

Aspirine en prévention primaire et patient diabétique

CREMA , 5 AVRIL 2023

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Vignette clinique

- ▶ Patiente de 55 ans, originaire de Roumanie
- ▶ Social : sans domicile fixe, aller-retours entre Genève et Roumanie
- ▶ Comorbidités: Obésité, dyslipidémie, HTA, **Diabète T2 sans atteinte d'organe** (HbA1c: 8%)
- ▶ Traitements: IEC, anticalcique, statine, jardiance, Januvia-metformine, ASA cardio
- ▶ Compliance douteuse, faible littératie en santé

Quel médicament est nécessaire ? Que faire de cette Aspirine?

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Aspirin in diabetic patients at primary prevention: insights of the VITAL cohort

D. Caldeira^{1,2,3} · M. Alves^{3,4,5} · J. J. Ferreira^{3,4} · F. J. Pinto^{1,2}

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CONCLUSION

- ▶ Le diabète est un facteur de risque important d'événements cardiovasculaire (CV)
- ▶ Il n'y a pas de bénéfice CV à proposer de l'aspirine en prévention primaire chez une population diabétique à haut risque CV

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A vous de jouer!

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Aspirine, prévention primaire et diabète?

- ▶ Une étude sur le sujet?
- ▶ Quelle(s) méthode(s)?
 - ▶ Pourquoi?
- ▶ Quelle population?
- ▶ Comment y arriver?

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Vos propositions:

Méthode?	Avantages?	Inconvénients?
...

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Quelle méthode pour arriver à ces conclusions?

Méthode	Avantages?	Inconvénients?
Etude randomisée contrôlée (RCT)? <ul style="list-style-type: none"> - Critères d'inclusion? - D'exclusion? - Intervention? - Outcome (s)? <ul style="list-style-type: none"> - Unique? - Composite? - Secondaire? 	<ul style="list-style-type: none"> - Hasard: distribution comparable des facteurs de confusion connus/inconnus - Blinding? - Intention to treat 	<ul style="list-style-type: none"> - \$\$\$ (biais de financement?) - N important pour puissance de l'étude - Questionnements éthiques - Intention to treat

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The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Effects of Aspirin for Primary Prevention in Persons with Diabetes Mellitus

The ASCEND Study Collaborative Group*

ETUDE PROSPECTIVE, RANDOMISEE, CONTRÔLEE, DOUBLE-AVEUGLE

POPULATION: N= 15'480, DM 94% T2, 63 Â, 96% white, BMI:30, >50% tabagisme actif ou ancien, DM depuis 7 ans, >80% score CV bas ou modéré

INTERVENTION : Aspirine 100mg/j vs **COMPARATEUR:** Placebo

OUTCOMES

- 1^e Efficacité: événement cardio vasc
- 1^e Safety: saignements majeurs
- 2nd: Incidence des cancers gastro-intestinaux (CaGI)

CCL: AAS = prévention CV primaire mais saignements majeurs et pas de différence incidence CaGI

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Quelle méthode pour arriver à ces conclusions?

Méthode	Avantages?	Inconvénients?
Revue systématique? Méta-analyse? - Stratégie de recherche? - Critères de sélection des études?	- Forte puissance - Niveau de preuve > 1 seule étude observationnelle	- Nombre important d'études disponibles - Niveau de preuve inférieur à un RCT - Etudes non publiées (biais de publication) - Biais de sélection

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JAMA | US Preventive Services Task Force | EVIDENCE REPORT

Aspirin Use to Prevent Cardiovascular Disease and Colorectal Cancer Updated Evidence Report and Systematic Review for the US Preventive Services Task Force

Janelle M. Guirguis-Blake, MD; Corinne V. Evans, MPP; Leslie A. Perdue, MPH;
Sarah I. Bean, MPH; Caitlyn A. Senger, MPH

REVUE SYSTEMATIQUE DE LITTÉRATURE ET META-ANALYSE

► Objectifs:

- Review des risques/ bénéfiques de l'aspirine en prévention primaire
- Aspirine en prévention primaire du cancer colo-rectal (CCR)

► Etudes sélectionnées

- RCT en anglais, AAS low-dose versus Placebo ou pas d'intervention
- 11 RCT (N= 134 470) et 1 étude pilote (N=400)

► Conclusion:

- AAS associée à une diminution significative des MACE
- AAS pas associée à une diminution de la mortalité CV toutes causes
- Peu d'évidence sur bénéfice pour le CCR
- AAS associée à une augmentation significative des saignements majeurs

