This HbA_{1c} believes that glycated haemoglobin should be used to diagnose diabetes ?

For the motion – Nick Wareham


The New York Times.

NEW YORK, TUESDAY, APRIL 5, 1921.

WASHINGTON TAKES ISSUE WITH BRITISH IN DISPUTE ON OIL

Russian Claims Harnessing of Air Energy; Soviet Holds It Is Greatest Discovery

REFUSES TO GIVE UP BLACKMAIL NOTES RECEIVED BY WARD

ARMY INVENTS MASK

MANY HELD IN TEXAS

Russian scientist, Professor Figu Posakoff, had discovered a method of "harnessing the latent energy of the atmosphere," the energy displayed in thunderstorms and other atmospheric catastrophes. Harnessing this energy would allow the Soviets to hurl objects "of any weight almost unlimited distances."

Disease

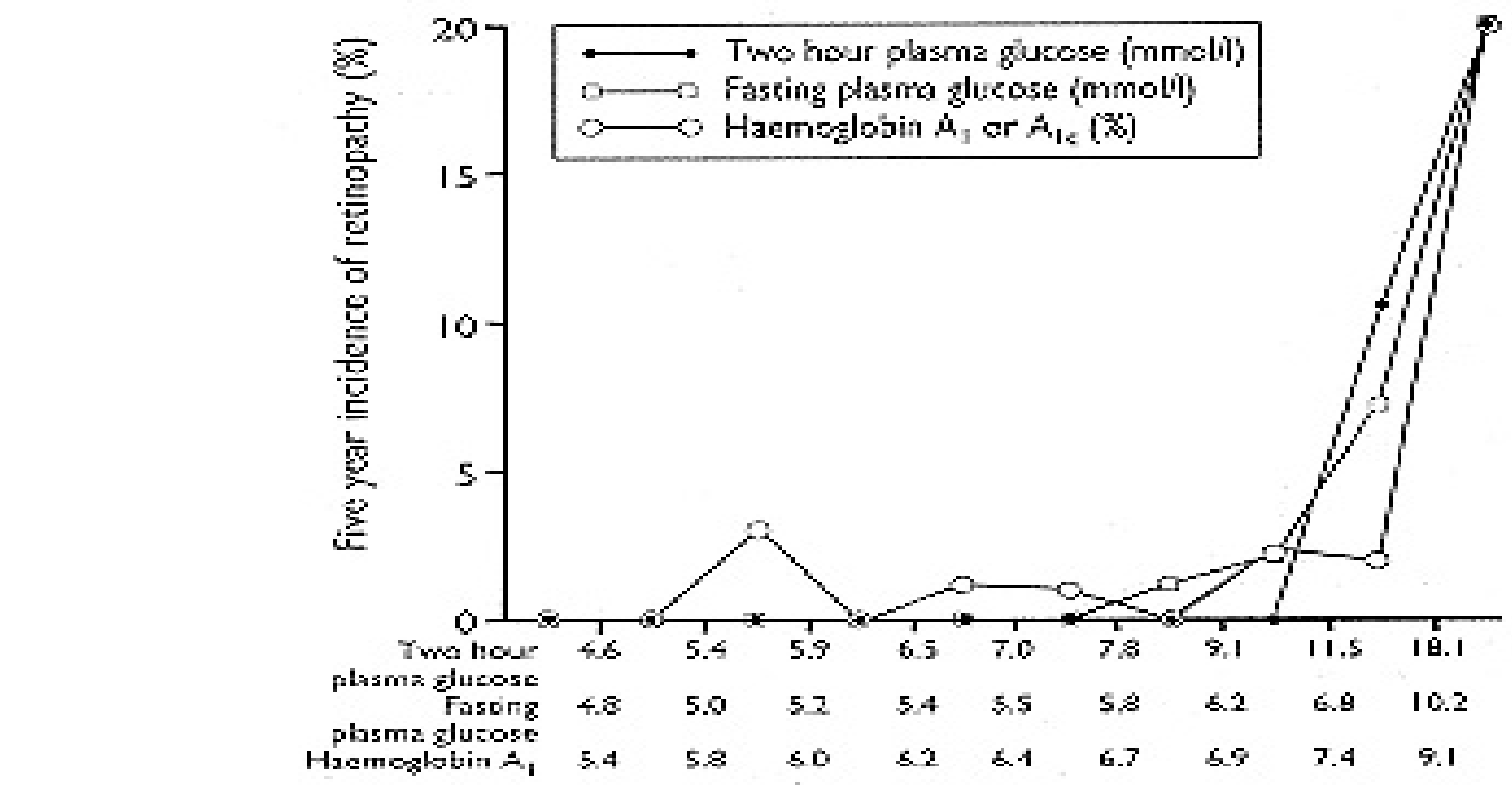
“The anatomic, biochemical, physiologic, or psychologic derangement whose etiology (if known) , maladaptive mechanisms, presentation, prognosis, and management we read about in medical texts.”

