Temporal Trends in Low-Dose Aspirin Use (from the CoLaus|PsyCoLaus Study)

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Although established in secondary prevention, the use of low-dose aspirin for primary cardiovascular prevention remains uncertain. We assessed the temporal trend of low-dose aspirin use in people at primary and secondary prevention over 14 years. We used data from the population-based CoLaus|PsyCoLaus study. A baseline survey was conducted from 2003 to 2006, involving 6,733 participants. The first and second follow-up investigations were performed from 2009 to 2012 and 2014 to 2017, respectively. Low-dose aspirin use was defined as ≤300 mg/daily oral administration or administration of an anticoagulant for similar indications. For primary prevention analysis, 6,555, 4,695, and 3,893 participants were included in the analysis at baseline, first and second follow-ups, respectively. Overall, low-dose aspirin use doubled between baseline (4.1%) and second follow-up (8.1%). Appropriate use of low-dose aspirin rose from 32% at baseline to 64% at the second follow-up for primary prevention. In secondary prevention, 71.8%, 75.9%, and 71.7% of participants were taking low-dose aspirin at baseline, first, and second follow-up, respectively. On the basis of a population-based cohort, the appropriateness of low-dose aspirin use increased over a 10-year follow-up in primary prevention, but its inappropriate use still concerned 44% of subjects. In secondary prevention, a quarter of individuals were not taking low-dose aspirin which remained stable over the analyzed period. **(Am J Cardiol 2023;190:61−66)**

The use of low-dose aspirin (≤300 mg orally daily) for primary cardiovascular prevention remains uncertain, as recent clinical trials have failed to show significant vascular benefit, except (marginally) in individuals with diabetes mellitus.[1] As the bleeding risk in people taking aspirin generally outweighs any cardiovascular benefit, current guidelines do not recommend using low-dose aspirin for the primary prevention of atherosclerotic cardiovascular disease (ASCVD).[2] In the baseline examination (2003 to 2006) of the population-based CoLaus|PsyCoLaus cohort, patients at intermediate risk of developing an ASCVD and diabetic subjects were more likely to take low-dose aspirin.[1] Conversely, 2% of the sample, considered at low cardiovascular risk, overused low-dose aspirin. Using data from the CoLaus|PsyCoLaus study, our aims were to (1) estimate the prevalence and temporal trend of low-dose aspirin use and factors associated with such use over a 10-year follow-up period; (2) investigate low-dose aspirin use in primary prevention according to 10-year cardiovascular risk derived from ESC-SCORE (European Society of Cardiology−Systematic COronary Risk Evaluation) equation for Switzerland; and (3) compare prospective use of low-dose aspirin in people with and without ASCVD.

Methods

The CoLaus|PsyCoLaus study is a prospective cohort established in 2003 to 06, including 6,734 participants, aged 35 to 75 years (54% women) and recruited from a random sample of the population of the city of Lausanne, Switzerland (participation rate 41%[3]). Prospective follow-ups of the baseline investigation were conducted from 2009 to 2012 and from 2014 to 2017. At each survey, participants answered questionnaires, underwent a clinical examination, and had blood samples drawn for analyses. Drugs were thoroughly collected. ASCVD were collected and adjudicated by trained specialists when participants reported an incident ASCVD and/or ASCVD-related procedure. The complete procedure has been already described.[4] The local Ethics Commission approved the CoLaus|PsyCoLaus study (www.cer-vd.ch; project number PB_2018-00038, reference 239/09). All participants gave their signed informed consent at each survey.

Low-dose aspirin use for cardiovascular prevention was defined by the association of 2 parameters: (1) daily use of ≤300 mg orally, (2) indication for which low-dose aspirin is recommended according to European guidelines in cardiology.[4] Low-dose aspirin users also included participants taking clopidogrel and those only taking an anticoagulant

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The CoLaus|PsyCoLaus study was and is supported by research grants from GlaxoSmithKline (Brentford, United Kingdom), the Faculty of Biology and Medicine of Lausanne (Lausanne, Switzerland), and the Swiss National Science Foundation (Bern, Switzerland) grants 33CSCO-122661, 33CS30-139468, 33CS30-148401, and 33CS30_177535/1.

