

# **INTERNET NEWS**












**(26 Oct 2023)**

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Khoa Gan, MEDIC**

## ORIGINAL RESEARCH ARTICLE

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# Long-Term Incidence of Ischemic Stroke After Transient Ischemic Attack: A Nationwide Study From 2014 to 2020

Naja Emborg Vinding, MD , Jawad H. Butt, MD , Marie Dam Lauridsen, MD, PhD , Søren Lund Kristensen, MD, PhD , Søren Paaske Johnsen, MD, PhD , Johanna Krøll, MB , Peter L. Graversen, MD , Christina Kruuse, MD, DMSc , Christian Torp-Pedersen, MD, DMSc , Lars Køber, MD, DMSc , and Emil L. Fosbøl, MD, PhD 

**Background:** The short-term incidence of ischemic stroke after a transient ischemic attack (TIA) is high. However, data on the long-term incidence are not well known but are needed to guide preventive strategies.

**Background:** The short-term incidence of ischemic stroke after a transient ischemic attack (TIA) is high. However, data on the long-term incidence are not well known but are needed to guide preventive strategies.

**Methods:** Patients with first-time TIA (index date) in the Danish Stroke Registry (January 2014–December 2020) were included and matched 1:4 with individuals from the background population and 1:1 with patients with a first-time ischemic stroke on the basis of age, sex, and calendar year. The incidences of ischemic stroke and mortality from index date were estimated by Aalen-Johansen and Kaplan-Meier estimators, respectively, and compared between groups using multivariable Cox regression.

**Results:** We included 21 500 patients with TIA, 86 000 patients from the background population, and 21 500 patients with ischemic stroke (median age, 70.8 years [25th–75th percentile, 60.8–78.7]; 53.1% males). Patients with TIA had more comorbidities than the background population, yet less than the control stroke population. The 5-year incidence of ischemic stroke after TIA (6.1% [95% CI, 5.7–6.5]) was higher than the background population (1.5% [95% CI, 1.4–1.6],  $P<0.01$ ; hazard ratio, 5.14 [95% CI, 4.65–5.69]) but lower than the control stroke population (8.9% [95% CI, 8.4–9.4],  $P<0.01$ ; hazard ratio, 0.58 [95% CI, 0.53–0.64]). The 5-year mortality for patients with TIA (18.6% [95% CI, 17.9–19.3]) was higher than the background population (14.8% [95% CI, 14.5–15.1],  $P<0.01$ ; hazard ratio, 1.26 [95% CI, 1.20–1.32]) but lower than the control stroke population (30.1% [95% CI, 29.3–30.9],  $P<0.01$ ; hazard ratio, 0.41 [95% CI, 0.39–0.44]).

**Conclusions:** Patients with first-time TIA had an ischemic stroke incidence of 6.1% during the 5-year follow-up period. After adjustment for relevant comorbidities, this incidence was approximately 5-fold higher than what was found for controls in the background population and 40% lower than for patients with recurrent ischemic stroke.

## Nonstandard Abbreviations and Acronyms

<b>ABCD<sup>2</sup> score</b>	age $\geq 60$ years, blood pressure $\geq 140/90$ mm Hg, clinical features, duration of TIA symptoms, and presence of diabetes
<b>HR</b>	hazard ratio
<b>PPV</b>	positive predictive value
<b>TIA</b>	transient ischemic attack

## Clinical Perspective


### What Is New?

- This is the first study to report long-term risk of ischemic stroke in patients with first-time transient ischemic attack (TIA) in a contemporary nationwide real-world setting.
- Patients with TIA were associated with a noteworthy 5-year incidence of ischemic stroke of 6.1% compared with 1.5% in the matched background population, corresponding to a 5-fold higher relative risk. Compared with patients with first-time ischemic stroke, the relative risk of recurrent stroke among patients with TIA was 40% lower.
- Importantly, this elevated risk after TIA persisted beyond the initial high-risk period and was evident regardless of whether the patients were defined as low-risk or high-risk patients with TIA.


### What Are the Clinical Implications?

- Our study indicates a potential role for extending the follow-up of patients with TIA beyond the initial high-risk period, highlighting the necessity for future trials to investigate the potential benefits of long-term antithrombotic strategies.
- These findings suggest that all patients with TIA should undergo a full diagnostic workup and should be treated similarly.

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## Risk and Prognosis of Cancer in Patients With Cerebral Venous Thrombosis Compared With the Danish General Population

Nils Skajaa , Dóra Körmendiné Farkas, Kasper Adelborg and Henrik Toft Sørensen

Originally published 30 Aug 2023 | <https://doi.org/10.1161/STROKEAHA.123.043590> | Stroke. 2023;54:2576–2582

### Abstract

#### BACKGROUND:

Whether cerebral venous thrombosis (CVT) is a marker of cancer in clinical practice remains unknown. Little is known about the prognosis of cancer detected subsequent to CVT.