Definitions of "normal" in common clinical use

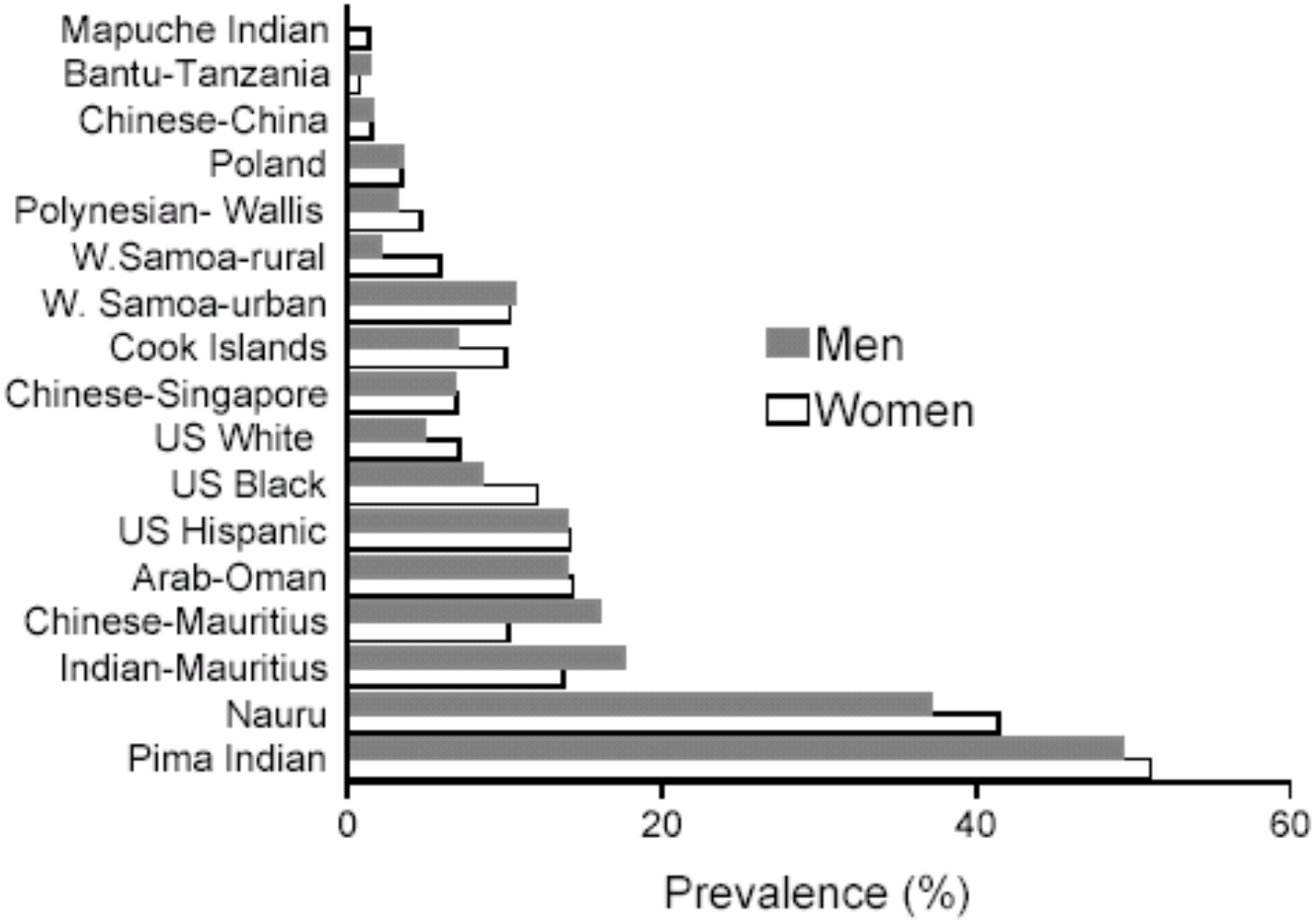
Property	Term	Consequences
Distribution of diagnostic test results has a certain shape	Gaussian	Ought to occasionally obtain minus values
Lies within a preset percentile of previous diagnostic test results	Percentile	All diseases have the same prevalence. Patients are normal only until they are "worked up“
Carries no additional risk of morbidity or mortality	Risk factor	Assumes that altering a risk factor alters risk
Socially or politically aspired to	Culturally desirable	Confusion over the role of medicine in society
Range of test results beyond which disease is, with known probability, present or absent	Diagnostic	Need to know predictive values that apply in your specific practice
Range of test results beyond which treatment does more good than harm	Therapeutic	Need to keep up with knowledge about treatment

Source: Sackett et al, Clinical Epidemiology: a basic science for clinical medicine

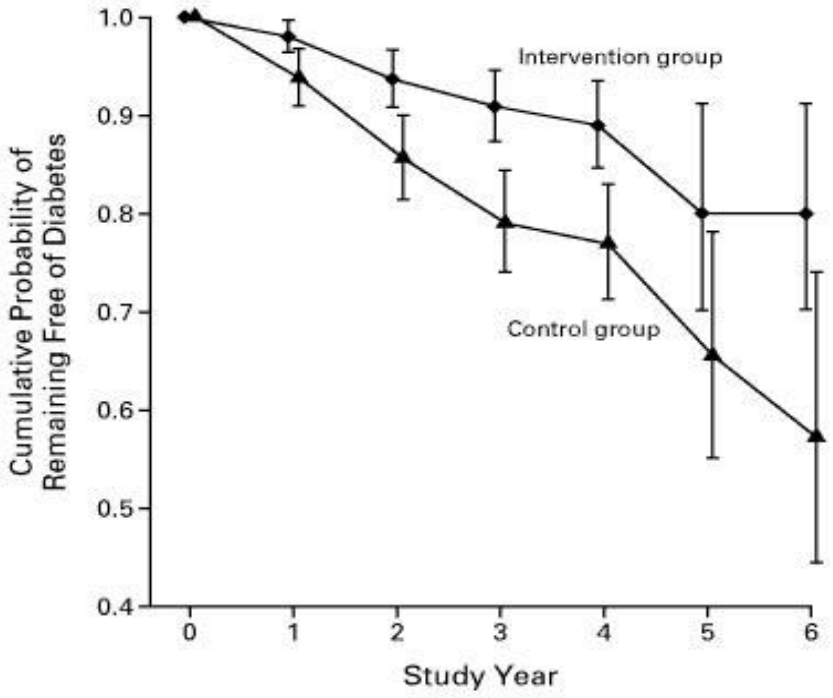
Classical justification for considering diabetes a categorical state



