Perturbed Risk Probabilities of Developing Diabetic Complications, Including Heart Attack, Stroke, Kidney Complications and Diabetic Retinopathy in Comparison with HbA1C Values over the Past 11.5 Years Using GH-Method: Math-Physical Medicine (No. 476)

Gerald C Hsu

EclaireMD Foundation, USA

*Corresponding author
Gerald C Hsu, EclaireMD Foundation, USA

Submitted: 16 July 2021; **Accepted**: 23 July 2021; **Published**: 11 Aug 2021

Abstract

This paper describes the author's math-physical assessment of his three perturbed annual risk probabilities on having atherosclerotic conditions, cardiovascular disease (CVD), stroke, renal complications & chronic kidney disease (CKD), and diabetic retinopathy (DR) over a period of 11.5 years from 1/1/2010- to 6/30/2021.

These three predicted risk probabilities are calculated using his developed metabolism index (MI) model created in 2014. In addition, he compared the perturbed three risk probabilities against HbA1C (A1C) values calculated from his A1C prediction model generated in 2015. It includes comparisons and verifications against his measured A1C values from various hospitals or medical clinical laboratories over the same time period.

Finally, he applies the perturbation theory of quantum mechanics or modern physics and utilized A1C value as his perturbation factor or slope to develop three sets of perturbed risk probabilities of having a CVD, CKD, and DR within the same time frame (2010 through 2021). He then further compare these three perturbed risk curves against the three calculated risk curves using the MI model.

Many published medical research papers discuss the risk of having diabetic complications using a similar phrase such as "each 1% of increased A1C would result into x% increase of risk of having some diabetic complication disease". Therefore, the author decides to select five key-years that correspond to annual A1C values close to an integer value (see below) for his follow-on comparison study between A1C and his three risk probabilities.

2010: 10%
2011: 9%
2014: 8%
2017: 7%
2021: 6.2%

Note the similar moving pattern of his A1C waveform which declines continuously from 10% in 2010 to 6.2% in 2021. All three perturbed risk probability waveforms follow similar declining patterns of A1C. The above conclusive statement can prove an extremely high correlation coefficients between A1C values and the 3 separated perturbed risk probabilities listed below:

Perturbed CVD vs. A1C: **95%**
Perturbed CKD vs. A1C: **89%**
Perturbed DR vs. A1C: **92%**

More importantly, all of the three disease categories listed below have extremely high prediction accuracies >95%.
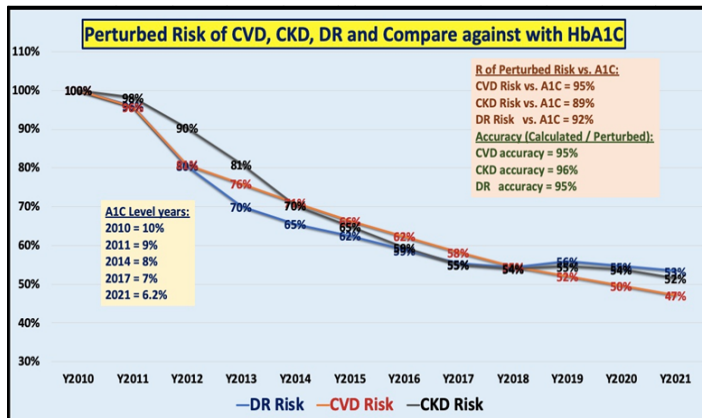
The prediction accuracy is defined as follows:

Prediction accuracy of risk
= (calculated average risks / perturbed average risks

CVD risk accuracy = **95%**
CKD risk accuracy = **96%**
DR risk accuracy = **95%**

In addition, the three correlation coefficients (i.e., waveform shape similarity) between calculated risk curve and perturbed risk curve are extremely high: 97% for DR, 98% for CVD, and 99% for CKD.

The evidence show that the perturbation method can achieve high-

ly accurate average risk values that produce similar curve shapes of the perturbed risk waveform in comparison against the calculated risk waveform based on MI.