See page 66 for disclosure information.

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0002-9149/

https://doi.org/10.1016/j.amjcard.2022.11.037

treatment (no concomitant antiplatelet treatment) but with an indication for an antiplatelet treatment.

Appropriateness of low-dose aspirin use in primary prevention was defined as follows: (1) correct use, when low-dose aspirin was taken in presence of a high or very-high 10-year risk of ASCVD or absence of low-dose aspirin use when the risk was low or intermediate; (2) overuse, when low-dose aspirin was taken despite a low or intermediate 10-year cardiovascular risk; and (3) underuse, when low-dose aspirin was not taken despite a high or very-high 10-year cardiovascular risk. In secondary prevention, the correct use of low-dose aspirin was defined based on participants taking low-dose aspirin in presence of an ASCVD.

We included all the participants recruited at baseline (2003 to 2006), first follow-up (2009 to 2012), and second follow-up (2014 to 2017) with available data on drug use, and clinical and biologic data to compute 10-year cardiovascular risk score.

Questionnaires querying socioeconomic status, lifestyle, and personal and family history were applied and were identical between surveys. Educational level was categorized into university, high school, and apprenticeship or mandatory. Smoking status was self-reported and categorized as never, former, and current. Positive family history of cardiovascular disease was defined based on the presence of ASCVD in a father before 55 years or a mother before 65 years.

Body weight and height were measured with participants barefoot and in light indoor clothes. Blood pressure was measured using an Omron HEM-907 (Omron Healthcare Co., Ltd., Kyoto, Japan) automated oscillometric sphygmomanometer after at least a 10-minute rest in a seated position, and the average of the last 2 measurements was used. Total cholesterol was assessed by cholesterol oxidase: P-aminophenazone, with maximum interbatch and intrabatch coefficients of variation (CVs) of 1.6% and 1.7%, respectively. High-density lipoprotein−cholesterol was assessed by cholesterol oxidase: P-aminophenazone + polyethylene glycol + cyclodextrin, with maximum inter and intra-batch CVs of 3.6% and 0.9%, respectively. Glucose was assessed by glucose dehydrogenase, with maximum inter and intra-batch CVs of 2.1% and 1.0%, respectively.

The risk of developing an ASCVD was estimated using the ESC-SCORE developed in 2003[5] and already validated in the CoLaus|PsyCoLaus study.[4,5] SCORE was recalibrated as previously described.[6] SCORE was computed for each participant in each survey. SCORE was preferred over the recently developed SCORE2[7] to minimize discrepancies between categories of risk (defined based on SCORE and valid from 2003 to 2021) and secular trends in aspirin use recommendations.

Results were expressed as number of participants (percentage) for categorical variables and as average (±SD) for continuous variables. Bivariate comparisons between participants receiving or not low-dose aspirin were performed using Pearson's chi-square for categorical variables and Student's *t* test for continuous variables. The associations between aspirin use and 10-year cardiovascular disease risk were analyzed by multivariable analysis using logistic regression as previously done.[1] Results are reported as odds ratio (OR), with 95% of confidence intervals (CIs). Statistical significance was considered for $p < 0.05$. Statistical analysis was conducted using Stata V16.1 (Stata Corp., College Station, Texas).

Results

For the analysis on primary prevention, 6,555 (53.2% women) participants were included at baseline. Participants' characteristics at baseline are presented in Table 1. Compared with nonaspirin users, people taking low-dose aspirin were older (61.7 [SD ± 10.6] vs 51.5 [SD ± 9.0] years, $p < 0.001$) and presented a higher prevalence of cardiovascular risks. In primary prevention (Figure 1), the percentage of participants taking low-dose aspirin doubled between baseline (4.1%) and the second follow-up (8.1%), with the same magnitude in men and women.