#### METHODS:

We used Danish nationwide registries (1996–2019) to identify patients with a first-time primary inpatient diagnosis of CVT without a history of cancer (N=811, 65% women, median age 42 years). We assessed the risk of an incident cancer diagnosis using standardized incidence ratios (SIRs). This measure contrasts the number of observed cancers among patients with CVT to the number of expected cancers where patients with CVT have the same cancer risk as the general population. We used Kaplan-Meier survival analysis and Cox regression to compare the survival of patients with both cancer and CVT with the survival of patients with cancer but without CVT, matched on cancer site, sex, age, and year of cancer diagnosis.

# Abstract

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Whether cerebral venous thrombosis (CVT) is a marker of cancer in clinical practice remains unknown. Little is known about the prognosis of cancer detected subsequent to CVT.

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We used Danish nationwide registries (1996–2019) to identify patients with a first-time primary inpatient diagnosis of CVT without a history of cancer (N=811, 65% women, median age 42 years). We assessed the risk of an incident cancer diagnosis using standardized incidence ratios (SIRs). This measure contrasts the number of observed cancers among patients with CVT to the number of expected cancers where patients with CVT have the same cancer risk as the general population. We used Kaplan-Meier survival analysis and Cox regression to compare the survival of patients with both cancer and CVT with the survival of patients with cancer but without CVT, matched on cancer site, sex, age, and year of cancer diagnosis.


## RESULTS:

Observing 43 incident cancer cases during follow-up, the overall SIR was unity (SIR, 1.04 [95% CI, 0.75–1.40]). However, the risk was  $\approx$ 7-fold the expected level in the first 3 months following CVT diagnosis (SIR, 7.00 [95% CI, 3.02–13.80]) and  $\approx$ 2-fold the expected level from 3 to 12 months following CVT diagnosis (SIR, 2.21 [95% CI, 0.89–4.56]). By 12 months following CVT diagnosis, the risk resembled the expected level (SIR, 0.76 [95% CI, 0.50–1.09]). Survival among cancer patients with prior CVT versus cancer patients without prior CVT was 91% versus 87% after 6 months and 65% versus 70% after 5 years. The adjusted hazard ratio of death was 0.78 (95% CI, 0.44–1.38).

## CONCLUSIONS:

Patients with CVT were not at overall increased risk of a cancer diagnosis, except in the first 3 months after diagnosis during which period the risk was elevated  $\approx$ 7-fold. The estimate from this early period, however, was based on only a few cancer diagnoses. Unlike other forms of venous thrombosis, a prior diagnosis of CVT did not negatively impact cancer survival.

ARTICLES | VOLUME 402, ISSUE 10397, P203-234, JULY 15, 2023

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# Global, regional, and national burden of diabetes from 1990 to 2021, with projections of prevalence to 2050: a systematic analysis for the Global Burden of Disease Study 2021

GBD 2021 Diabetes Collaborators <sup>†</sup> • Show footnotesOpen Access • Published: June 22, 2023 • DOI: [https://doi.org/10.1016/S0140-6736\(23\)01301-6](https://doi.org/10.1016/S0140-6736(23)01301-6) •