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Recommandations USPTF 2022

Summary of Recommendations

Adults aged 40 to 59 years with a 10% or greater 10-year cardiovascular disease (CVD) risk	The decision to initiate low-dose aspirin use for the primary prevention of CVD in adults aged 40 to 59 years who have a 10% or greater 10-year CVD risk should be an individual one. Evidence indicates that the net benefit of aspirin use in this group is small. Persons who are not at increased risk for bleeding and are willing to take low-dose aspirin daily are more likely to benefit.	C
Adults 60 years or older	The USPSTF recommends against initiating low-dose aspirin use for the primary prevention of CVD in adults 60 years or older.	D

USPSTF indicates US Preventive Services Task Force.

Table. Summary of USPSTF Rationale

Rationale	Assessment
Benefits of aspirin use	Adequate evidence that low-dose aspirin has a small benefit to reduce risk for cardiovascular events (nonfatal myocardial infarction and stroke) in adults 40 years or older who have no history of CVD but are at increased CVD risk. Evidence shows that the absolute magnitude of benefit increases with increasing 10-year CVD risk and that the magnitude of the lifetime benefits is greater when aspirin is initiated at a younger age.
Harms of aspirin use	Adequate evidence that aspirin use in adults increases the risk for gastrointestinal bleeding, intracranial bleeding, and hemorrhagic stroke. The USPSTF determined that the magnitude of the harms is small overall but increases in older age groups, particularly in adults older than 60 years.
USPSTF assessment	The USPSTF concludes with moderate certainty that aspirin use for the primary prevention of CVD events in adults aged 40 to 59 years who have a 10% or greater 10-year CVD risk has a small net benefit. The USPSTF concludes with moderate certainty that initiating aspirin use for the primary prevention of CVD events in adults 60 years or older has no net benefit.

Abbreviations: CVD, cardiovascular disease; USPSTF, US Preventive Services Task Force.

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Quelle méthode pour arriver à ces conclusions?

Méthode	Avantages?	Inconvénients?
Etude observationnelle? Prospective? Rétrospective? <ul style="list-style-type: none"> • Cas-Témoin? • Transversale? • Cohorte? 	<ul style="list-style-type: none"> - Registres existants - Si rétroS: simple, rapide, moins \$ 	<ul style="list-style-type: none"> - \$\$\$ - Temps important (si maladie rare) - Risque de perte de vue des individus - si rétroS: biais d'attribution (exposition)

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Revenons-en à notre étude

Aspirin in diabetic patients at primary prevention: insights of the VITAL cohort

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► Analyse rétrospective de la cohorte VITAL

► The VITamin D and Omega-3 Trial (VITAL)

- Etude de l'impact de la supplémentation en VitD et Oméga3 pour la prévention primaire CV et oncologique
- RCT, double aveugle, suivi sur 5 ans par des questionnaires Population multiethnique (>25% afroA), N> 20'000, H> 50â F>55â
- **EXCL:** d' ATCD de cancer/IM/AIT/Angor/revascularisation/IRC/cirrhose hépatique
- **Avantage :** grand échantillon, patient-e-s poly morbides, multiethnique

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Fig. 1 Flowchart showing the patients according to baseline diabetes status and aspirin use in diabetics