Factors associated with the prescription of aspirin in primary prevention were higher age, being a smoker and obese, and having hypertension and diabetes (Supplementary Table 1). These factors were consistent across follow-up surveys. Educational level, family history of ASCVD, and gender were not associated with low-dose aspirin use either at baseline or at follow-ups. Hypercholesterolemia was associated with taking low-dose aspirin only in the first follow-up ($p < 0.001$). The percentage of participants underusing aspirin (Figure 2) was 68%, 51%, and 36% at baseline, first, and second follow-up, respectively. The number of subjects overusing it (that is, taking aspirin while being at (very-)low and intermediate risk) rose from 4% at baseline to 7% and 8% at first and second follow-ups, respectively. The percentage of participants at very high risk of ASCVD and taking aspirin (Figure 3) was 15.2% at baseline, 24% at the first follow-up, and 24.7% at the second follow-up.

For the secondary prevention analysis, 149 participants (28.9% women) were included at baseline of whom 107 were taking low-dose aspirin (Supplementary Table 2). Factors associated at baseline and follow-ups 1 and 2 with the prescription of aspirin in people in secondary prevention are described in Supplementary Table 3. None of them was steadily associated with low-dose aspirin use over time. Only being a former smoker was associated with taking low-dose aspirin at baseline ($p = 0.01$). Being hypertensive was associated with low-dose aspirin use in secondary prevention only in the second survey ($p = 0.045$) but not at baseline or first follow-up.

Combining all participants (at primary and secondary prevention), the overall use of low-dose aspirin increased from 6.4% at baseline to 6.7% at the first follow-up and 8.2% at the second follow-up (Figure 4). The percentage of men taking low-dose aspirin remained stable between baseline (8.4%) and second follow-up (8.4%). In terms of consistency of low-dose aspirin use over time, 62 participants were taking low-dose aspirin at baseline but not at the first follow-up, among whom 18 were on low-dose aspirin at the second follow-up again. A total of 459 individuals did not use low-dose aspirin at baseline but were taking it during follow-ups. The percentage of women taking low-dose aspirin doubled between baseline (4.7%) and second follow-up (8.0%) (Figure 4). Trends of low-dose aspirin use by age group are presented in Supplementary Table 4.

Table 1
Baseline characteristics of participants according to low-dose aspirin use in primary prevention

Characteristics	Total	Non-aspirin users	Low-dose aspirin users	p Value
n	6,555	6,231	324	
Women (%)	3,484 (53.2)	3,347 (53.7)	137 (42.3)	<0.001
Age (years)	52.4±10.7	51.9±10.5	62.5±8.8	<0.001
Age groups (%)				<0.001
35−44 y	1,968 (30.0)	1,954 (31.4)	14 (4.3)	
45−54 y	1,938 (29.6)	1,893 (30.4)	45 (13.9)	
55−64 y	1,716 (26.2)	1,582 (25.4)	134 (41.4)	
≥65 y	933 (14.2)	802 (12.9)	131 (40.4)	
Education (%)				<0.001
High	1,294 (19.8)	1,258 (20.2)	36 (11.1)	
Middle	1,587 (24.2)	1,511 (24.3)	76 (23.5)	
Low	3,666 (56.0)	3,454 (55.5)	212 (65.4)	
Body mass index (kg/m^2)	25.7±4.5	25.6±4.4	28.0±5.2	<0.001
BMI categories (%)				<0.001
Normal (18−25 kg/m^2)	3,189 (48.7)	3,092 (49.6)	97 (29.9)	
Overweight (25−30 kg/m^2)	2,384 (36.4)	2,251 (36.1)	133 (41.1)	
Obese (≥30 kg/m^2)	982 (15.0)	888 (14.3)	94 (29.0)	
Smoking status (%)				<0.001
Never	2,694 (41.1)	2,596 (41.7)	98 (30.3)	
Former	2,089 (31.9)	1,952 (31.3)	137 (42.3)	
Current	1,772 (27.0)	1,683 (27.0)	89 (27.5)	
Diabetes mellitus (%)	407 (6.2)	327 (5.3)	80 (24.7)	<0.001
Hypertension (%)	2,355 (35.9)	2,109 (33.9)	246 (75.9)	<0.001
Lipid values (mmol/L)				
Total cholesterol	5.58±1.04	5.6±1.03	5.37±1.05	<0.001
LDL cholesterol	3.34±0.92	3.35±0.91	3.12±0.91	<0.001
HDL cholesterol	1.63±0.44	1.64±0.44	1.56±0.44	0.001
Statin use (%)	575 (8.8)	444 (7.1)	131 (40.4)	<0.001
10-y CVD risk (%)				<0.001
<1.5%	4,270 (65.1)	4,200 (67.4)	70 (21.6)	
1.5%−2.4%	532 (8.1)	496 (8.0)	36 (11.1)	
2.5%−4.9%	545 (8.3)	496 (8.0)	49 (15.1)	
5.0%−9.9%	601 (9.2)	545 (8.8)	56 (17.3)	
≥10%	607 (9.3)	494 (7.9)	113 (34.9)	
Family history of CHD (%)	2,194 (33.5)	2,064 (33.1)	130 (40.1)	0.009