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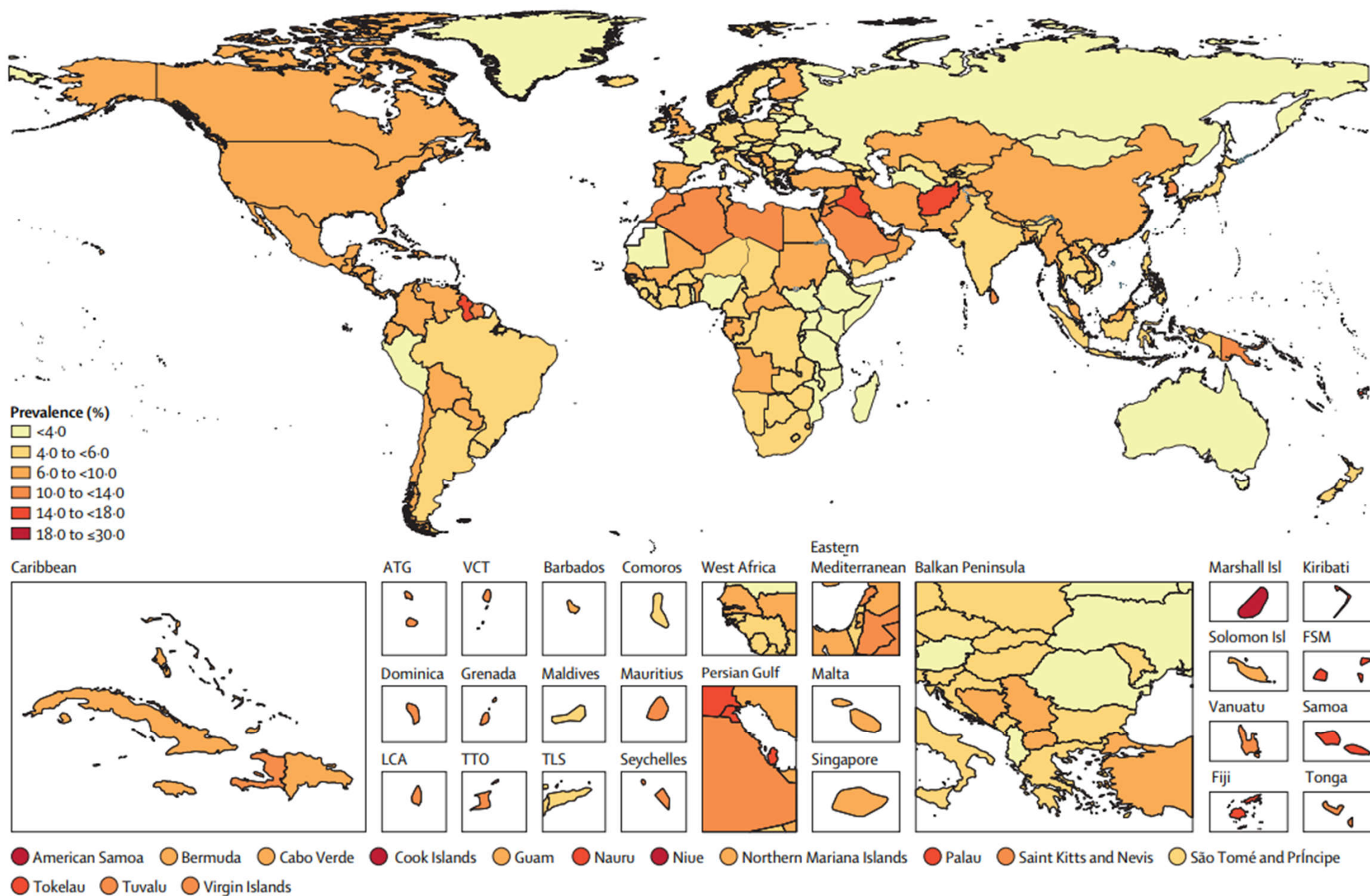
## Summary

### Background

Diabetes is one of the leading causes of death and disability worldwide, and affects people regardless of country, age group, or sex. Using the most recent evidentiary and analytical framework from the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD), we produced location-specific, age-specific, and sex-specific estimates of diabetes prevalence and burden from 1990 to 2021, the proportion of type 1 and type 2 diabetes in 2021, the proportion of the type 2 diabetes burden attributable to selected risk factors, and projections of diabetes prevalence through 2050.

