Review / Derleme

The Role of Aspirin in Primary Prevention According to Current Guidelines: Recommendations for Family Physicians

Güncel Kılavuzlara Göre Aspirinin Birincil Korunmadaki Rolü: Aile Hekimleri için Öneriler

Gülşah ONUR[1], Nadide YILDIZ[1], Hilal AKSOY[1], İzzet FİDANCI[1], Duygu AYHAN BAŞER[1]

Abstract

Family physicians, who are the leaders of primary health care institutions that patients can access easily, should recommend aspirin to patients with suitable indications for primary or secondary protection by evaluating the benefit-harm relationship via the principle of "Primum non nocere". Studies which were conducted in Turkish primary care settings mentioned that there is an irrational and inappropriate use of aspirin in the primary prevention of atherosclerotic cardiovascular diseases. Aspirin has a role in the primary prevention of cardiovascular diseases, in reducing the incidence of colorectal cancer, in protection related to increased thrombosis risk by some oncology drugs, and in protection from pregnancy complications. Recommendations from current guidelines will lead the way to family physicians regarding the use of aspirin.

Keywords: Aspirin, family practice, primary prevention, guideline

Özet

Hastaların kolaylıkla ulaşabileceği birinci basamak sağlık kuruluşlarının öncüsü olan aile hekimleri, "Primum non nocere" ilkesi ile yarar-zarar ilişkisini değerlendirerek birincil veya ikincil koruma için uygun endikasyonu olan hastalara aspirin önermelidir. Türkiye'de birinci basamakta yapılan çalışmalarda aterosklerotik kardiyovasküler hastalıkların birincil korunmasında aspirinin akılcı olmayan ve uygunsuz kullanımı söz konusudur. Aspirinin kardiyovasküler hastalıkların primer önlenmesinde, kolorektal kanser insidansının azaltılmasında, bazı onkoloji ilaçlarının tromboz riskini artırmasına bağlı korunmada ve gebelik komplikasyonlarından korunmada rolü vardır. Güncel kılavuzlara ait öneriler, birincil korunmada aspirin kullanımı konusunda aile hekimlerine rehber olacaktır.

Anahtar kelimeler: Aspirin, aile hekimliği, primer korunma, rehber

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[1]Department of Family Medicine, Faculty of Medicine, Hacettepe University, Ankara, TURKEY

Address for Correspondence / Yazışma Adresi: Gülşah ONUR. Department of Family Medicine, Faculty of Medicine, Hacettepe University, Altındağ/Ankara, TURKEY E-posta: gulsahonur94@gmail.com Tel: +905309527822

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Introduction

Primary healthcare institutions are the first point of contact for every individual in the community. Maintaining health and well-being by using health maintenance and disease prevention strategies is one of the core competencies of the family medicine discipline. Primary care physicians who provide person-centered care and a comprehensive approach are in a position to perform preventive medicine most effectively.[1] Preventive health services are divided into several groups: Primordial prevention includes preventing the occurrence of risk factors before they occur and improving health, primary prevention includes preventing the occurrence of diseases in individuals at risk, secondary prevention includes early diagnosis and early intervention to diseases, tertiary prevention includes preventing or delaying the occurrence of complications and dysfunctions related to diseases, and quaternary prevention includes preventing overmedication.[2] Patients and physicians usually prefer acetylsalicylic acid (ASA) for the prevention of cardiovascular diseases, which are common in society.[3,4,5,6,7,8] Family physicians, who are the leaders of primary health care institutions that patients can access easily, should recommend ASA to the patients with suitable indications for primary or secondary protection by evaluating the benefit-harm relationship in the motto of preventive medicine and the principle of "Primum non nocere". This review includes recommendations for family physicians concerning the use of aspirin in primary prevention in current guidelines.