Perturbed Risk of CVD, CKD, DR and Compare against with HbA1C

Introduction

This paper describes the author's math-physical assessment of his three perturbed annual risk probabilities on having atherosclerotic conditions, cardiovascular disease (CVD), stroke, renal complications & chronic kidney disease (CKD), and diabetic retinopathy (DR) over a period of 11.5 years from 1/1/2010- to 6/30/2021.

These three predicted risk probabilities are calculated using his developed metabolism index (MI) model created in 2014. In addition, he compared the perturbed three risk probabilities against HbA1C (A1C) values calculated from his A1C prediction model generated in 2015. It includes comparisons and verifications against his measured A1C values from various hospitals or medical clinical laboratories over the same time period.

*Finally, he applies the perturbation theory of quantum mechanics or modern physics and utilized A1C value as his perturbation factor or slope to develop three sets of **perturbed** risk probabilities of having a CVD, CKD, and DR within the same time frame (2010 through 2021). He then further compare these three perturbed risk curves against the three calculated risk curves using the MI model.*

Methods
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 published 400+ 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 biochemical medicine (BCM) approach versus the MPM approach. The third paper, No. 397, depicts a general flow diagram containing ~10 key MPM research methods and different tools.

In short, the author studies and analyzes various digital footprints of human disease's biophysical phenomena using academic tools he has learned about mathematics, physics, engineering, and computer science.

The Author's T2D History

The author has been a severe T2D patient since 1996. He weighed 220 lb. (100 kg, BMI 32.5) at that time. By 2010, he still weighed 198 lb. (BMI 29.2) with an average daily glucose of 250 mg/dL (HbA1C of 10%). During that year, his triglycerides reached to 1161 and albumin-creatinine ratio (ACR) at 116. He also suffered from five cardiac episodes within a decade. In 2010, three independent physicians warned him regarding his needs of kidney dialysis treatment and his future high risk of dying from his severe diabetic complications. Other than cerebrovascular disease (stroke), he has suffered most of 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 conditions: weight, postprandial plasma glucose (PPG), fasting plasma glucose (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) to 33 inches (84 cm), average finger glucose reading from 250 mg/dL to 120 mg/dL, and lab-tested A1C from 10% to ~6.5%. One of his major accomplishments is that *he no longer takes any diabetes medications since 12/8/2015.*

In 2017, he has achieved excellent results on all fronts, especially 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 dinning 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 approximately 400 medical papers in 100+ journals, but he has also reached his best health conditions for the past 26 years. By the beginning of 2021, his weight was further reduced to 165 lbs. (BMI 24.4) along with a 6.2% A1C value, without having any medication interventions or insulin injections. These good results are due to his non-traveling, low-stress, and regular daily life routines. Of course, his knowledge of chronic diseases, practical lifestyle management experiences, and his developed various high-tech tools contribute to his excellent health status since 1/19/2020.

On 5/5/2018, he applied a continuous glucose monitoring (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 present day. In his research work, he uses his CGM sensor glucose at 15-minute time intervals (96 data per day). The difference is only 0.3% between the average glucose of 114.96 mg/dL for the 5-minute time interval and the average glucose of 115.35 mg/dL for the 15-minute time interval during 2/19/20-7/6/21.

His developed A1C prediction model has two existing versions, one for finger-pierced glucose and the other for sensor-collected glucose. The average A1C values for the period from 5/5/2018 to 7/13/2021 are 6.58% for finger and 6.85% for sensor with a 4% difference.

Therefore, over the past 11.5 years, he could study and analyze his collected 2+ million data regarding health status, medical conditions, and lifestyle management details. He applies his knowledge, models, and tools from mathematics, physics, engineering, and computer science to conduct medical research work. His research work is aimed at achieving both "high precision" with a believable "quantitative proof" in the medical findings.