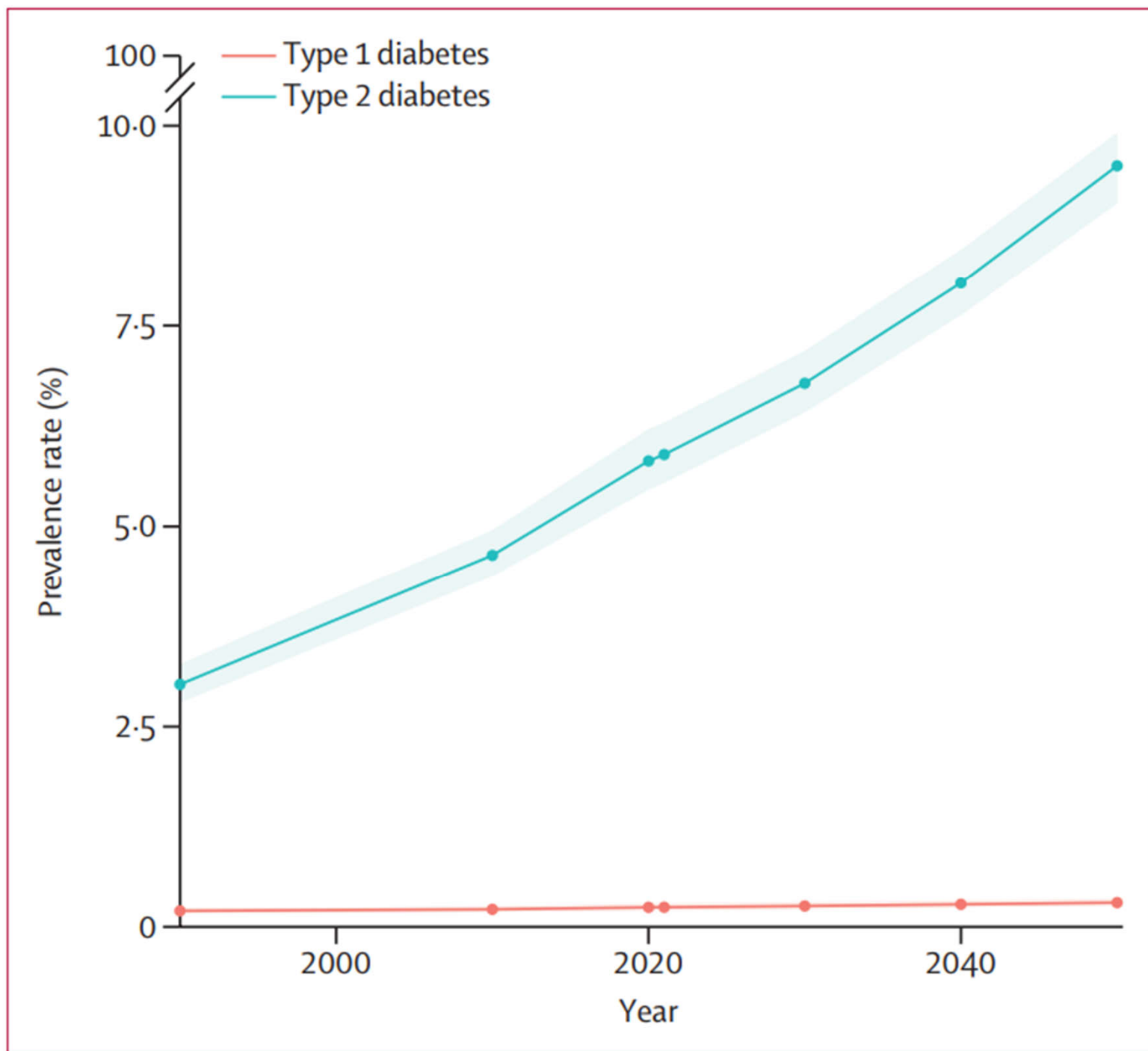
### Methods

Estimates of diabetes prevalence and burden were computed in 204 countries and territories, across 25 age groups, for males and females separately and combined; these estimates comprised lost years of healthy life, measured in disability-adjusted life-years (DALYs; defined as the sum of years of life lost [YLLs] and years lived with disability [YLDs]). We used the Cause of Death Ensemble model (CODEm) approach to estimate deaths due to diabetes, incorporating 25 666 location-years of data from vital registration and verbal autopsy reports in separate total (including both type 1 and type 2 diabetes) and type-specific models. Other forms of diabetes, including gestational and monogenic diabetes, were not explicitly modelled. Total and type 1 diabetes prevalence was estimated by use of a Bayesian meta-regression modelling tool, DisMod-MR 2.1, to analyse 1527 location-years of data from the



**Figure 1: Age-standardised total diabetes prevalence rates in 2021**

ATG=Antigua and Barbuda. VCT=Saint Vincent and the Grenadines. LCA=Saint Lucia. TTO=Trinidad and Tobago. Isl=Islands. FSM=Federated States of Micronesia. TLS=Timor-Leste.



**Figure 4:** Global age-standardised prevalence of type 1 and type 2 diabetes from 1990 through 2050 forecasts

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## TOPIC CHALLENGE : SEPTEMBER CHALLENGE



What is the primary risk factor for type 2 diabetes worldwide?

According to a recent systematic analysis of the Global Burden of Diabetes Disease Study 2021, which of the following is found to be the primary risk factor for type 2 diabetes worldwide?

Correct! The answer is:

<b>A</b>	Tobacco use	<b>B</b>	Low physical activity
<b>C</b>	Uncontrolled diet	<input checked="" type="checkbox"/>	High body mass index

### Commented Answer

A recent systematic analysis of the Global Burden of Disease Study 2021's global, regional, and national burden of diabetes from 1990 to 2021 found that high body mass index was the primary risk factor for type 2 diabetes worldwide, accounting for 52.2% (25.5%-71.8%) of global type 2 diabetes disability-adjusted life years (DALYs). In addition to the various other risk factors, dietary risks were accountable for 25.7% (8.6%-40.7%), environmental or occupational risks were responsible for 19.6% (12.7%-26.5%), the use of tobacco contributed to 12.1% (4.5%-20.9%), low physical activity was responsible for 7.4% (3.0%-11.2%), and alcohol use was accountable for 1.8% (0.3%-3.9%) of type 2 diabetes DALYs.