Global variation in T2DM risk



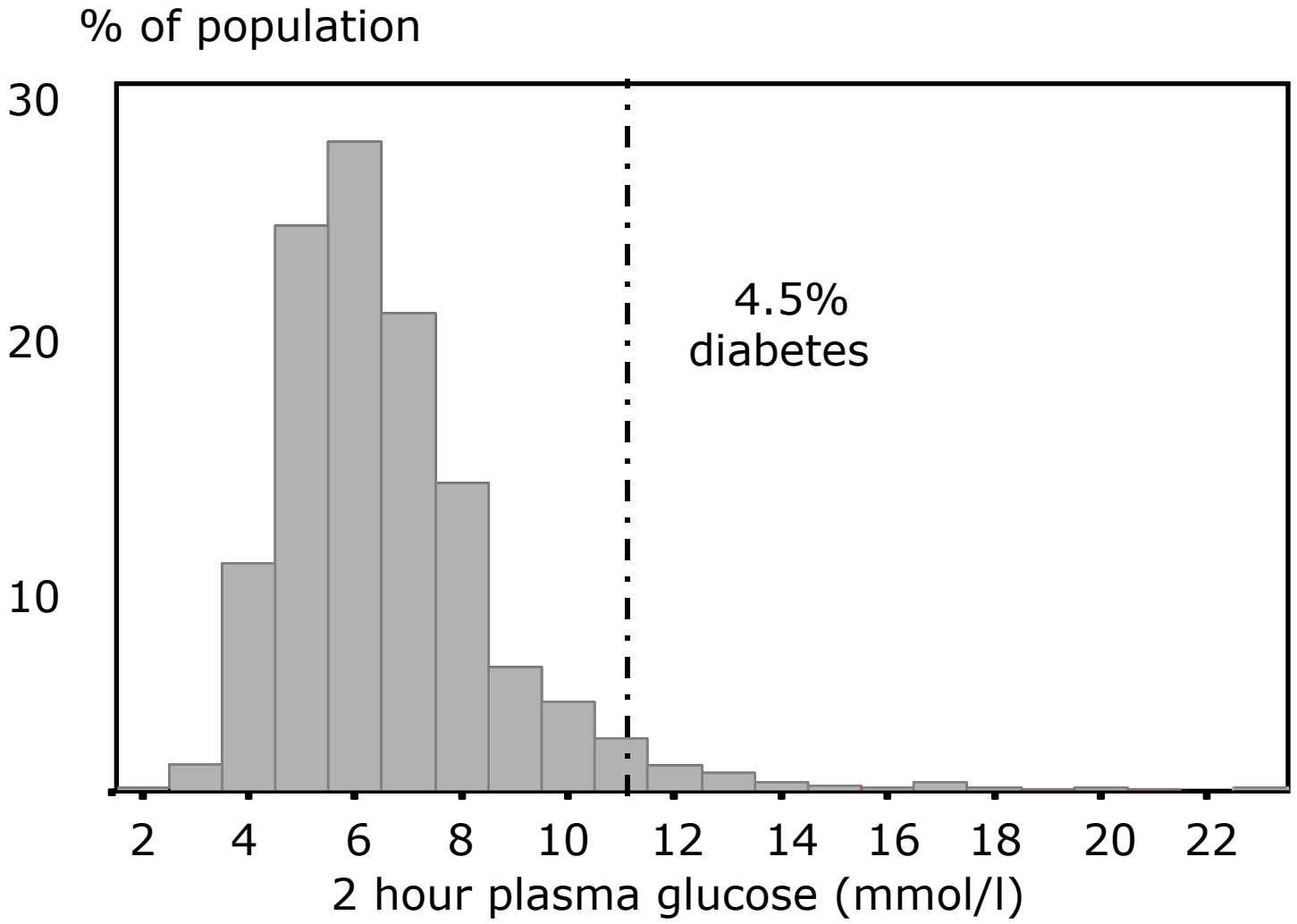
The Finnish Prevention Study



Subjects at Risk						
Total no.	507	471	374	167	53	27
Cumulative no. with diabetes:						
Intervention group	5	15	22	24	27	27
Control group	16	37	51	53	57	59

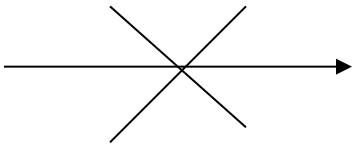
Source: Tuomilheto et al. New England J Med 2001

Population Distribution of 2-Hour Glucose in a Previously Unscreened Population: Ely Study



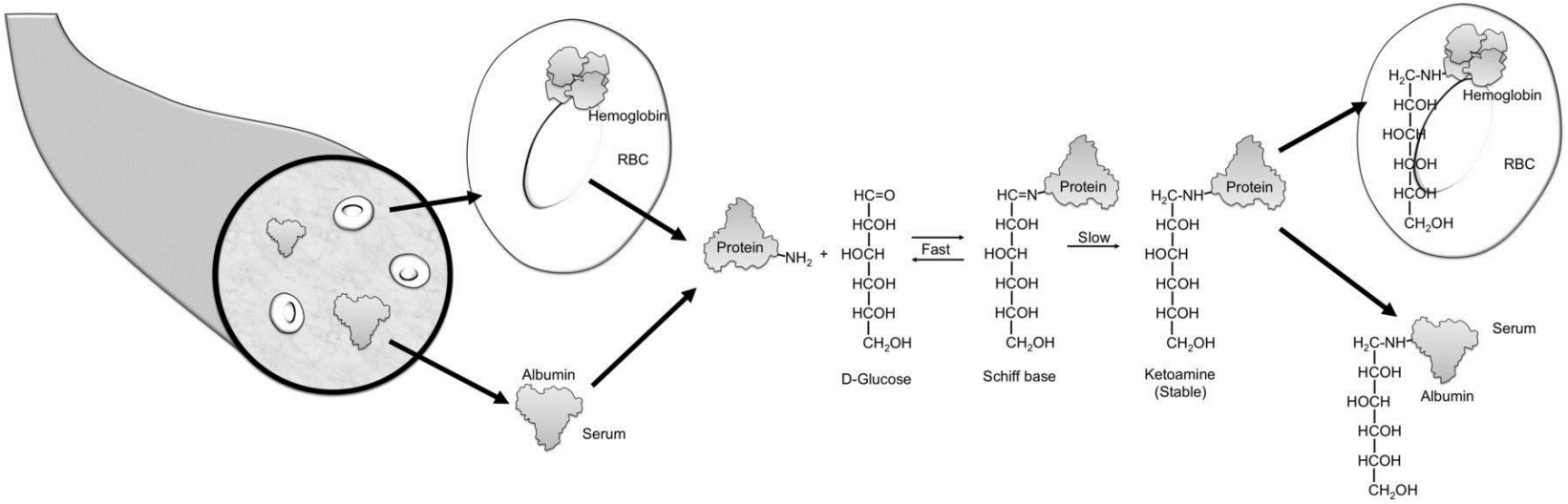
Source: Williams et al. Diabetic Med 1995

- The purpose of a diagnostic label is to inform action, either by the practitioner or by the patient

Epidemiology  **Clinical practice**

Disconnect between research, epidemiology and clinical practice

Formation of glycated protein.