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

• *2000-2013:* Self-study diabetes and food nutrition, developing a data collection and analysis software.
• *2014:* Developed a mathematical model of metabolism, using engineering modeling and advanced mathematics.
• *2015:* Weight & FPG prediction models, using neuroscience.
• *2016:* PPG & A1C prediction models, using optical physics, artificial intelligence (AI), and neuroscience.
• *2017:* Complications due to macro-vascular research, such as CVD, coronary heart diseases (CHD) and stroke, using pattern analysis and segmentation analysis.
• *2018:* Complications due to micro-vascular research such as kidney, bladder, foot, and eye issues.
• *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 fungal infection, and linkage between metabolism and immunity, learning about certain infectious diseases, such as COVID-19.
• *2021:* Applications of linear elastic glucose theory (LEGT) and perturbation theory on medical research subjects, such as chronic diseases and their complications, cancer, and dementia.

Again, to date, he has collected more than two million data regarding his medical conditions and lifestyle details. In addition, he has written 475 medical papers and published ~400 paper in 100+ various medical journals. Moreover, he has also given ~120 presentations at ~65 international medical conferences. He has continuously dedicated his time and efforts on medical research and also wanted to share his findings and learnings with other diabetes patients worldwide.

Lifestyle, Metabolism, Immunity, Diseases, and Death
The most effective defense against infectious diseases, which caused ~10% of total death cases prior to 2019, is our immune system. In addition, the *immune system* is closely related to overall *metabolic* conditions. We can safely say that metabolism and immunity are two sides of one coin. If we consider cancer and dementia as part of "chronic diseases", then the metabolic-related death cases would reach approximately 70-80% of total death cases prior to 2019. After 2020, the number of COVID deaths would disturb the established statistical patterns prior to 2020.

Nevertheless, in order to strengthen our overall metabolism, we must manage our daily *lifestyle* to build a strong and firm foundation over an extended period of time for our health.

In short, lifestyle is similar to the individual weapon quality and overall weaponry production capacity of an arsenal based on the overall educational, technological, and industrial power of a nation. But, metabolism is similar to the effectiveness and destruction power of the military forces, including the weapons available to individual soldiers which are produced by an arsenal. Immunity is similar to the overall military strength of the armed forces (assembly of strong soldiers with powerful weapons), while diseases (chronic, cancer, and infectious) are similar to an enemy's invasion force. Lastly, the study of death is similar to the investigation of outcomes of a war, which is the probability and rate of people death.

Categories of Risk Model
Instead of using traditional biology and chemistry, the author utilized mathematics, physics, engineering modeling, and computer science tools to conduct his medical research.

The framework of his mathematical risk probability model of having diabetic complications, including atherosclerotic conditions, CHD, CVD, stroke, CKD, and DR, includes the following four parts with brief descriptions:

(A) Genetics includes age, race, and health/medical history of family members.

(B) Personal background involves personal bad habits (cigarette smoking, alcohol intake, and illicit drug use), obesity (weight and waistline due to overeating and bad life habits), and personal medical history. Weight problems and bad habits are difficult to change over a short period of time. They are a type of "semi-permanent" issues while genetics are "permanent" issues which cannot be altered or controlled by any patient.

(C) Medical condition consist of blood vessels blockage (glucose and lipids) or blood vessels rupture or leakage (glucose and blood pressure) resulting from obesity, diabetes, hypertension, hyperlipidemia, and other metabolic conditions. In his opinion, glucose is the *primary criminal*, where blood pressure and lipids are the *accomplices*. When combined, they will damage almost all of the internal organs through the blood circulatory system (both macro- and micro- vascular systems) and their related nearby nervous system. This is the root cause of atherosclerosis, CHD, CVD, stroke, CKD, diabetic retinopathy, neuropathy, foot ulcer, and more.

The combined contribution to kidney complications include glucose, blood pressure, kidney, glomeruli, bladder, urinary tract, etc. In addition to glucose and blood pressure, either the albumin to creatinine ratio (ACR) or the glomerular filtration rate (GFR) should be included to evaluate the risk probability of having CKD.

In addition, HbA1C, systolic blood pressure (SBP), and triglycerides are three primary factors that contribute to DR.