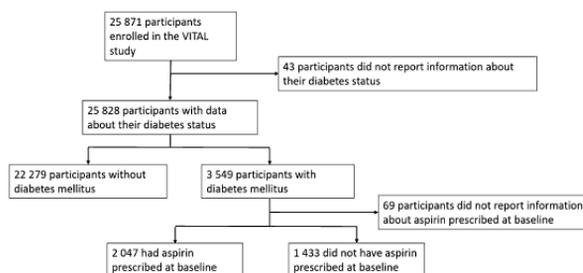


Table 1 Baseline characteristics

	Global VITAL cohort (n = 25,828)		P value	Diabetic participants (n = 3549)		P value
	Diabetes (n = 3549)	No Diabetes (n = 22,279)		Aspirin (n = 2047)	No aspirin (n = 1433)	
Age (years) (mean, SD)	66.6 (7.0)	66.6 (7.1)	0.720	67.0 (6.8)	66.0 (7.2)	<0.001
Age > 70 years (% , n)	30.4 (1079)	30.3 (6760)	0.942	31.9 (654)	28.1 (402)	0.014
Sex (men) (% , n)	48.4 (1718)	49.6 (11,043)	0.200	51.3 (1051)	44.6 (639)	<0.001
BMI (kg/m ²) (mean, SD)	31.9 (6.9)	27.5 (5.3)	<0.001	31.9 (6.8)	31.9 (7.0)	0.908
Obese (% , n)	52.6 (1867)	24.3 (5405)	<0.001	52.5 (1074)	53.2 (762)	0.680
Hypertension (% , n)	79.7 (2799)	45.1 (9976)	<0.001	82.6 (1676)	75.3 (1065)	<0.001
Baseline statins (% , n)	60.4 (2092)	30.9 (6788)	<0.001	67.1 (1361)	50.5 (714)	<0.001
Current smoking (% , n)	9.2 (321)	6.9 (1511)	<0.001	7.6 (154)	11.6 (165)	<0.001
Parental history of MI (% , n)	19.2 (585)	15.5 (3064)	<0.001	20.2 (360)	17.7 (215)	0.09
Aspirin use (% , n)	58.8 (2047)	43.2 (9504)	<0.001	100 (2047)	0 (0)	–

BMI Body mass index, MI Myocardial infarction, SD Standard deviation

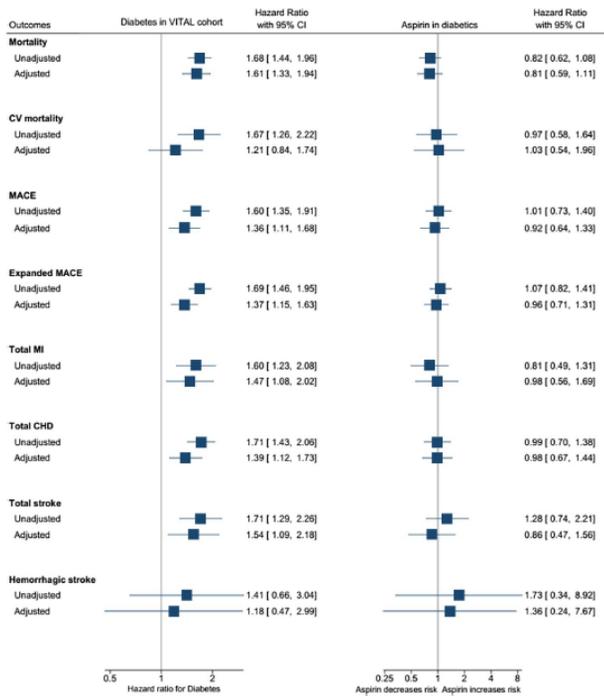
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Outcomes

- ▶ 1^{ère} Outcome= MACE (évènement CV majeur) composite

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Fig. 2 Plot showing the estimates (unadjusted and adjusted) in hazard ratios for diabetes (left side) and for aspirin in diabetic patients (right side). Adjusted estimates accounted for age, sex, body mass index, smoking status, parental history of myocardial infarction, hypertension, statins use. *CHD*: Coronary heart disease; *CI* Confidence interval, *CV* Cardiovascular, *MACE* Major adverse cardiovascular events, *MI* Myocardial infarction



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CONCLUSION

- ▶ Le diabète est un facteur de risque important d'événements cardiovasculaire (CV) dans un population contemporaine
- ▶ Il n'y a pas de bénéfice CV à proposer de l'aspirine en prévention primaire chez une population diabétique à haut risque CV

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Limitations et commentaires de cette étude

- ▶ Etude basée sur la Cohorte de l'étude VITAL
 - ▶ Pas d'info. sur: HbA1c, risque CV, statut social
 - ▶ Patients compliants et impliqués dans leurs prises en charges
 - ▶ Etude rétrospective: Biais d'attribution
 - ▶ Pas de données sur les complications hémorragiques (uniquement AVC)
- ▶ Pas représentative de notre patiente
- ▶ Âge est > aux recommandations USPTF 2022
- ▶ Pas de plu values par rapport à l'étude ASCEND 2018

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Que répondez-vous à notre patiente?

- Discussion partagée

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MERCI DE VOTRE ATTENTION

Questions?