Hypertension was defined as a systolic blood pressure ≥140 mm Hg and/or diastolic blood pressure ≥90 mm Hg. Results are expressed as the number of participants (column %) for categorical variables and as average±SD for continuous variables. Between-group comparisons were performed using chi-square for categorical variables and Student *t* test for continuous variables.

BM = body mass index; CHD = coronary heart disease; CVD = cardiovascular diseases; HDL = high-density lipoprotein; LDL = low-density lipoprotein.

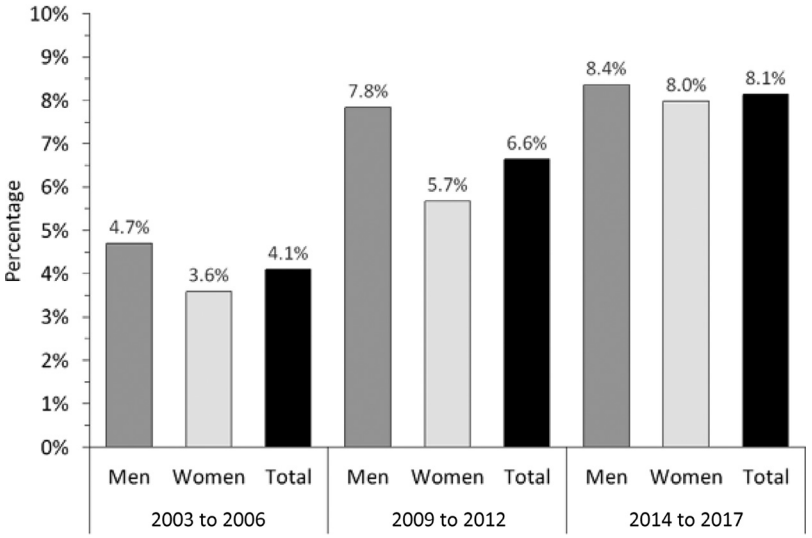

Figure 1. Evolution of low-dose aspirin use in primary prevention at baseline (2003 to 2006), first (2009 to 2012) and second (2014 to 2017) follow-ups.