(D) Lifestyle management details contain exercise, water intake, sleep (hours, wake up time, and sleep quality), stress (more than 20 different kind of stressors, including more than 20 different psychological conditions), food and meals (quantity such as portion size for weight control, carbs/sugar intake amount for glucose control, plus food quality for nutritional balance and correct diet), and regularity of daily life routines for longevity concerns.

Based on these four parts (A, B, C, and D), and his collected personal big data (2+ million data), he established assumptions with different weighting factors, existing conditions, practice guidelines, and mathematical models based on his 11.5 years of medical research. He built his learned knowledge from reading many biomedical books and medical journals, along with his own findings of his research work, to calculate 7 different risk probability percentages of 7 groups: A, B, C, D, A+B+C, A+B+D, and A+B+C+D.

He developed a software module in his eclaireMD APP on his iPhone to automatically assess and calculate the above-mentioned numerical process of risk probability of having a CVD/CHD/Stroke, CKD, or DR for patients with existing chronic diseases, particularly diabetes.

A Combined Risk Evaluation Model

Based on the information from many medical papers he has read, the author conducted a study on his own diabetic complications development and progression for the past 11.5-years (2010-2021). He has collected and further calculated the following data categories associated with his own medical conditions:

Weight: Body weight, BMI
Glucose: 1 FPG, 3 PPG, 1 daily A1C
Blood Pressure: SBP, DBP, pulse
Lipids: Triglycerides, HDL, LDL

The data for the top three categories were accumulated (weight, glucose, BP, lipids, ACR) or calculated (A1C, BMI and predicted glucoses) on a daily basis. However, his lipid and ACR results were obtained from >30 hospital lab-tests with an average testing period of every four months.

He selected the following medical conditions as his **baseline** or **normal** conditions for his DR risk probability analysis:

Weight: 170 lbs. (BMI=25.0)
Glucose: 120 mg/dL
Triglycerides: 150 mg/dL
SBP: 120 mm Hg
HbA1C: 6.0%

All of his collected data are further normalized according to these established baselines; therefore the final normalized values are located within a range between 0.5 (healthy years of 2017-2021) and 2.5 (unhealthy years of 2010-2012). The worst case occurred in 2010 when he weighed 198 lbs. (BMI 30), peak/average glucoses of 280/240 mg/dL, and A1C of 10%. On the other hand, in 2020-2021, he weighed 168 lbs. (BMI 24.9), finger glucose reading of

106 mg/dL, sensor glucose of 116 mg/dL, and A1C of 6.2%.

Different weighting factor for each contribution element would change the combined result to a certain degree. For example, the following weighting factors are used for his calculation of risk probability:

Glucose:	*40%*
BP:	*30%*
Weight:	*20%*
Lipids:	*10%*

When ACR is added into the model, all of the assigned weighting factors must be re-arranged to sum up to 100%.

After calculating his 4 medical condition categories, he then analyzes his 6 lifestyle management categories such as diet, exercise, sleep, stress, water intake, and daily life routines, to obtain a combined score for lifestyle.

The last category is related to his basic conditions including genetics (family medical histories), bad habits (smoking, alcohol intake), illicit drug use, and certain harmful environmental factors (including but not limited to pollution, radiation, toxic, others).

When he calculates his combined MI, he applies the following different weighing factors for each of these 3 groups:

Medical Conditions:	*50%*
Lifestyle Management:	*40%*
Basic Conditions:	*10%*

It is obvious that the MI model is more sophisticated and covers a wider scope than the A1C model. However, an A1C-alone model can sufficiently provide an accurate-enough results on risk calculations.

It should be noted here that the risk probability percentages are expressed on a "relative" scale, not on an "absolute" scale.