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Référence

- ▶ Aspirin in diabetic patients at primary prevention: insights of the VITAL cohort, D. Caldeira, M. Alves, J. J. Ferreira, F. J. Pinto, October 2022
- ▶ Manson JE, et al. The VITamin D and OmegA-3 Trial (VITAL): rationale and design of a large randomized controlled trial of vitamin D and marine omega-3 fatty acid supplements for the primary prevention of cancer and cardiovascular disease. Contemp Clin Trials. 2012 Jan
- ▶ US Preventive Services Task Force; Davidson KW, et al.. Aspirin Use to Prevent Cardiovascular Disease: US Preventive Services Task Force Recommendation Statement. JAMA. 2022 Apr
- ▶ Guirguis-Blake Jmet al.. Aspirin Use to Prevent Cardiovascular Disease and Colorectal Cancer: Updated Evidence Report and Systematic Review for the US Preventive Services Task Force. JAMA. 2022 Apr 26.
- ▶ Epimed, L'épidémiologie expliquée aux cliniciens, O.Kherad, M. Blondon, C. Toso

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Take home message

Figure 1. Clinician Summary: Aspirin Use to Prevent Cardiovascular Disease

What does the USPSTF recommend?	<p>For adults aged 40 to 59 years with an estimated 10% or greater 10-year cardiovascular disease (CVD) risk: The decision to initiate low-dose aspirin use for the primary prevention of CVD in this group should be an individual one. Grade: C</p> <p>For adults 60 years or older: Do not initiate aspirin for the primary prevention of CVD. Grade: D</p>
To whom does this recommendation apply?	This recommendation applies to adults 40 years or older without signs or symptoms of CVD or known CVD and who are not at increased risk for bleeding (eg, no history of gastrointestinal ulcers, recent bleeding, or other medical conditions, or taking medications that increase bleeding risk).
What's new?	<ul style="list-style-type: none"> • The USPSTF has changed the age ranges and grades of its recommendation on aspirin use. • The USPSTF currently recommends considering initiating aspirin in persons with an estimated 10% or greater CVD risk at a younger age: 40 years instead of 50 years. • Aspirin should be initiated selectively based on individual decision-making rather than routinely for all persons in the recommended age and CVD risk group. • There is a new recommendation not to initiate aspirin in adults 60 years or older for primary prevention. • The evidence is unclear whether aspirin use reduces the risk of colorectal cancer incidence or mortality.
How to implement this recommendation?	<ul style="list-style-type: none"> • Consider the patient's age. • For adults aged 40 to 59 years: Estimate CVD risk using a CVD risk estimator. • In patients whose estimated CVD risk is 10% or greater, use shared decision-making, taking into account potential benefits and harms of aspirin use, as well as patients' values and preferences, to inform the decision about initiating aspirin. • For patients initiating aspirin use, it would be reasonable to use a dose of 81 mg/d. • For adults 60 years or older: Do not initiate aspirin for primary prevention of CVD.

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Take home message

What additional information should clinicians know about this recommendation?	<ul style="list-style-type: none"> • Age is one of the strongest risk factors for CVD. • Males have a higher prevalence of CVD than females. Among both sexes, Black persons have the highest prevalence of CVD. • Aspirin reduces the risk of cardiovascular events, but it increases the risk for gastrointestinal bleeding, intracranial bleeding, and hemorrhagic stroke. • Both CVD risk and risk for gastrointestinal bleeding, intracranial hemorrhage, and hemorrhagic stroke (with or without aspirin use) increase with age. • For patients who are eligible and choose to start taking aspirin, the benefits become smaller with advancing age, and data suggest that clinicians and patients should consider stopping aspirin use around age 75 years.
Why is this recommendation and topic important?	CVD is the leading cause of mortality in the US, accounting for more than 1 in 4 deaths. Each year, an estimated 605 000 Americans have a first heart attack and about 610 000 experience a first stroke.
What are additional tools and resources?	<ul style="list-style-type: none"> • The Million Hearts initiative provides information on improving cardiovascular health and preventing heart attack and stroke at https://millionhearts.hhs.gov/ • The Centers for Disease Control and Prevention have resources related to risk of heart disease and the prevention of heart disease for patients and health professionals at https://www.cdc.gov/heartdisease/index.htm • The National Heart, Lung, and Blood Institute has patient resources related to coronary heart disease at https://www.nhlbi.nih.gov/health-topics/coronary-heart-disease
Where to read the full recommendation statement?	Visit the USPSTF website (https://www.uspreventiveservicestaskforce.org/uspstf/) or the JAMA website (https://jamanetwork.com/collections/44068/united-states-preventive-services-task-force) to read the full recommendation statement. This includes more details on the rationale of the recommendation, including benefits and harms; supporting evidence; and recommendations of others.

The USPSTF recognizes that clinical decisions involve more considerations than evidence alone. Clinicians should understand the evidence but individualize decision-making to the specific patient or situation.

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