The history of aspirin, one of the most commonly used drugs in the world, began thousands of years ago with the use of willow tree bark containing salicylate to treat pain and fever.[9] Hippocrates and Galen were the first scientists who kept medical records about the analgesic and anti-inflammatory effects of willow tree bark.[10] In 1897, Chemist Felix Hoffman acetylated the hydroxyl group on the benzene ring of salicylic acid, thus making ASA, which is frequently found in our prescriptions today.[9] In 1948 Lawrence Craven and 1949 Paul Gibson suggested that aspirin may be effective in the protection against cardiovascular diseases.[11] Aspirin inhibits COX-1 and COX-2 enzymes irreversibly. Low-dose aspirin shows anti-aggregant effect by inhibiting COX-1 and high doses show an anti-inflammatory effect by inhibiting COX-2. Intermediate doses have antipyretic, and analgesic effects. Aspirin has oral, rectal, and intravenous usage forms.[12]

The Role of Aspirin in the Primary Prevention of Cardiovascular Disease:

Aspirin is commonly recommended for secondary prevention of atherosclerotic cardiovascular diseases (ASCVD). However, its use in primary prevention is controversial because the benefit-risk proportion is not clear. This state of uncertainty is also reflected in international guidelines:

In the last version of the ACC/AHA (American College of Cardiology/American Heart Association) Guideline on the Primary Prevention of Cardiovascular Disease, the recommendation class for prophylactic aspirin was lowered compared to previous guidelines.[13] Considering the benefits and side effects, previous guidelines recommended the use of prophylactic aspirin only in patients with a high risk of ASCVD.[14,15] Data from some studies suggest that the benefits of aspirin use in primary prevention outweigh the risks in people with a 10-year ASCVD risk estimate above 10%.[16] However, the proportional benefits of aspirin in the prevention of nonfatal heart attack and stroke are less prominent in recent studies.[17] Thus, according to the recently published guideline, low-dose aspirin may be noted for the primary prevention of ASCVD in selected patients aged 40-70 years, who are at higher risk of ASCVD but without increased bleeding risk (Class of Recommendation (COR) IIb, Level of Evidence (LOE) A). At this point, in the selection of the patient group to give aspirin, an individual approach should be taken for every patient with detailed anamnesis and physical examination. A 10-year ASCVD risk estimate should be made, the family history of early myocardial infarction (MI) should be questioned, blood lipid and glucose values should be examined, and it should be evaluated whether these are at the target values. The physician should consider patient-specific multifactorial factors and decide on a case-by-case basis whether reducing the risk of ischemic events is worth increasing the risk of bleeding. Meta-analyses recommend that low-dose aspirin (75-100 mg orally per day) is equal to high-dose aspirin in reducing the risk of ASCVD, but high-dose aspirin is associated with a higher risk of bleeding. For this reason, low-dose aspirin should be given to this selected group of patients for primary prevention of ASCVD. Again, according to this guideline, low-dose aspirin shouldn't be routinely administered to the geriatric population over 70 years of age for the primary prevention of ASCVD due to the increased risk of bleeding (COR III, LOE B-R). Additionally, for adults under 40 years of age, routine aspirin administration is not recommended because there is unsatisfactory evidence to assess the risk-benefit proportion of routine aspirin in the primary prevention of ASCVD. People who have high risk of bleeding, regardless of age, should not be given aspirin for primary prevention of ASCVD (COR III, LOE C-LD).[13]

According to the last version of the ESC (European Society of Cardiology) Guidelines on Cardiovascular Disease Prevention in Clinical Practice, aspirin can be given for primary prevention in patients under 70 years of age with diabetes and high or very high risk of ASCVD, if there is no contraindication for aspirin (COR IIb, LOE A). The persons under 70 years of age with high or very high risk of ASCVD, decisions should be made on a case-by-case

basis, taking into account both ischemic risk and bleeding risk. Further studies are needed in this patient group.[18] According to recent meta-analyses, there is no reduction in all-cause or cardiovascular mortality rate with aspirin, but there is a reduction in the risk of nonfatal MI and ischemic stroke. On the other side, aspirin increases the risk of intracranial and gastrointestinal bleeding, but there is no consequential increase in the risk of fatal bleeding.[19,20,21] The risk of bleeding is especially increased in the elderly.[18]