A Special Note on HbA1C

There are many contributing factors to high glucose including two main biological factors which are pancreatic beta cell damage and being overweight (obesity). In total, there are 24 influential factors, such as food, exercise, weather temperature, sleep, stress, and more. Among those many influential factors, the two most prominent are carbs/sugar intake amount (~39% contribution) and post-meal exercise level (~41% contribution). Not only does exercise reduce inflammation in the organs but also highly effective in decreasing glucose level quickly; therefore, the "post-meal" exercise impacts PPG more obviously. Although some human psychological behaviors, such as overeating and being sedentary, are quite common for most people, the required knowledge of diet is indeed far broader and more complicated than the required knowledge of daily exercise routines in terms of scope and depth of knowledge, variety of choices, and degree of difficulty.

Once diet and exercise are in place, most likely, glucose and

HbA1C will be under controlled. Having glucose control combined with the management of both blood pressure (reduce salt consumption, avoid stress, exercise) and lipid (avoid fat, reduce cholesterol consumption, exercise), the blood system (both artery and micro-vessels) will then be in a healthy state. This will definitely reduce the risks of having vascular disease such as CVD/CHD and stroke along with micro-vessels and nervous system problems, such as CKD or diabetic neuropathy, bladder infection, foot ulcer, diabetic retinopathy, erectile dysfunction, constipation, even diabetic fungal infection, and so forth.

Perturbation Theory of Quantum Mechanics or Modern Physics

The author applies the first-order interpolation perturbation method to obtain his "perturbed PPG" waveforms based on one selected carbs/sugar intake amount functioning as the *perturbation factors*, which is the "Slope". He uses the "measured PPG" waveform as his reference or baseline waveform.

The following polynomial function is used as the perturbation equation:

$$A = f(x)$$
$$= A0 + (A1*x) + (A2*x**2)+(A3*x**3) + ... + (An*x**n)$$

Where A is the perturbed glucose, Ai is the measured glucose, and **x is the perturbation factor** *based on a chosen carbs/sugar intake amount.*

For this particular study, he choose his **Ai as A1, where i=1**. In this way, the above equation can then be simplified into the first-order perturbation equation as follows:

$$A = f(x) = A0 + (A1*x)$$

Or the first-order interpolation perturbation equation can also be expressed in the following general format:

$$A i = A1 + (A2-A1)*(slope 1)$$

Where:
A1 = original risk A at year 1
A2 = advanced risk A at year 2
(A2-A1) = (Risk A at Year 2 - Risk A at Year 1)

The perturbation factor or **Slope** is an arbitrarily selected parameter that controls the size of the perturbation. The author has chosen a function of HbA1C value, as his perturbation factor or slope, which is further defined below:

In this particular study, he selects 5.0% as the low-bound A1C value and 10.0% as the high-bound A1C value, while uses 6.2% as his selected or perturbed A1C value.

Then the "slope" becomes:

Slope
= (Selected A1C - Low-bound A1C) / (High-bound A1C - Low-bound A1C)

It should be noted that, for achieving a better predicted glucose value, the selected carbs amount should be within the range of the high-bound A1C and the low-bound A1C, where these two boundary A1C values should be wide enough in magnitude to include the perturbed value in between.

Therefore, in this particular study, his slope or perturbation factor value has been calculated as:

Slope from Carbs
= (6.2-5.0) / (10.0-5.0)
= 0.24 or 24%

Results

Figure 1 illustrates the combination of 3 **perturbed** risk probability curves (CVD, CKD, and DR) and their associated data table, including the perturbation factor calculation.