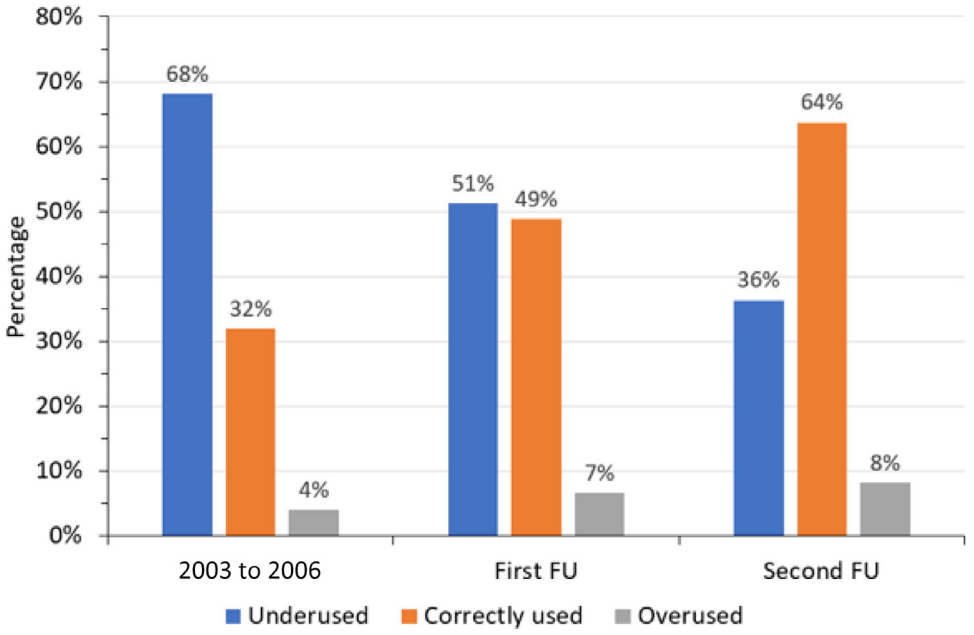

Figure 2. Trend in low-dose aspirin use, according to the appropriateness of use in primary prevention at baseline (2003 to 2006), first (2009 to 2012) and second (2014 to 2017) FUs. Correct use of low-dose aspirin was defined as low-dose aspirin us taken in presence of a high or very-high 10-year risk of ASCVD or absence of low-dose aspirin use when the risk was low or intermediate; overuse corresponds to low-dose aspirin use despite a low or intermediate 10-year cardiovascular risk; and underuse, when low-dose aspirin was not taken despite a high or very-high 10-year cardiovascular risk. FU = follow-up.

From baseline to first follow-up and from first to second follow-ups, 1,426 and 571 individuals were lost to follow-up, respectively. Characteristics of participants lost to follow-up (deaths excluded) are presented in Supplementary Table 5. Participants who had a low education level were obese, and had hypertension were more often lost to follow-up from baseline to follow-up 1. Participants lost from follow-up 1 to follow-up 2 were more often men, 45 to 55 years of age, had a low education level, were overweight or obese, were current smokers, and had hypertension. Overall, 65.6% of participants lost from baseline to follow-up 1% and 59.8% from follow-up 1 to follow-up 2 had a low education level. A total of 19.8% of participants lost to follow-up from baseline to follow-up, and 1% and 19.4% from follow-up 1 to follow-up 2 respectively, were overweight. Overall, 42.7% of participants lost from baseline to follow-up 1%, and 44.5% from follow-up 1 to follow-up 2 had hypertension.

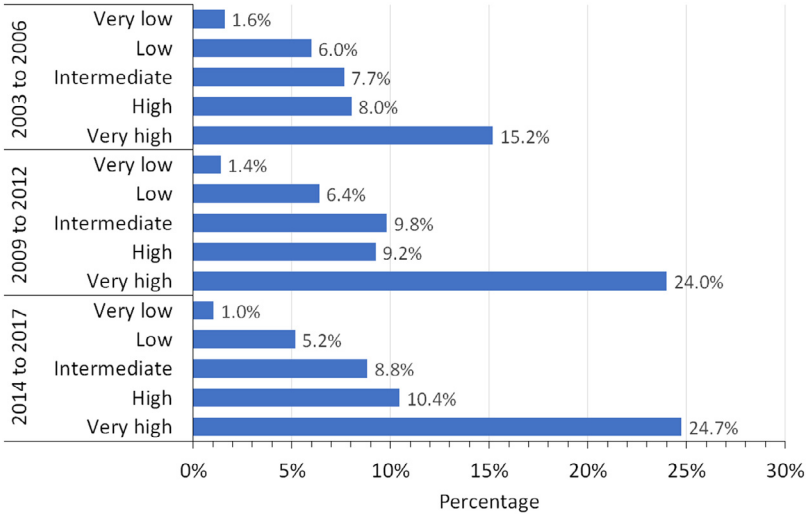

Figure 3. Distribution of aspirin use in primary prevention according to 10-year cardiovascular risk as defined by the ESC-SCORE of 2019, at baseline (2003 to 2006), first (2009 to 2012), and second (2014 to 2017) follow-ups.