According to the USPSTF (United States Preventive Services Task Force) Recommendation Statement on the Aspirin Use to Prevent Cardiovascular Disease published in 2022, the suggestions related to initiating low-dose aspirin for the primary prevention of ASCVD in adults aged 40-59 years with a 10-year risk of cardiovascular disease of 10% or more should be individualized (LOE C). Evidence suggests that the net benefit of using aspirin use in this group is minor. The USPSTF recommends aspirin shouldn't be initiated for primary prevention in adults aged 60 years and older (LOE D).[22]

According to the "Guidelines for the Diagnosis, Treatment and Follow-up of Diabetes Mellitus and its Complications" published by the Turkish Society of Endocrinology and Metabolism (TEMD) in 2022, studies conducted in recent years have shown that the place of aspirin in primary prevention in diabetic patients is arguable.[23,24,25,26] Aspirin increases the risk of bleeding, particularly gastrointestinal system bleeding. Therefore, aspirin is not recommended for people with a 10-year risk of cardiovascular events below 5%. 75-150 mg of aspirin daily is recommended for primary prevention in diabetic patients with a 10-year risk of cardiovascular events above 5%. However, aspirin should be given for secondary prevention in patients with diabetes and ASCVD.[27]

In summary, the ACC/AHA guideline recommends the use of low-dose aspirin for primary prevention in selected patients aged 40-70 years with a high risk of ASCVD and no increased risk of bleeding; the ESC guideline similarly recommends it in selected patients under the age of 70 years with a high/very high risk of ASCVD and no contraindications for aspirin use; and the USPSTF recommends it in patients aged 40-59 years with a 10-year cardiovascular disease risk above 10%. For diabetic patients, the ESC guideline recommends it in patients under 70 years of age with a high/very high risk of ASCVD, and the TEMD recommends it in patients with a 10-year risk of cardiovascular events above 5%. The ACC/AHA guideline does not recommend the routine use of aspirin for primary prevention in the geriatric population aged 70 years and older and in adults under 40 years of age, and the USPSTF does not recommend the routine use of aspirin for primary prevention in adults aged 60 years and older. The common point of the guidelines is that aspirin is not recommended for people at high risk of bleeding and aspirin is recommended for people at high risk of atherosclerotic cardiovascular disease. Individual approach is very important in this context.

When we look at the studies conducted in recent years on the use of aspirin in the primary prevention of ASCVD in our country; 1132 adult patients using aspirin for primary prevention were included in the multicentered cross-sectional study published in 2021, which was provided with data from 30 different cardiology outpatient clinics in 14 different cities from 7 regions of Turkey. In this study, inappropriate aspirin use for primary prevention was found in 100% of patients according to the 2016 ESC guideline and in 89% of patients according to the 2019 ACC/AHA guideline.[3] In another cross-sectional study conducted on 119 adult patients who requested an appointment at the family medicine outpatient clinic, published in 2021, 42.01% of the patients stated a reason for using aspirin other than the physician's recommendation. It was determined that aspirin use was appropriate for the purpose in only 26% of the patients who used aspirin without a physician's recommendation.[4] These current studies conducted in our country show that there is an irrational and inappropriate use of aspirin in the primary prevention of ASCVD.