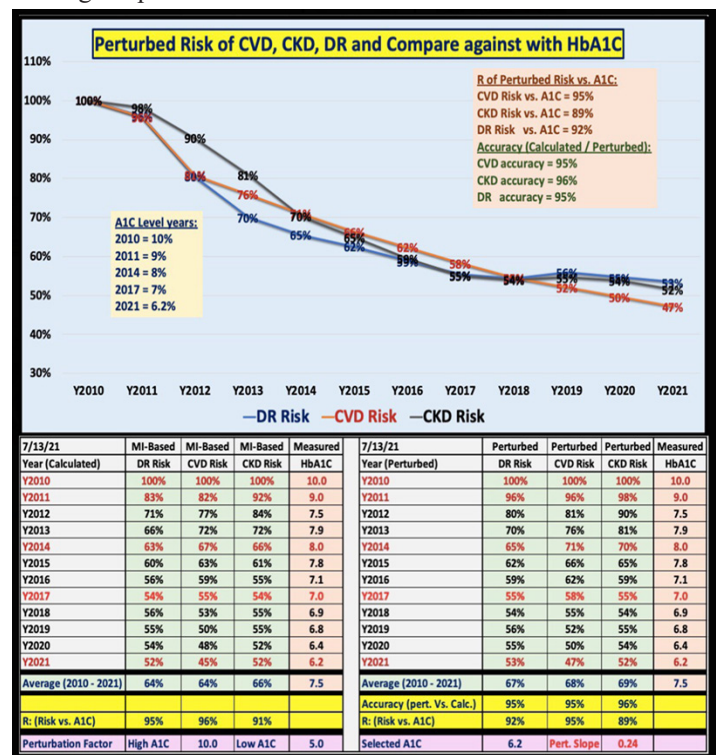| 7/13/21 Year (Calculated)	MI-Based DR Risk	MI-Based CVD Risk	MI-Based CKD Risk	Measured HbA1C	7/13/21 Year (Perturbed)	Perturbed DR Risk	Perturbed CVD Risk	Perturbed CKD Risk	Measured HbA1C
Y2010	100%	100%	100%	10.0	Y2010	100%	100%	100%	10.0
Y2011	83%	82%	92%	9.0	Y2011	96%	96%	98%	9.0
Y2012	71%	77%	84%	7.5	Y2012	80%	81%	90%	7.5
Y2013	66%	72%	72%	7.9	Y2013	70%	76%	81%	7.9
Y2014	63%	67%	66%	8.0	Y2014	65%	71%	70%	8.0
Y2015	60%	63%	61%	7.8	Y2015	62%	66%	65%	7.8
Y2016	56%	59%	55%	7.1	Y2016	59%	62%	59%	7.1
Y2017	54%	55%	54%	7.0	Y2017	55%	58%	55%	7.0
Y2018	56%	53%	55%	6.9	Y2018	54%	55%	54%	6.9
Y2019	55%	50%	55%	6.8	Y2019	56%	52%	55%	6.8
Y2020	54%	48%	52%	6.4	Y2020	55%	50%	54%	6.4
Y2021	52%	45%	52%	6.2	Y2021	53%	47%	52%	6.2
Average (2010 - 2021)	64%	64%	66%	7.5	Average (2010 - 2021)	67%	68%	69%	7.5
					Accuracy (pert. Vs. calc.)	95%	95%	96%	
R: (Risk vs. A1C)	95%	96%	91%		R: (Risk vs. A1C)	92%	95%	89%	
Perturbation Factor	High A1C	10.0	Low A1C	5.0	Selected A1C	6.2	Pert. Slope	0.24	

Figure 1: Perturbed risk probability of having CVD, CKD, and DR during 2010-2021

The most important observation, through visual checking, is that these **3 perturbed** *risk waveforms are starting from a 100% baseline in 2010 and declining year-after-year. This is similar to the three calculated risk waveforms using the MI model. These perturbed risk probability percentages are also expressed on a "relative" scale, not on an "absolute" scale.*

Using statistical calculation, the numerical correlation coefficients of these risks of having three diabetic complication diseases versus HbA1C values are:

Perturbed CVD risk vs. HbA1C: R=95%
Perturbed CKD risk vs. HbA1C: R=89%
Perturbed DR risk vs. HbA1C: R=92%

Here, the HbA1C values are also declining year-after-year with the support of the following summarized table which are extracted from the detailed data table of the lower diagram in Figure 1.