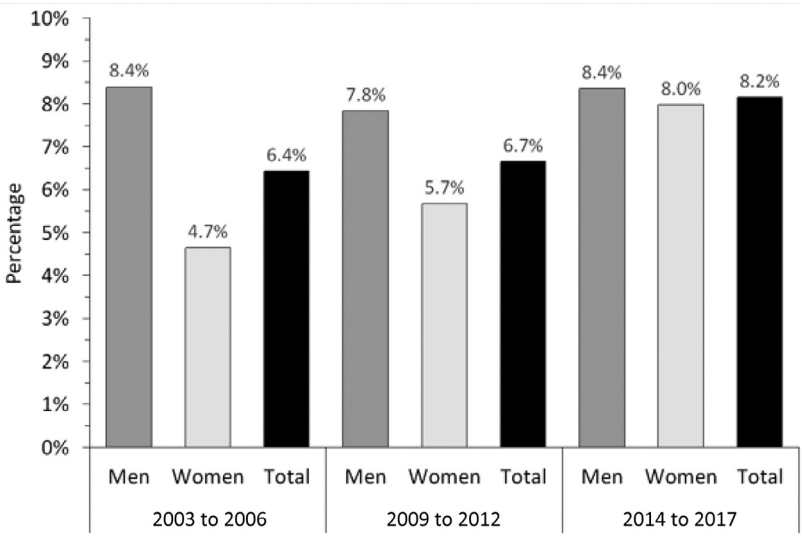

Figure 4. Evolution of low-dose aspirin use in primary and secondary prevention at baseline (2003 to 2006), first (2009 to 2012) and second (2014 to 2017) follow-ups.

Discussion

Using a population-based cohort with a 10-year follow-up, our findings showed an overall increase in low-dose aspirin use with a twofold higher rate of low-dose aspirin use in primary prevention across the time. In addition, women had more frequent low-dose aspirin intake at second follow-up compared with baseline for primary and secondary prevention combined, accounting for the overall increase in low-dose aspirin use. Our results also showed an overall better use of low-dose aspirin over time, especially in primary prevention with 64% of participants taking it adequately. The use of low-dose aspirin in secondary prevention remained stable, with about 1 in 4 participants with an ASCVD not using it.

The number of participants taking low-dose aspirin in primary prevention doubled between 2003 and 2006 and from 2014 to 2017 from 4% to 8%. The percentage of low-dose aspirin use in primary prevention may have followed ESC guidelines, which recommended 2004 low-dose aspirin use in high-risk patients (despite lack of evidence at that time).[8] As for the most recent recommendations, the 2021 ESC recommendations on cardiovascular prevention did not recommend low-dose aspirin routinely to patients without established ASCVD, but did not exclude that the benefits outweigh the risks in some patients at high or very-high cardiovascular disease risk.[9] Moreover, the 2019 American College of Cardiology/ American Heart Association guidelines recommended aspirin for primary prevention only in patients aged 40 to 70 at a high ASCVD risk and low bleeding risk.[10]

Women were twice more likely to take low-dose aspirin at the second follow-up compared with baseline (for primary and secondary prevention combined), whereas in men low-dose aspirin use remained stable. As fewer women are included in clinical trials than men, it is known that cardiovascular risk estimation has limitations in women compared with men.[11] Therefore, fewer women were likely to be classified in the high-risk cardiovascular category and thus might have been treated less aggressively and received less aspirin for prevention at baseline.[11] Awareness about gender differences in diagnosis, prevention, and treatment of ASCVD has been raised during the last decade.[11–13] Over time, this can explain the increase in low-dose aspirin use among women who tended to have the same rate of treatment as men in our cohort (8.0% for women and 8.4% for men at the second follow-up).