Kerry J. Welsh et al. Dia Care 2016;39:1299-1306

American Diabetes Association.

Committee on Diagnosis of Diabetes

Advantages of A1C vs FPG or 2HPG

The HbA1c assay (standardized and aligned to the DCCT/UKPDS assay) has the following advantages compared with the currently used laboratory measurements of glucose:

1. Better index of overall glycemic exposure
2. At least as good at predicting risk for long-term complications (retinopathy)
3. Similar standardization
4. Substantially less pre-analytic instability
5. Substantially less biologic variability

Committee on Diagnosis of Diabetes

Advantages of A1C vs FPG or 2HPG (cont.)

The HbA1c assay (standardized and aligned to the DCCT/UKPDS assay) has the following advantages compared with the currently used laboratory measurements of glucose:

6. No need for fasting or timed samples
7. Relatively unaffected by acute (e.g. stress or illness-related) perturbations in glucose levels
8. Used to guide management and adjust therapy

Limitations

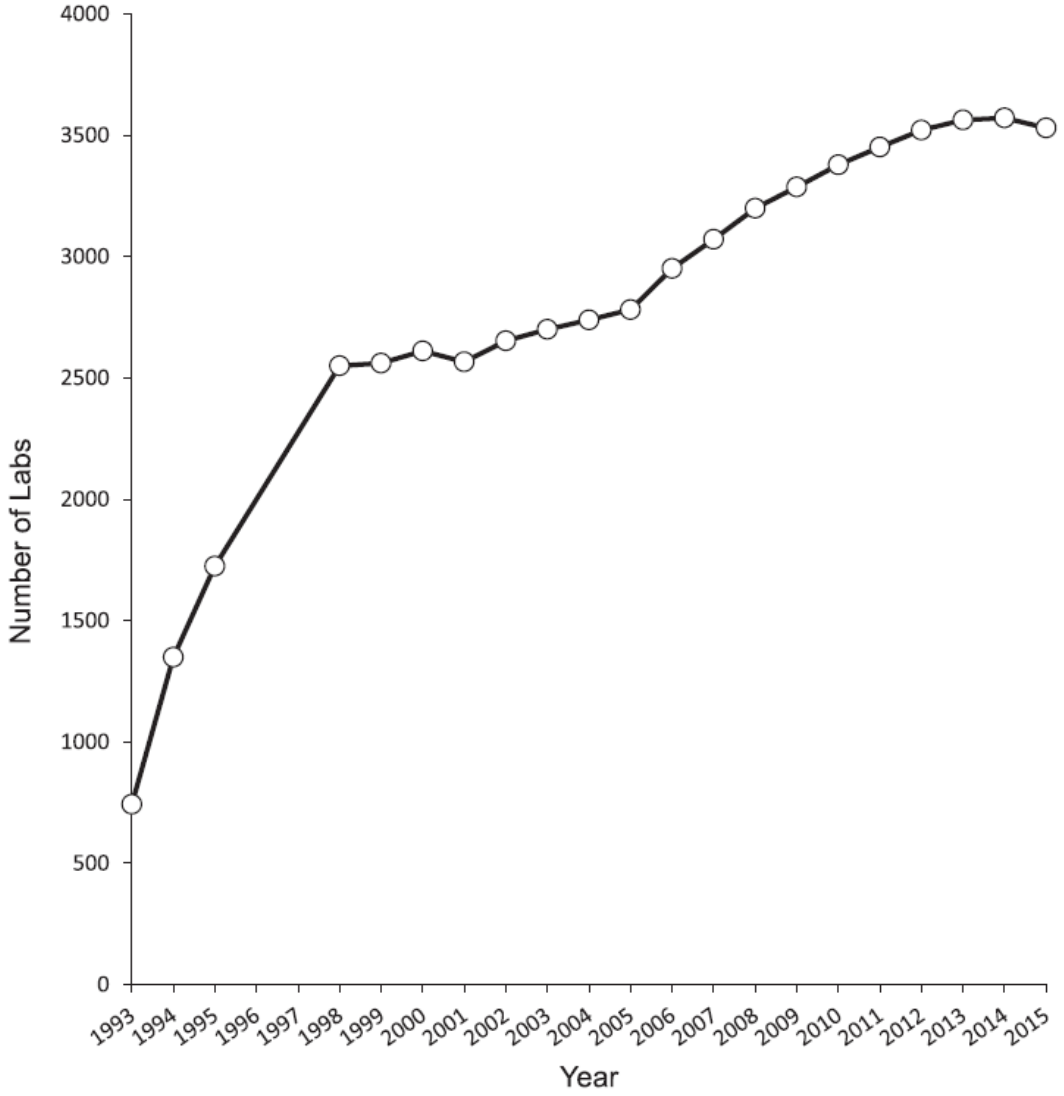
- A1C may not be easily available or affordable in some parts of the world
- Interfering factors (e.g.hemoglobinopathies) may require use of specific methods
- Conditions that affect red cell turnover may cause spurious results
- Clinicians should be aware of these limitations and should use the traditional means of diagnosis (e.g. FPG) when an A1C can’t be performed

Expert Committee on Diagnosis of Diabetes

Conclusions: Diagnosis of diabetes

- The A1C assay is an accurate, precise measure of chronic glycemia and correlates well with risk of developing chronic complications