### References

GBD 2021 Diabetes Collaborators. Global, regional, and national burden of diabetes from 1990 to 2021, with projections of prevalence to 2050: a systematic analysis for the Global Burden of Disease Study 2021. Lancet. 2023 June 22. Epub ahead of print.

Original Research

## Blood Pressure Level in Late Adolescence and Risk for Cardiovascular Events

### A Cohort Study

Helene Rietz, MD , Johanna Pennlert, MD, PhD , Peter Nordström, MD, PhD , and ... [See More](#) 

[Author, Article, and Disclosure Information](#)

<https://doi.org/10.7326/M23-0112>

[Eligible for CME Point-of-Care](#)

## Abstract

### Background:

Not enough is known about the association between blood pressure (BP) in adolescence and future cardiovascular events.

### Objective:

To measure this association using the 2017 American College of Cardiology/American Heart Association guidelines for classifying BP elevation.

### Design:

Cohort study.

**Setting:**

Sweden.

**Participants:**

Males in late adolescence who were conscripted into the military from 1969 to 1997.

**Measurements:**

Baseline BP was measured at conscription. The primary outcome was a composite of cardiovascular death or first hospitalization for myocardial infarction, heart failure, ischemic stroke, or intracerebral hemorrhage.

**Results:**

**Results:**

The study included 1 366 519 males with a mean age of 18.3 years. The baseline BP was classified as elevated (120 to 129/<80 mm Hg) for 28.8% of participants and hypertensive ( $\geq$ 130/80 mm Hg) for 53.7%. During a median follow-up of 35.9 years, 79 644 had a primary outcome. The adjusted hazard ratio was 1.10 for elevated BP (95% CI, 1.07 to 1.13), 1.15 for stage 1 isolated systolic hypertension (ISH) (CI, 1.11 to 1.18), 1.23 for stage 1 isolated diastolic hypertension (IDH) (CI, 1.18 to 1.28), 1.32 for stage 1 systolic–diastolic hypertension (SDH) (CI, 1.27 to 1.37), 1.31 for stage 2 ISH (CI, 1.28 to 1.35), 1.55 for stage 2 IDH (CI, 1.42 to 1.69), and 1.71 for stage 2 SDH (CI, 1.58 to 1.84). The cumulative risk for cardiovascular events also increased gradually across BP stages, ranging from 14.7% for normal BP to 24.3% for stage 2 SDH at age 68 years.

**Limitation:**

This was an observational study of Swedish men.

**Conclusion:**

Increasing BP levels in late adolescence are associated with gradually increasing risks for major cardiovascular events, beginning at a BP level of 120/80 mm Hg.



[Journal List](#) > [eClinicalMedicine](#) > [v.63; 2023 Sep](#) > PMC10480545

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PMCID: PMC10480545

Published online 2023 Aug 30. doi: [10.1016/j.eclinm.2023.102196](#)

PMID: [37680941](#)

### Increased risk of colon cancer after acute appendicitis: a nationwide, population-based study

[Manon Viennet](#),<sup>a</sup> [Solène Tapia](#),<sup>b</sup> [Jonathan Cottenet](#),<sup>b</sup> [Alain Bernard](#),<sup>b</sup> [Pablo Ortega-Deballon](#),<sup>a,c,d,\*</sup> and [Catherine Quantin](#)<sup>b,c</sup>

## Summary

**Background** Acute appendicitis is the most common digestive disease requiring emergency surgery. Colorectal cancer is the third most common cancer in France. An increased risk of colorectal cancer after acute appendicitis has been suggested. We aimed to assess the frequency of hospitalization for colon cancer after appendicitis in a nationwide analysis.

**Methods** Using the French Hospital Discharge Database (PMSI), we included all patients aged 18–59 years presenting with acute appendicitis between 2010 and 2015. Univariate and multivariate analyses were performed to compare colon cancer occurrence in these patients vs a control-matched population with a hospital stay for trauma in the same period. Patients presenting strong risk factors for colorectal cancer were excluded.

**Findings** A total of 230,349 patients with acute appendicitis (exposed group) were included. We used a propensity score to match each exposed patient with two unexposed patients (controls) to ensure the comparability of the groups, resulting in a control group of 460,698 patients. Univariate analysis found significantly more colon cancer in the appendicitis group, especially during the first year after appendicitis (5 per 10,000 vs 1 per 10,000,  $p < 0.000$ , this corresponds to 111 patients in the appendicitis group), namely within the first 6 months. Survival analysis confirmed patients treated for appendicitis present a 4 times higher risk of being diagnosed with colon cancer than control patients during the first year of follow-up (sHR = 4.67 (95% CI: 3.51–6.21), and 8 times higher during the first 6 months (sHR = 8.39; 95% CI: 5.41–12.99). The association was even more marked for right-sided colon cancer (sHR = 8.25; 95% CI: 5.03–13.54 during the 1st year). While the risk of diagnosis of colon cancer was also significant for patients over 40 years, it was even greater in patients under 40 years, who had between a 6-fold and 12-fold increase in risk.