The Role of Aspirin in the Primary Prevention of Colorectal Cancers:

Publications are showing that aspirin decreases the risk of colorectal cancer, but further studies are needed. If we look at the data from the current literature on the role of aspirin in primary prevention of colorectal cancer, in the analysis of two cohort studies involving a total of 94540 participants in 2021, regular aspirin use at the age of 70 years and older was relevant with a lower risk of colorectal cancer compared to non-regular use. However, this risk reduction was only remarkable in people who started using aspirin before the age of 70 and continued to take it into their 70s. Starting aspirin at an older age was not relevant with a lower risk of colorectal cancer.[28] The systematic review published in 2022 for the USPSTF included randomized clinical trials comparing low-dose aspirin (Maximum 100 mg orally per day) given for primary prevention with placebo. According to this study, there is restricted evidence for the benefits of aspirin use in preventing colorectal cancer; results were highly variable according to the length of follow-up and statistically significant only when long-term observational follow-up beyond randomized trials was considered.[29] In a meta-analysis of 11 randomized controlled trials, high-dose aspirin (500-1200 mg orally daily) was associated with a reduced incidence of colorectal cancer; however, this data is based on a limited number of studies. There is no consequential reduction in the incidence of colorectal cancer with moderate doses (164-325 mg orally daily) or low doses (50-163 mg orally daily) of aspirin.[30]

In the BSG/ACPGBI/UKCGG (British Society of Gastroenterology/Association of Coloproctology of Great Britain and Ireland/United Kingdom Cancer Genetics Group) Guidelines for the Management of Hereditary Colorectal Cancer, which was last published in 2020, aspirin prophylaxis is recommended for primary prevention in patients with Lynch Syndrome because it reduces the risk of colorectal cancer (COR I, LOE B). Studies have shown that aspirin decreases this risk by nearly half compared to placebo. This effect only occurs with regular aspirin use for 3-5 years. Using of aspirin for less than 2 years does not provide a benefit in decreasing the incidence of cancer or improving survival in individuals with Lynch Syndrome. There is ambiguity about the ideal dose of aspirin recommended for patients with Lynch Syndrome. In this guideline, 300 mg aspirin daily if the body mass index (BMI) is 25 kg/m^2 and above and 150 mg aspirin daily if the BMI is below 25 kg/m^2 is suggested for patients with Lynch Syndrome until further studies are conducted.[31] In the EHTG/ESCP (European Hereditary Tumor Group/European Society of Coloproctology) Guidelines for Lynch Syndrome published in 2021, daily aspirin use decreases the risk of colorectal cancer in patients with Lynch Syndrome (COR II). The recommended dose is at least 75-100 mg daily. For people over 70 kg, this dose should be increased.[32]

The Role of Aspirin in Primary Protection in Oncology:

Aspirin is often recommended for primary prevention in oncology because of its anti-thrombotic effect. According to a report published by the American Heart Association in 2022, low-dose aspirin should be given to patients in primary prevention who are taking dexamethasone in combination with immunomodulatory drugs due to an increased risk of thrombosis. In patients with newly diagnosed multiple myeloma or patients at risk of multiple venous thrombo-embolism, low molecular weight heparin prophylaxis is preferred because it is more effective than aspirin. Patients receiving dexamethasone treatment together with ponatinib should also receive prophylactic low-dose aspirin, and hospitalized patients in this patient group should receive low molecular weight heparin due to multiple venous thromboembolism risk factors.[33]

The Role of Aspirin in Primary Protection During Pregnancy:

To prevent preeclampsia in women, aspirin may be given to women in the risk group for primary prevention. The 2018 ACOG (American College of Obstetricians and Gynecologists) Commission Opinion recommends that women with one or more high-risk characteristics (such as chronic hypertension, history of preeclampsia, multiple gestation, diabetes, kidney disease, and autoimmune disease) or women with more than one moderate risk factor (such as BMI of 30 kg/m^2 or more, nulliparity, maternal age 35 years or older, family history of preeclampsia, black race, low socioeconomic status, adverse pregnancy outcomes) should take low-dose aspirin (81 mg orally daily) starting from 12 to 28 weeks of gestation (ideally before 16 weeks) and continue until delivery to prevent preeclampsia. The use of low-dose aspirin during pregnancy is safe, and the risk of complications to the mother and/or fetus is low. In pregnant women who are not at high risk of preeclampsia, current evidence does not recommend prophylactic use of low-dose aspirin for the prevention for miscarriage, fetal growth restriction, stillbirth, or preterm birth.[34] The 2021 USPSTF Recommendation Statement on the Aspirin Use to Prevent Preeclampsia and Related Morbidity and Mortality recommends the use of low-dose aspirin (81 mg orally daily) to prevent preeclampsia after 12 weeks of gestation for women at high risk of preeclampsia (LOE B).[35]

