (89 kg, BMI 26.0), waistline from 44 inches (112 cm, nonalcoholic fatty liver disease/NAFLD) to 33 inches (84 cm), average finger glucose reading from 250 mg/dL to 120 mg/dL, and the lab-tested A1C from 10% to ~6.5%. One of his major accomplishments is that he no longer takes any diabetes medication since 12/8/2015.

In 2017, he has achieved excellent results on all fronts, especially his glucose control. However, during the pre-COVID period of 2018 and 2019, he traveled to approximately 50+ international cities to attend 65+ medical conferences and made ~120 oral presentations. This hectic schedule inflicted damage to his diabetes control, through dining out frequently, post-meal exercise disruption, jet lag, and along with the overall metabolism impact due to his irregular life patterns through a busy travel schedule; therefore, his glucose control and overall metabolism state were somewhat affected during this two-year heavier traveling period.

During 2020 with a COVID-19 quarantined lifestyle, not only has he published ~400 medical papers in 100+ journals, but he has also reached his best health condition for the past 26 years. By the beginning of 2021, his weight was further reduced to 165 lbs. (BMI 24.4) along with a 6.1% A1C value (daily average glucose at 105 mg/dL), without having any medication intervention or insulin injections. These good results are due to his non-traveling, low-stress, and regular daily life routines. His knowledge of chronic diseases, practical lifestyle management experiences and developed various high-tech tools contributed to his excellent health status since 1/19/2020, which is the start date of being self-quarantined.

On 5/5/2018, he applied a CGM sensor device on his upper arm and checks his glucose measurements every 5 minutes for a total of ~288 times each day. He has maintained the same measurement pattern to the present day. In his research work, he uses the CGM sensor glucose at a time-interval of 15 minutes (96 data per day). By the way, the difference of average sensor glucose between 5-minute intervals and 15-minute intervals is only 0.4% (average glucose of 114.81 mg/dL for 5-minutes and average glucose of 114.35 mg/dL for 15-minutes with a correlation of 93% between these two sensor glucose curves) during the period from 2/19/20-8/13/21.

Therefore, over the past 11 years, he could study and analyze the collected 2+ million data regarding his health status, medical conditions, and lifestyle details. He applies his knowledge, models, and tools from mathematics, physics, engineering, and computer science to conduct his medical research work. His medical research work is based on the aim of achieving high precision with quantitative proof in the medical findings.

The following timetable provides a rough sketch of the emphasis of his medical research during each stage:

2000-2013: Self-study diabetes and food nutrition, developing a data collection and analysis software.

2014: Develop a mathematical model of metabolism using engineering modeling and advanced mathematics.

2015: Weight and FPG prediction models using neuroscience.

2016: PPG and HbA1C prediction models using optical physics, artificial intelligence (AI), and neuroscience.

2017: Complications due to macro-vascular research such as cardiovascular disease (CVD), coronary heart disease (CHD), and stroke using pattern analysis and segmentation analysis.

2018: Complications due to micro-vascular research such as chronic kidney disease (CKD), bladder, foot, and eye issues such as diabetic retinopathy (DR).

2019: CGM big data analysis, using wave theory, energy theory, frequency domain analysis, quantum mechanics, and AI.

2020: Cancer, dementia, longevity, geriatrics, DR, hypothyroidism, diabetic foot, diabetic fungal infection, linkage between metabolism and immunity, and learning about certain infectious diseases such as COVID-19.

2021: Applications of linear elastic glucose theory (LEGT) and perturbation theory from quantum mechanics on medical research subjects, such as chronic diseases and their complications, cancer, and dementia. Using metabolism and immunity as the base, he expands his research into cancers, semantic, and COVID-19.

To date, he has collected more than two million data regarding his medical conditions and lifestyle details. In addition, he has written 498 medical papers and published 400+ articles in 100+ various medical journals, including 6 special editions with selected 20-25 papers for each edition. Moreover, he has given ~120 presentations at ~65 international medical conferences. He has continuously dedicated his time and effort on medical research work and shared his findings and learnings with other patients worldwide.

2.3 Biomarker density (BMD%)

For the case of one particular patient i, the collected biomarker data can be expressed by pairs of data in the format of (t ij, X ij), j = 1 … T, where the t ij represents the recording time and X ij is the biomarker level at time instant t ij, and T is the overall observation length of the weight. For the case in this article, the total T is 110 (e.g., from 41 mmHg to 150 mmHg with an equal interval of 1 mmHg between two BP end-points).

Therefore, he can describe the above mathematical problem in a more simplified equation for one patient only. The biomarker density% (BMD% or D%) for one patient can be defined in terms of a continuous format as follows:

$$D(x) = \frac{1}{T} \int_{0}^{T} (Y(t)\,dt) / T$$

with $x1 < Y(t) < x2$

where x1 and x2 are boundaries of his selected biomarker range.