**Interpretation** In this population-based study, we found that acute appendicitis seems to be a warning sign for colon cancer (reverse causality) in both middle-aged and younger adults. The risk of presenting with cancer colon was higher during the first six months after acute appendicitis. This raises the issue of routine diagnostic work-up in adults presenting with acute appendicitis.

**Funding** Regional Council of Burgundy.

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ORIGINAL ARTICLE | ARTICLES IN PRESS

# High accuracy of a blood ctDNA-based multimodal test to detect colorectal cancer

X. Bessa <sup>1</sup>, #  • J. Vidal J <sup>2</sup>, # • J. Carles Balboa • ... C. Álvarez <sup>1</sup> • B. Bellosillo <sup>4</sup> •

C. Montagut <sup>2</sup>, <sup>5</sup>  • [Show all authors](#) • [Show footnotes](#)

**Open Access** • Published: October 05, 2023 • DOI: <https://doi.org/10.1016/j.annonc.2023.09.3113>

Highlights

Abstract

Keywords

Introduction

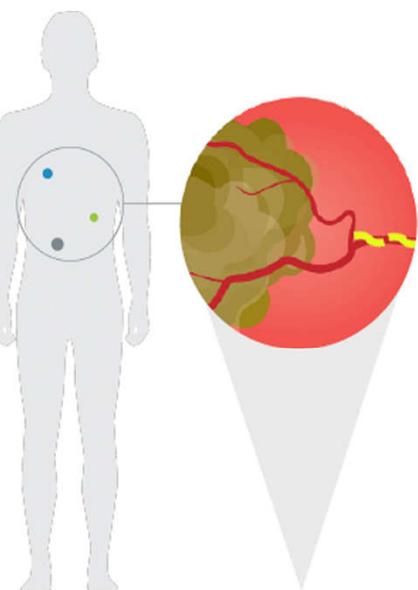
Patients and  
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Results

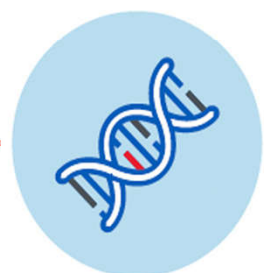
Discussion

## Highlights

- Effectiveness of CRC screening programs are limited by the low adherence of the population to screening recommendations.
- A novel blood multimodal ctDNA-based assay was tested in FIT-positive individuals from a screening program and CRC patients.
- CRC was detected with high accuracy (93% sensitivity; 90% specificity). Sensitivity to detect precancerous lesions was 23%.
- A blood test including genomics, epigenomics, fragmentomics and proteomics may increase the effectiveness of CRC screening.

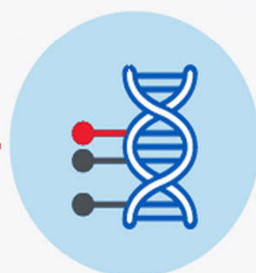


## Genomic Alterations

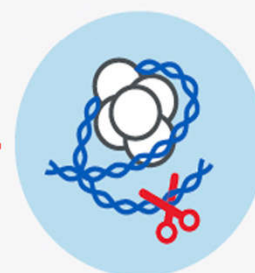


Assessment of ctDNA mutations known to be present in cancer

## Epigenomic Modifications

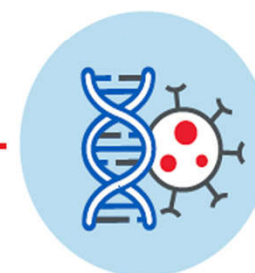


Analysis of which genes are turned on or off throughout the genome



Assessment of ctDNA fragment size can indicate the presence of cancer

## Proteomics



Expression of certain proteins may be associated with cancer

## Background

Detection of circulating tumor DNA (ctDNA) is a minimally invasive and convenient blood-based screening strategy that may increase effectiveness of colorectal cancer (CRC) screening.

## Patients and methods

A novel multimodal ctDNA-based blood assay that integrates genomics, epigenomics and fragmentomics, as well as proteomics in a refined version, was tested in blood samples from two cohorts: (1) consecutive FIT-positive individuals from the CRC Barcelona stool-based screening program; (2) patients diagnosed with CRC. Primary endpoint was the performance of the test to detect CRC at different TNM stages. Secondary endpoint was the ability of the test to detect advanced precancerous lesions (advanced adenoma or advanced serrated lesion).