- The A1C assay has numerous advantages compared with laboratory measures of glucose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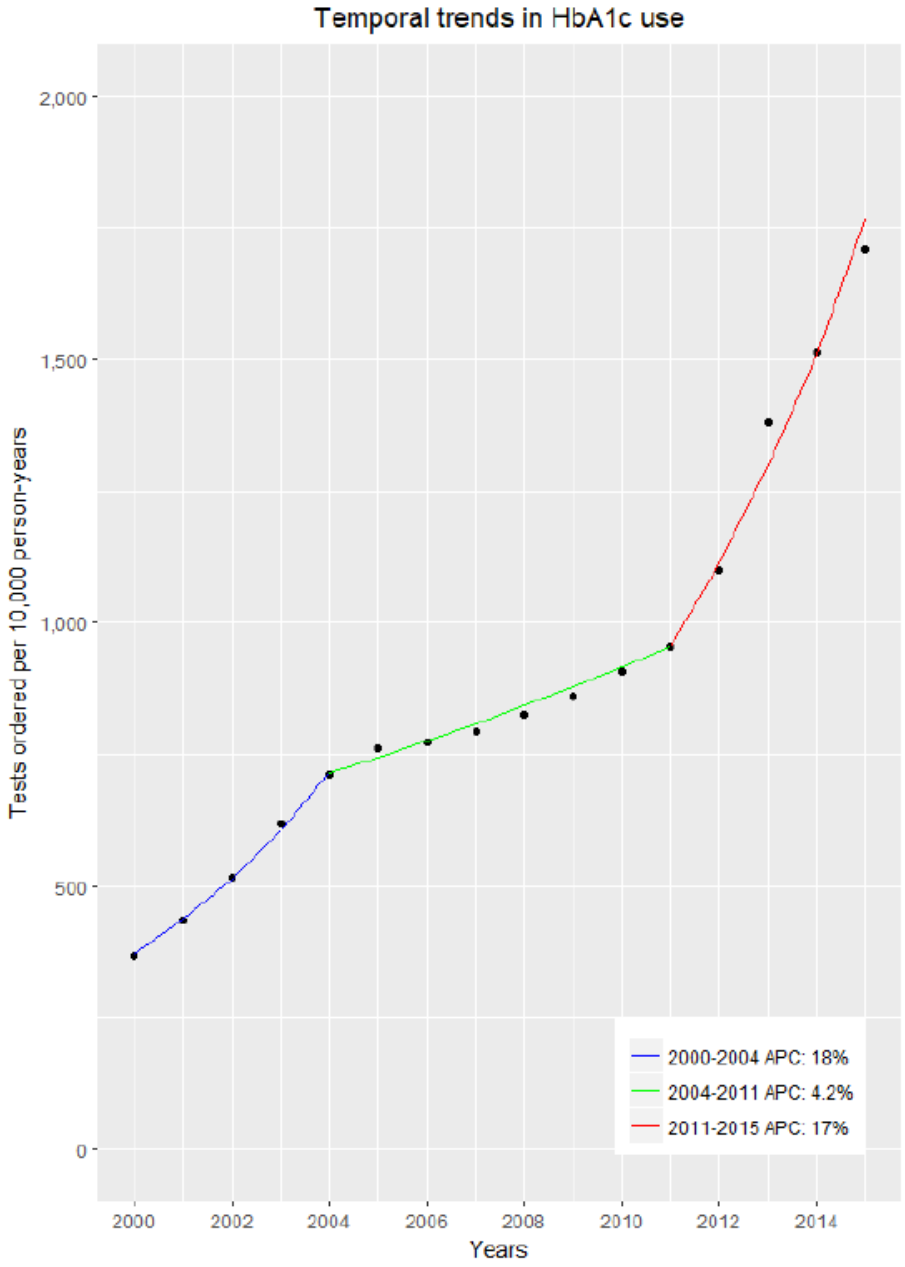
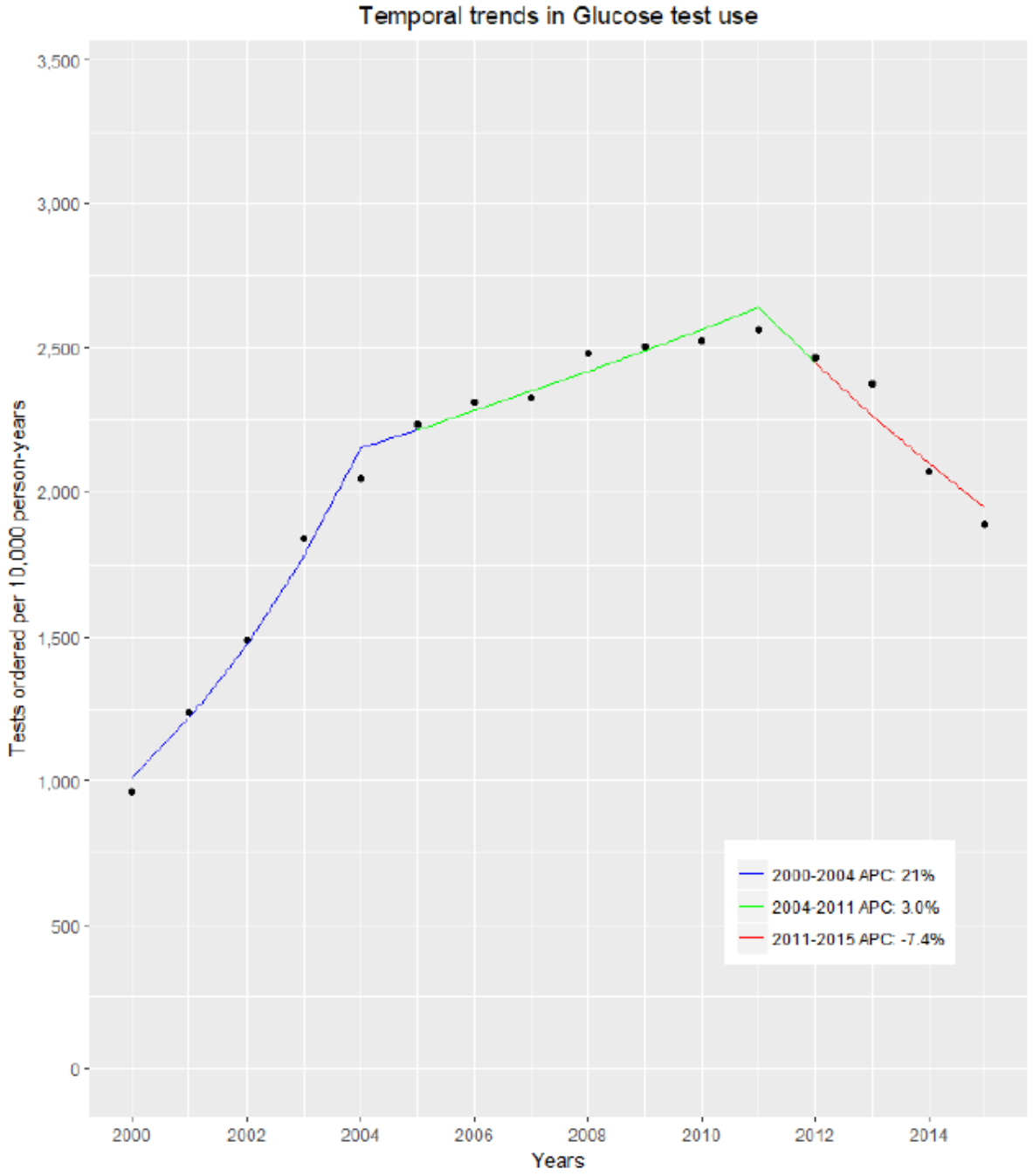