2010: 10%
2011: 9%
2014: 8%
2017: 7%
2021: 6.2%

In addition, the predicted risks using the perturbation theory have achieved the following extremely high prediction accuracies:

CVD Accuracy = 95%
CKD Accuracy = 96%
DR   Accuracy = 95%

Figure 2 reflects three diagrams: upper diagram for CVD, middle diagram for CKD, and lower diagram for DR. They show the comparisons between the calculated risk curve using the MI model and perturbed curve using the perturbation model. The high correlation coefficients of 98% for CVD, 99% for CKD, and 97% for DR have demonstrated that the waveform shapes are almost identical between the calculated risks and perturbed risks.
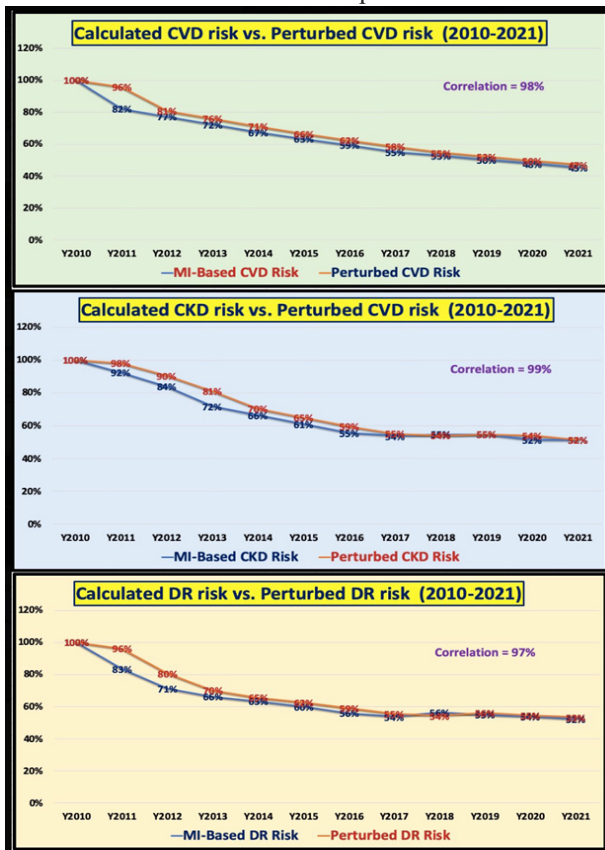

Figure 2: Calculated risk vs. Perturbed risk of CVD, CKD, and

DR during 2010-2021

These two figures have shown that *the perturbation method can achieve highly accurate average risk values that produce almost identical curve shapes of the perturbed risk waveform in comparison with the calculated risk waveform based on metabolism index.*

Conclusions

Many published medical research papers discuss the risk of having diabetic complications using a similar phrase such as "each 1% of increased A1C would result into x% increase of risk of having some diabetic complication disease". Therefore, the author decides to select five key-years that correspond to annual A1C values close to an integer value (see below) for his follow-on comparison study between A1C and his three risk probabilities.

2010: 10%
2011: 9%
2014: 8%
2017: 7%
2021: 6.2%

Note the similar moving pattern of his A1C waveform which declines continuously from 10% in 2010 to 6.2% in 2021. All three perturbed risk probability waveforms follow similar declining patterns of A1C. The above conclusive statement can prove an extremely high correlation coefficients between A1C values and the 3 separated *perturbed* risk probabilities listed below:

Perturbed CVD vs. A1C: 95%
Perturbed CKD vs. A1C: 89%
Perturbed DR   vs. A1C: 92%

More importantly, all of the three disease categories listed below have extremely high prediction accuracies >95%.

The prediction accuracy is defined as follows:

Prediction accuracy of risk
= (calculated average risks / perturbed average risks

CVD risk accuracy = 95%
CKD risk accuracy = 96%
DR risk accuracy =   95%

In addition, the three correlation coefficients (i.e., waveform shape similarity) between calculated risk curve and perturbed risk curve are extremely high: 97% for DR, 98% for CVD, and 99% for CKD.

The evidence show that *the perturbation method can achieve highly accurate average risk values that produce similar curve shapes of the perturbed risk waveform in comparison against the calculated risk waveform based on MI.*

References
For editing purposes, 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.