## Results

A total of 623 blood samples were analyzed in the primary analysis. Sensitivity and specificity of the assay to detect CRC was 93% and 90%, respectively. The sensitivity of CRC detection according to TNM stages was 84% stage I, 94% stage II, 96% stage III, 100% stage IV. Sensitivity to detect advanced precancerous lesions was 23% with a refined version of the test (including protein and updating bioinformatic thresholding).

## Conclusion

A blood-based multimodal ctDNA assay detected colorectal cancer with high accuracy. This minimally invasive, accessible, and convenient assay may help to increase the effectiveness of CRC screening.

RESEARCH ARTICLE | VOLUME 79, ISSUE 4, P1006-1014, OCTOBER 2023

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# Machine learning for individualized prediction of hepatocellular carcinoma development after the eradication of hepatitis C virus with antivirals

[Tatsuya Minami](#) <sup>†</sup> • [Masaya Sato](#) <sup>†</sup> • [Hidenori Toyoda](#) • ... [Mitsuhiro Fujishiro](#) • [Kazuhiko Koike](#) •

## Highlights

- A novel machine learning model for HCC prediction in patients after SVR was developed, named the SMART model.
- The SMART model consists of seven readily available parameters: age, platelet count, serum AFP, GGT, albumin and AST levels, and BMI.
- Using an online app, the SMART model can generate an individualized predictive curve for HCC development for each patient.
- Risk stratification by the SMART model could contribute to personalized and cost-effective HCC surveillance after SVR.

Machine learning for individualized prediction of hepatocellular carcinoma development after the eradication of hepatitis C virus with antivirals - Journal of Hepatology (journal-of-hepatology.eu)

## Background & Aims

Accurate risk stratification for hepatocellular carcinoma (HCC) following the achievement of a sustained virologic response (SVR) is necessary for optimal surveillance. We aimed to develop and validate a machine learning (ML) model to predict the risk of HCC after achievement of an SVR in individual patients.

## Methods

In this multicenter cohort study, 1,742 patients with chronic hepatitis C who achieved an SVR were enrolled. Five ML models were developed including DeepSurv, gradient boosting survival analysis, random survival forest (RSF), survival support vector machine, and a conventional Cox proportional hazard model. Model performance was evaluated using Harrel's c-index and was externally validated in an independent cohort (977 patients).

## Results

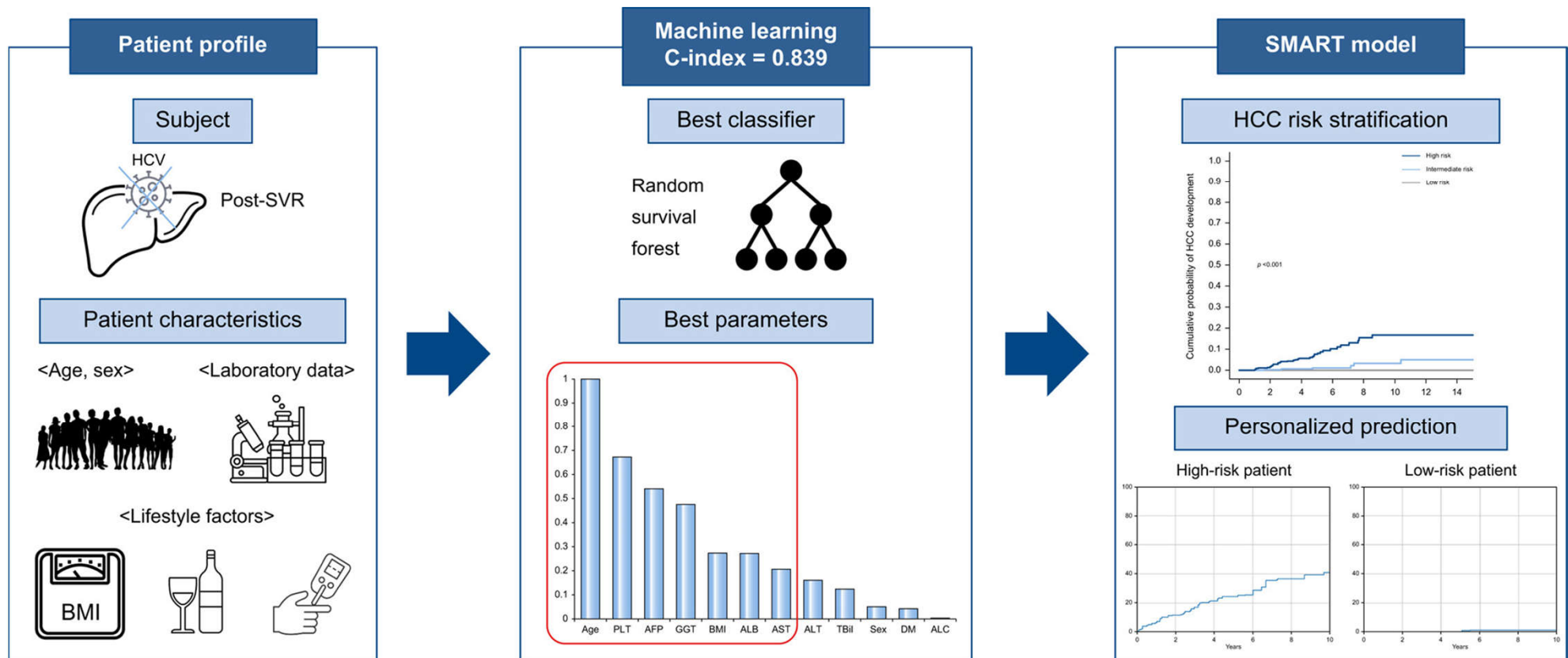
During the mean observation period of 5.4 years, 122 patients developed HCC (83 in the derivation cohort and 39 in the external validation cohort). An RSF model, based on seven parameters at the achievement of an SVR, showed the best discriminative ability, with a c-index of 0.839 in the external validation cohort and a high discriminative ability when patients were categorized into three risk groups ( $p < 0.001$ ). Furthermore, using an app that has been made available online, this RSF model (termed the SMART model) enabled the generation of an individualized predictive curve for HCC occurrence for each patient.