Temporal trends in HbA1c use
2,000
1,500
1,000
500
0
Tests ordered per 10,000 person-years
2000
2002
2004
2006
2008
2010
2012
2014
Years
2000-2004 APC: 18%
2004-2011 APC: 4.2%
2011-2015 APC: 17%


Temporal trends in Glucose test use
Tests ordered per 10,000 person-years
3,500
3,000
2,500
2,000
1,500
1,000
500
0
2000
2002
2004
2006
2008
2010
2012
2014
Years
2000-2004 APC: 21%
2004-2011 APC: 3.0%
2011-2015 APC: -7.4%

Comparison of tests without reference to the "truth" is a barren exercise

Efficacy and effectiveness of screen and treat policies in prevention of type 2 diabetes: systematic review and meta-analysis of screening tests and interventions

Eleanor Barry,[1] Samantha Roberts,[1] Jason Oke,[1] Shanti Vijayaraghavan,[2] Rebecca Normansell,[3] Trisha Greenhalgh[1]

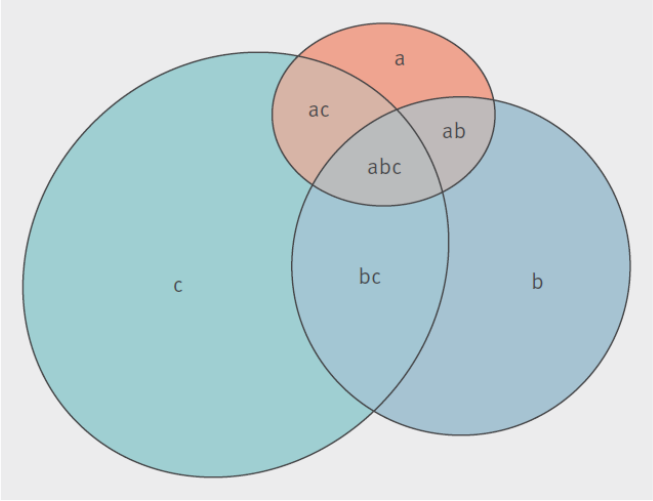


Fig 4 | Prevalence of pre-diabetes by diagnostic test with IEC and WHO criteria, showing overlap with all three tests. Prevalence of pre-diabetes was 27%. Of those with abnormal results, a=4.7% isolated IFG; b=24.4% isolated IGT; c=47.8% isolated HbA_{1c}; ab=2.9% IFG+IGT; ac=4.1% IFG+HbA_{1c}; bc=12.2% IGT+HBA_{1c}; abc=3.9% IGT+IFG+HbA_{1c}; d (area outside ellipse)=72% (normal result)

Table 1—Nonglycemic factors that may influence HbA_{1c}

Factors that may influence interpretation of HbA_{1c}

1. Physiological (e.g., age, race)
2. Chronic renal failure
3. Iron-deficiency anemia
4. Erythrocyte life span
5. Glycation "phenotypes"
6. Drugs (e.g., dapsone, antiretroviral)
7. Other (e.g., vitamin C, vitamin E)

Factors that may interfere with HbA_{1c} measurement

1. Uremia
2. Hemoglobin variants
3. Drugs (e.g., opiates)
4. Other (e.g., bilirubin, triglyceride, alcohol)

Table 2—Adjusted hazard ratios (95% CI)* of cardiovascular and all-cause mortality according to categories of HbA_{1c} and fasting glucose† at baseline in persons without diagnosed diabetes, by race/ethnicity group, U.S. adults aged 18 years or older (NHANES III, 1988–1994), *N* = 12,722

	HbA_{1c} <5.0%	HbA_{1c} 5.0–5.6%	HbA_{1c} 5.7–6.5%	HbA_{1c} ≥6.5%
Cardiovascular mortality, *n* = 804 deaths				
Non-Hispanic white	0.74 (0.38–1.41)	1 (ref)	1.13 (0.83–1.53)	1.39 (0.77–2.51)
Non-Hispanic black	0.94 (0.45–1.96)	1 (ref)	1.10 (0.78–1.56)	2.25 (0.89–5.64)
Mexican American	0.60 (0.18–1.98)	1 (ref)	1.15 (0.63–2.10)	3.90 (1.86–8.17)
All-cause mortality, *n* = 3,415 deaths				
Non-Hispanic white	1.18 (0.91–1.54)	1 (ref)	1.12 (0.96–1.32)	1.50 (1.09–2.05)
Non-Hispanic black	1.27 (0.88–1.81)	1 (ref)	1.14 (0.98–1.32)	2.00 (1.40–2.85)
Mexican American	0.99 (0.60–1.63)	1 (ref)	1.15 (0.84–1.58)	1.74 (1.13–2.67)