There was an overall better use of low-dose aspirin combining both primary and secondary prevention (Figure 2). For the primary prevention, our results have shown that the number of participants taking correctly low-dose aspirin doubled between baseline and second follow-up. However, the percentage of participants at high-risk of ASCVD taking aspirin was only 8.0% at baseline and reached 10.4% at the second follow-up. As for the very-high-risk category, only 15% were taking low-dose aspirin at baseline and 24.7% at the second follow-up. This shows improvements in the use of aspirin for primary prevention of ASCVD but this also shed light on the high and very-high risk categories of participants who are undertreated. This shows the ambiguity of the European and American cardiology societies' recommendations saying that there are no proved benefits outweighing the potential risks in prescribing low-dose aspirin for primary prevention except for patients in a high or very-high-risk category with low bleeding risk; use of low-dose aspirin in this context being an individual decision.[9,10]

There are limitations to this study that should be accounted for. First, the CoLaus|PsyCoLaus study may not be representative of other populations. However, the population structure and prevalence of cardiovascular risk factors were in line with previous findings in Switzerland and Europe.[14,15] Second, not all antiplatelets were taken into account. Nevertheless, using clopidogrel and anticoagulant (including direct-acting oral anticoagulants) as proxies of low-dose aspirin use allows capturing most of the participants taking antiplatelets (or anticoagulants functioning as

antiplatelets). For example, ticagrelor was only introduced in late 2011 in Switzerland and was mainly restricted to in-hospital use. Finally, this study was observational and population based. Any variation could have thus arisen because of the preferences of participants and physicians, or healthy volunteer bias encountered in such cohorts.[16]

In our cohort, the use of low-dose aspirin rose over a 10-year follow-up, with an increase in its appropriate use for people at primary prevention. However, overuse of low-dose aspirin (i.e., in people at (very-)low and intermediate risk) also increased to reach 8% of participants. Differences between men and women tended to decrease over time, suggesting that a different approach between men and women in cardiovascular prevention is less frequent. Future interventions should focus on better information for physicians and patients on the indication of low-dose aspirin use.

Disclosures

The authors have no conflicts of interest to declare.

Data availability

The CoLaus|PsyCoLaus cohort data used in this study cannot be fully shared as they contain potentially sensitive patient information. As discussed with the competent authority, the Research Ethic Committee of the Canton of Vaud, transferring or directly sharing this data would be a violation of the Swiss legislation aiming to protect the personal rights of participants. Nonidentifiable, individual-level data are available for interested researchers, who meet the criteria for access to confidential data sharing, from the CoLaus|PsyCoLaus Datacenter (CHUV, Lausanne, Switzerland). Instructions for gaining access to the CoLaus data used in this study are available at https://www.colaus-psycolaus.ch/professionals/how-to-collaborate/.

Supplementary materials

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.amjcard.2022.11.037.