The biomarker density% (BMD% or D%) equation for one patient, such as himself, can also be defined in terms of a discrete format as follows:

$$D(x) = \frac{1}{T} \left(\sum_{j=1}^{T} Y(tj)\right) / T$$

with $x1 < Y(t) < x2$

where x1 and x2 are boundaries of his selected biomarker range.

He then developed his app software program using the above-described algorithm.

3. RESULTS

Figure 1 is the only diagram generated for this study. It shows the combination of 5 biomarkers on a common scale.

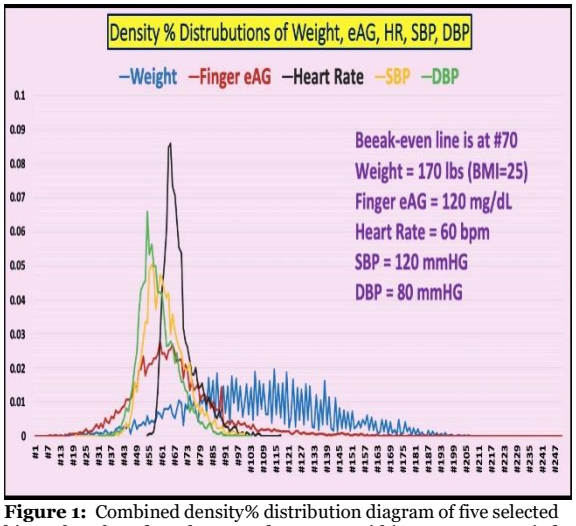

Figure 1: Combined density% distribution diagram of five selected biomarkers based on the same data range within a common period of 7.5 years (4/1/2014-9/13/2021).

This conclusive density% distribution diagram demonstrates the following three conclusions:

(1) Most of his four biomarkers, glucose, SBP, DBP, and HR, are within their normal range.

(2) The peaks of finger glucose and HR are located about #67 while the peaks of SBP and DBP are located around #55. All of them are below #70 which means that the peaks are within the healthy range.

(3) His weight density% are located within the range of #80 (171 lbs.) to #150 (178 lbs.) which reveals that during the majority of the past 7.5 years, his body weight was in the overweight category.

4. CONCLUSION

In summary, the author has chosen to perform his research work using the tools of BMD% with his collected 5 daily biomarker data over the same period of 7.5 years (4/1/2014-9/13/2021).

Each one of these 5 selected biomarkers has its unique biomarker data range and specifically defined biomarker's normal conditions. As a result, this makes the combined study and data presentation quite difficult. For example, his target weight is 170 lbs. (equal to BMI 25 for his case), target glucose is 120 mg/dL, target HR is 60-100 bpm (but chose 60 bpm), target SBP is 120 mmHg, and target DBP is 80 mmHg. In order to combine these 5 biomarkers into one single diagram, he must redefine a common general-scale for the data range from 1 to 250 with equal intervals of 1. With this new numbering system, he can then align these 5 different normal conditions or target values at #70. Now, he is able to plot all 5 density% curves into a combined single diagram with their relative positions indicating their relative biomedical meanings.

Through a closer examination of this combined diagram, he can provide the following three conclusive statements:

Since all 5 biomarkers have been rearranged according to a common scale (from #1 to #250 with #70 as the normal condition), he can then use an eyeball-viewing method to examine these biomarker curves. Other than the weight curve, all the other 4 biomarkers have their majority of data being distributed below #70 which means that most of these 4 biomarkers, glucose, SBP, DBP, and HR, are within their normal range.

(1) The peaks of finger glucose and HR are located around #67 while the peaks of SBP and DBP are located around #55. All of them are below #70 which indicates being in a healthy range.

(2) The weight density distribution curve appears different from the other 4 biomarker curves. From the time-domain analysis, his body weight decreased from 180 lbs. in 2014 to below 170 lbs. during 2020-2021. Therefore, in this density-domain analysis, the majority of his weight density% are located within the range of #80 (171 lbs.) to #150 (178 lbs.). This fact indicates that during the majority of the 7.5 years, his body weight was in the overweight category.

By combining the two different analysis methods, the traditional time-domain analysis and the newly defined density-domain analysis, he can then explore additional insights on the five biomarkers.

5. REFERENCES

For editing purposes, the majority of the references in this paper, which are self-references, have been removed for this article. Only references from other authors' published sources remain. The bibliography of the author's original self-references can be viewed at www.eclairemd.com.

1) Matabuena M, Petersen A, Vidal JC, et al. Glucodensities: A new representation of glucose profiles using distributional data analysis. Stat Methods Med Res. 30(6);1445–1464:2021.

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