	Fasting glucose <90 mg/dL	Fasting glucose 90–99 mg/dL	Fasting glucose 100–125 mg/dL	Fasting glucose ≥126 mg/dL
Cardiovascular mortality, $n = 363$ deaths†				
Non-Hispanic white	0.96 (0.51–1.80)	1 (ref)	1.43 (0.87–2.35)	1.82 (0.98–3.36)
Non-Hispanic black	0.77 (0.29–2.05)	1 (ref)	0.97 (0.45–2.07)	1.60 (0.42–6.13)
Mexican American	1.96 (0.86–4.47)	1 (ref)	1.11 (0.55–2.24)	1.22 (0.39–3.84)
All-cause mortality, $n = 1{,}536$ deaths†				
Non-Hispanic white	0.96 (0.76–1.21)	1 (ref)	1.16 (0.97–1.38)	1.47 (1.04–2.08)
Non-Hispanic black	1.09 (0.71–1.66)	1 (ref)	1.16 (0.85–1.59)	2.40 (1.50–3.84)
Mexican American	0.84 (0.46–1.53)	1 (ref)	0.97 (0.61–1.52)	1.48 (0.69–3.17)

*Adjusted for age, sex, lipids, BMI, waist-to-hip ratio, education, smoking status, hypertension, and physical activity; †Subsample of 5,676 participants who attended the morning examination and had measurements of fasting plasma glucose.

Epidemiology → **Clinical practice**

Reconnection between epidemiology, research and clinical practice

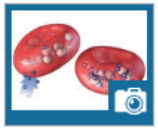
Glycohemoglobin (HbA1c, A1c)

Test Overview

A glycohemoglobin test, or hemoglobin A1c, is a blood test that checks the amount of sugar (glucose) bound to the hemoglobin in the red blood cells. When hemoglobin and glucose bond, a coat of sugar forms on the hemoglobin. That coat gets thicker when there's more sugar in the blood. A1c tests measure how thick that coat has been over the past 3 months, which is how long a red blood cell lives. People who have diabetes or other conditions that increase their blood glucose levels have more glycohemoglobin (sugar bound to hemoglobin) than normal.

Media Gallery

(1 picture)



Learn more about Hemoglobin

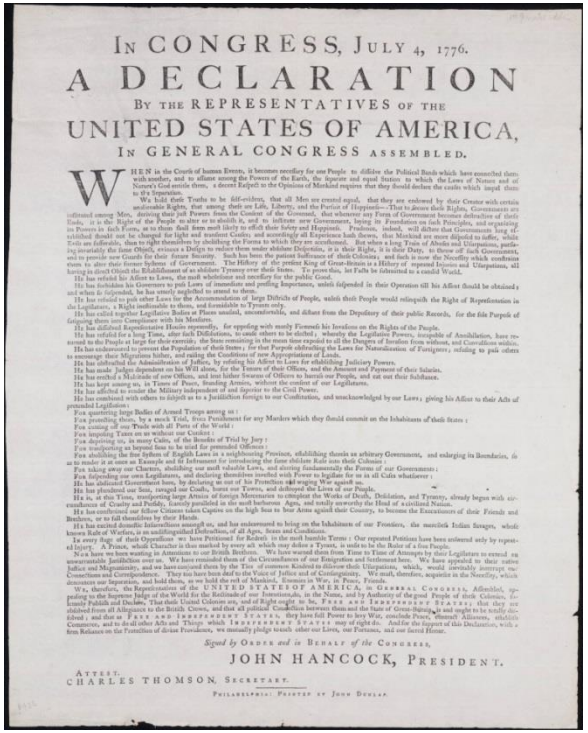
An A1c test can be used to diagnose prediabetes or diabetes. The A1c test checks the long-term control of blood glucose levels in people with diabetes. Most doctors think checking an A1c level is the best way to check how well a person is controlling his or her diabetes. This test may not be appropriate for everyone because many things can affect the life span of red blood cells, such as the second or third trimester of pregnancy, a recent blood loss or a blood transfusion, sickle cell disease, hemodialysis, or erythropoietin (ESA) medicine.

A home blood glucose test measures the level of blood glucose only at that moment. Blood glucose levels change during the day for many reasons, including medicine, diet, exercise, and the level of insulin in the blood.

It is useful for a person who has diabetes to have information about the long-term control of

An A1c test can be used to diagnose prediabetes or
diabetes. The A1c test checks the long-term control of blood glucose levels in people with diabetes. Most doctors think checking an A1c level is the best way to check how well a person is controlling his or her diabetes. This test may not be appropriate for everyone because many things can affect the life span of red blood cells, such as the second or third trimester of pregnancy, a recent blood loss or a blood transfusion, sickle cell disease, hemodialysis, or erythropoietin (ESA) medicine.

We hold these truths to be self-evident …..



IN CONGRESS, JULY 4, 1776.

A DECLARATION

BY THE REPRESENTATIVES OF THE

UNITED STATES OF AMERICA,

IN GENERAL CONGRESS ASSEMBLED.

WHEN in the Course of human Events, it becomes necessary for one People to dissolve the Political Bands which have connected them with another, and to assume among the Powers of the Earth, the separate and equal Station to which the Laws of Nature and of Nature's God entitle them, a decent Respect to the Opinions of Mankind requires that they should declare the causes which impel them to the Separation.