## Conclusions

We developed and externally validated an RSF model with good predictive performance for the risk of HCC after an SVR. This model can be used for risk stratification and, subject to validation and cost-effectiveness analysis, could be applied to personalized surveillance approaches in each country.

## Impact and implications



A novel prediction model for hepatocellular carcinoma (HCC) occurrence in patients after hepatitis C virus eradication was developed using machine learning algorithms. This model, using seven commonly measured parameters, has been shown to have a good predictive ability for HCC development and could be used as part of a personalized surveillance approach. Further studies will be required before this model can be considered in surveillance policies tailored to the medical situation in each country.



ORIGINAL RESEARCH ARTICLE | ARTICLES IN PRESS

# Red meat intake and risk of type 2 diabetes in a prospective cohort study of United States females and males

Xiao Gu • Jean-Philippe Drouin-Chartier • Frank M. Sacks • Frank B. Hu • Bernard Rosner •

Walter C. Willett  

Published: October 19, 2023 • DOI: <https://doi.org/10.1016/j.ajcnut.2023.08.021>

Abstract

Keywords

Linked Article

References

Article info

Related Articles

## Abstract

### Background

Studies with methodological advancements are warranted to confirm the relation of red meat consumption to the incidence of type 2 diabetes (T2D).

### Objective

We aimed to assess the relationships of intakes of total, processed, and unprocessed red meat to risk of T2D and to estimate the effects of substituting different protein sources for red meats on T2D risk.

Red meat intake and risk of type 2 diabetes in a prospective c...

Abstract

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estimate the effects of substituting different protein sources for red meats on T2D risk.

Methods

Our study included 216,695 participants (81% females) from the Nurses' Health Study (NHS), NHS II, and Health Professionals Follow-up Study (HPFS). Red meat intakes were assessed with semiquantitative food frequency questionnaires (FFQs) every 2 to 4 y since the study baselines. We used multivariable-adjusted proportional hazards models to estimate the associations between red meats and T2D.

Results

Over 5,483,981 person-years of follow-up, we documented 22,761 T2D cases. Intakes of total, processed, and unprocessed red meat were positively and approximately linearly associated with higher risks of T2D. Comparing the highest to the lowest quintiles, hazard ratios (HR) were 1.62 (95% confidence interval [CI]: 1.53, 1.71) for total red meat, 1.51 (95% CI: 1.44, 1.58) for processed red meat, and 1.40 (95% CI: 1.33, 1.47) for unprocessed red meat. The percentage lower risk of T2D associated with substituting 1 serving/d of nuts and legumes for total red meat was 30% (HR = 0.70, 95% CI: 0.66, 0.74), for processed red meat was 41% (HR = 0.59, 95% CI: 0.55, 0.64), and for unprocessed red meat was 29% (HR = 0.71, 95% CI: 0.67, 0.75); Substituting 1 serving/d of dairy for total, processed, or unprocessed red meat was also associated with significantly lower risk of T2D. The observed associations became stronger after we calibrated dietary intakes to intakes assessed by weighed diet records.

Conclusions

Our study supports current dietary recommendations for limiting consumption of red meat intake and emphasizes the importance of different alternative sources of protein for T2D prevention.

# Nên: Hạn chế





Thank  
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