1. Rodondi N, Cornuz J, Marques-Vidal P, Butler J, Hayoz D, Pécoud A, Paccaud F, Waeber G, Vollenweider P. Aspirin use for the primary prevention of coronary heart disease: a population-based study in Switzerland. *Prev Med* 2008;46:137–144.
2. Piepoli MF, Hoes AW, Agewall S, Albus C, Brotons C, Catapano AL, Cooney MT, Corra U, Cosyny B, Deaton C, Graham I, Hall MS, Hobbs FDR, Lochen ML, Löllgen H, Marques-Vidal P, Perk J, Prescott E, Redon J, Richter DJ, Sattar N, Smulders Y, Tiberi M, van der Worp HB, van Dis I, Verschuren WMM, Binno S, ESC Scientific Document Group. 2016 European Guidelines on cardiovascular disease prevention in clinical practiceThe Sixth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice. *Eur Heart J* 2016;37:2315–2381.
3. Firmann M, Mayor V, Vidal PM, Bochud M, Pécoud A, Hayoz D, Paccaud F, Preisig M, Song KS, Yuan X, Danoff TM, Stirnadel HA, Waterworth D, Mooser V, Waeber G, Vollenweider P. The CoLaus study: a population-based study to investigate the epidemiology and genetic determinants of cardiovascular risk factors and metabolic syndrome. *BMC Cardiovasc Disord* 2008;8:6.
4. Beuret H, Hausler N, Nanchen D, Méan M, Marques-Vidal P, Vaucher J. Comparison of Swiss and European risk algorithms for cardiovascular prevention in Switzerland. *Eur J Prev Cardiol* 2021;28:204–210.
5. Conroy RM, Pyörälä K, Fitzgerald AP, Sans S, Menotti A, De Backer G, De Bacquer DD, Ducimetière P, Jousilahti P, Keil U, Njølstad I, Oganov RG, Thomsen T, Tunstall-Pedoe H, Tverdal A, Wedel H, Whincup P, Wilhelmsen L, Graham IM, SCORE project group. Estimation of ten-year risk of fatal cardiovascular disease in Europe: the SCORE project. *Eur Heart J* 2003;24:987–1003.
6. Marques-Vidal P, Rodondi N, Bochud M, Pécoud A, Hayoz D, Paccaud F, Mooser V, Waeber G, Vollenweider P. Predictive accuracy and usefulness of calibration of the ESC SCORE in Switzerland. *Eur J Cardiovasc Prev Rehabil* 2008;15:402–408.
7. SCORE2 working group and ESC Cardiovascular risk collaboration. SCORE2 risk prediction algorithms: new models to estimate 10-year risk of cardiovascular disease in Europe. *Eur Heart J* 2021;42:2439–2454.
8. Patrono C, Bachmann F, Baigent C, Bode C, De Caterina R, Charbonnier B, Fitzgerald D, Hirsh J, Husted S, Kvasnicka J, Montalescot G, García Rodríguez LA, Verheugt F, Vermylen J, Wallentin L, Priori SG, Alonso Garcia MA, Blanc JJ, Budaj A, Cowie M, Dean V, Deckers J, Fernández Burgos E, Lekakis J, Lindahl B, Mazzotta G, Morais J, Oto A, Smiseth OA, Morais J, Deckers J, Ferreira R, Mazzotta G, Steg PG, Teixeira F, Wilcox R, European Society of Cardiology. Expert consensus document on the use of antiplatelet agents. The task force on the use of antiplatelet agents in patients with atherosclerotic cardiovascular disease of the European Society of Cardiology. *Eur Heart J* 2004;25:166–181.
9. Visseren FLJ, Mach F, Smulders YM, Carballo D, Koskinas KC, Bäck M, Benetos A, Biffi A, Boavida JM, Capodanno D, Cosyns B, Crawford C, Davos CH, Desormais I, Di Angelantonio E, Franco OH, Halvorsen S, Hobbs FDR, Hollander M, Jankowska EA, Michal M, Sacco S, Sattar N, Tokgozoglu L, Tonstad S, Tsioufis KP, van Dis I, van Gelder IC, Wanner C, Williams B. ESC National Cardiac Societies. ESC Scientific Document Group. 2021 ESC Guidelines on cardiovascular disease prevention in clinical practice. *Eur J Prev Cardiol* 2021;42:3227–3337.
10. Arnett DK, Blumenthal RS, Albert MA, Buroker AB, Goldberger ZD, Hahn EJ, Dennison Himmelfarb C, Khera A, Lloyd-Jones D, McEvoy JW, Michos ED, Miedema MD, Muñoz D, Smith SC Jr, Virani SS, Williams KA Sr, Yeboah J, Ziaeian B. 2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation* 2019;140:e596-646.
11. Saeed A, Kampangkaew J, Nambi V. Prevention of cardiovascular disease in women. *Methodist deBakey Cardiovasc J* 2017;13:185–192.
12. Gan SC, Beaver SK, Houck PM, MacLehose RF, Lawson HW, Chan L. Treatment of acute myocardial infarction and 30-day mortality among women and men. *N Engl J Med* 2000;343:8–15.
13. Anderson RD, Pepine CJ. Gender differences in the treatment for acute myocardial infarction: bias or biology? *Circulation* 2007;115:823–826.
14. Insam C, Paccaud F, Marques-Vidal P. The region makes the difference: disparities in management of acute myocardial infarction within Switzerland. *Eur J Prev Cardiol* 2014;21:541–548.
15. Romanens M, Szucs T, Sudano I, Adams A. Agreement of PROCAM and SCORE to assess cardiovascular risk in two different low risk European populations. *Prev Med Rep* 2019;13:113–117.
16. Fry A, Littlejohns TJ, Sudlow C, Doherty N, Adamska L, Sprosen T, Collins R, Allen NE. Comparison of sociodemographic and health-related characteristics of UK Biobank participants with those of the general population. *Am J Epidemiol* 2017;186:1026–1034.