We hold these Truths to be self-evident, that all Men are created equal, that they are endowed by their Creator with certain unalienable Rights, that among these are Life, Liberty, and the Pursuit of Happiness.—That to secure these Rights, Governments are instituted among Men, deriving their just Powers from the Consent of the Governed, that whenever any Form of Government becomes destructive of these Ends, it is the Right of the People to alter or to abolish it, and to institute new Government, laying its Foundation on such Principles, and organizing its Powers in such Form, as to them shall seem most likely to effect their Safety and Happiness. Prudence, indeed, will dictate that Governments long established should not be changed for light and transient Causes; and accordingly all Experience hath shewn, that Mankind are more disposed to suffer, while Evils are sufferable, than to right themselves by abolishing the Forms to which they are accustomed. But when a long Train of Abuses and Usurpations, pursuing invariably the same Object evinces a Design to reduce them under absolute Despotism, it is their Right, it is their Duty, to throw off such Government, and to provide new Guards for their future Security. Such has been the patient Sufferance of these Colonies; and such is now the Necessity which constrains them to alter their former Systems of Government. The History of the present King of Great-Britain is a History of repeated Injuries and Usurpations, all having in direct Object the Establishment of an absolute Tyranny over these States. To prove this, let Facts be submitted to a candid World.

He has refused his Assent to Laws, the most wholesome and necessary for the public Good.

He has forbidden his Governors to pass Laws of immediate and pressing Importance, unless suspended in their Operation till his Assent should be obtained; and when so suspended, he has utterly neglected to attend to them.

He has refused to pass other Laws for the Accommodation of large Districts of People, unless those People would relinquish the Right of Representation in the Legislature, a Right inestimable to them, and formidable to Tyrants only.

He has called together Legislative Bodies at Places unusual, uncomfortable, and distant from the Depository of their public Records, for the sole Purpose of fatiguing them into Compliance with his Measures.

He has dissolved Representative Houses repeatedly, for opposing with manly Firmness his Invasions on the Rights of the People.

He has refused for a long Time, after such Dissolutions, to cause others to be elected; whereby the Legislative Powers, incapable of Annihilation, have returned to the People at large for their exercise; the State remaining in the mean time exposed to all the Dangers of Invasion from without, and Convulsions within.

He has endeavoured to prevent the Population of these States; for that Purpose obstructing the Laws for Naturalization of Foreigners; refusing to pass others to encourage their Migrations hither, and raising the Conditions of new Appropriations of Lands.

He has obstructed the Administration of Justice, by refusing his Assent to Laws for establishing Judiciary Powers.

He has made Judges dependent on his Will alone, for the Tenure of their Offices, and the Amount and Payment of their Salaries.

He has erected a Multitude of new Offices, and sent hither Swarms of Officers to harrass our People, and eat out their Substance.

He has kept among us, in Times of Peace, standing Armies, without the consent of our Legislatures.

He has affected to render the Military independent of and superior to the Civil Power.

He has combined with others to subject us to a Jurisdiction foreign to our Constitution, and unacknowledged by our Laws; giving his Assent to their Acts of pretended Legislation:

For quartering large Bodies of Armed Troops among us:

For protecting them, by a mock Trial, from Punishment for any Murders which they should commit on the Inhabitants of these States:

For cutting off our Trade with all Parts of the World:

For imposing Taxes on us without our Consent:

For depriving us, in many Cases, of the Benefits of Trial by Jury:

For transporting us beyond Seas to be tried for pretended Offences:

For abolishing the free System of English Laws in a neighbouring Province, establishing therein an arbitrary Government, and enlarging its Boundaries, so as to render it at once an Example and fit Instrument for introducing the same absolute Rule into these Colonies:

For taking away our Charters, abolishing our most valuable Laws, and altering fundamentally the Forms of our Governments:

For suspending our own Legislatures, and declaring themselves invested with Power to legislate for us in all Cases whatsoever:

He has abdicated Government here, by declaring us out of his Protection and waging War against us.

He has plundered our Seas, ravaged our Coasts, burnt our Towns, and destroyed the Lives of our People.

He is, at this Time, transporting large Armies of foreign Mercenaries to compleat the Works of Death, Desolation, and Tyranny, already begun with circumstances of Cruelty and Perfidy, scarcely paralleled in the most barbarous Ages, and totally unworthy the Head of a civilized Nation.

He has constrained our fellow Citizens taken Captive on the high Seas to bear Arms against their Country, to become the Executioners of their Friends and Brethren, or to fall themselves by their Hands.

He has excited domestic Insurrections amongst us, and has endeavoured to bring on the Inhabitants of our Frontiers, the merciless Indian Savages, whose known Rule of Warfare, is an undistinguished Destruction, of all Ages, Sexes and Conditions.

In every stage of these Oppressions we have Petitioned for Redress in the most humble Terms: Our repeated Petitions have been answered only by repeated Injury. A Prince, whose Character is thus marked by every act which may define a Tyrant, is unfit to be the Ruler of a free People.

Nor have we been wanting in Attentions to our British Brethren. We have warned them from Time to Time of Attempts by their Legislature to extend an unwarrantable Jurisdiction over us. We have reminded them of the Circumstances of our Emigration and Settlement here. We have appealed to their native Justice and Magnanimity, and we have conjured them by the Ties of our common Kindred to disavow these Usurpations, which, would inevitably interrupt our Connections and Correspondence. They too have been deaf to the Voice of Justice and of Consanguinity. We must, therefore, acquiesce in the Necessity, which denounces our Separation, and hold them, as we hold the rest of Mankind, Enemies in War, in Peace, Friends.

We, therefore, the Representatives of the UNITED STATES OF AMERICA, in GENERAL CONGRESS, Assembled, appealing to the Supreme Judge of the World for the Rectitude of our Intentions, do, in the Name, and by Authority of the good People of these Colonies, solemnly Publish and Declare, That these United Colonies are, and of Right ought to be, FREE AND INDEPENDENT STATES; that they are absolved from all Allegiance to the British Crown, and that all political Connection between them and the State of Great-Britain, is and ought to be totally dissolved; and that as FREE AND INDEPENDENT STATES, they have full Power to levy War, conclude Peace, contract Alliances, establish Commerce, and to do all other Acts and Things which INDEPENDENT STATES may of right do. And for the support of this Declaration, with a firm Reliance on the Protection of divine Providence, we mutually pledge to each other our Lives, our Fortunes, and our sacred Honor.

Signed by ORDER *and in* BEHALF *of the* CONGRESS,

JOHN HANCOCK, PRESIDENT.

ATTEST.
CHARLES THOMSON, SECRETARY.

PHILADELPHIA: PRINTED BY JOHN DUNLAP.