Side Effects and Contraindications of Aspirin:

The most common side effect of aspirin, which is in the non-steroidal anti-inflammatory drug (NSAID) group, is gastritis due to gastrointestinal irritation, peptic ulcer, and gastrointestinal bleeding. Other side effects of aspirin include hypersensitivity reactions to NSAIDs, Reye's syndrome, increased risk of intracranial hemorrhage, and hemorrhagic stroke. Aspirin is contraindicated in patients with factors that increase the risk of bleeding, such as a history of bleeding, active peptic ulcer, thrombocytopenia, coagulopathy, chronic kidney disease, alcohol consumption, and concomitant use of other drugs that increase bleeding (NSAIDs, steroids, warfarin, and oral anticoagulants). It is also contraindicated in patients with severe hepatic impairment, aspirin allergy or intolerance, ibuprofen allergy, asthma patients with NSAID-associated bronchospasm, dengue fever, yellow hemorrhagic fever, and Glucose-6-phosphate dehydrogenase deficiency. Children under 16 should not use aspirin, except for Kawasaki disease. Breastfeeding women should not use it. Uncontrolled hypertension is a relative contraindication due to increased risk of intracranial hemorrhage. [12,13,36]

Conclusion:

In conclusion, aspirin can be given to selected patient groups for primary prevention, considering the benefits and risks. Treating diseases after they occur can be difficult and expensive. Primary prevention interventions aim to prevent diseases before they occur. Preventive healthcare is a fundamental aspect of family medicine. Family physicians, who have the responsibility to improve the health and well-being of individuals and society through

appropriate and effective interventions, also have to protect people with risk factors from diseases within the scope of preventive healthcare. The clinician should take an individual and holistic approach to each patient. Aspirin has a role in the primary prevention of cardiovascular diseases, in reducing the incidence of colorectal cancer, in protection related to increased thrombosis risk by some oncology drugs, and in protection from pregnancy complications. Further research is still needed on these subjects. It is crucial for family physicians to identify patients who require aspirin for primary prevention, conduct risk and side effect assessments, and stay updated with the current literature on these issues. At the same time, interventions to increase patients' health literacy and rational drug use can be planned to prevent inappropriate, incorrect, and off-label aspirin use.

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The authors have no competing interests to declare that are relevant to the content of this article.

References

1. The European Definition of General Practice / Family Medicine, WONCA EUROPE 2023 Edition [Internet]. Available from: https://www.woncaeurope.org/file/41f61fb9-47d5-472184e603f4afa6588/WONCA_European_Definitions_2_v7.pdf [Cited 09 Jan 2024]
2. Kisling LA, M Das J. Prevention strategies. Treasure Island (FL): StatPearls [Internet]. Publishing; 2023 Jan. [Updated 2023 Aug 1]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK537222/ [Cited 09 Jan 2024]
3. Çelik O, Çil C. Aterosklerotik hastalığın primer korumasında aspirin kullanımının uygunluğu: ASSOS çalışmasının altgrup analizi. Medical Journal of Mugla Sitki Kocman University 2021 Apr;8(1):43-46. doi:10.47572/muskutd.857550 [In Turkish]
4. Bulca Acar A, Özen M. Aile hekimliği polikliniğine başvuran hastalarda aspirin kullanımının değerlendirilmesi. Cukurova Medical Journal 2021 Sep;46(3):1026-1032. doi:10.17826/cumj.907395. [In Turkish]
5. Ponir C, Seals A, Caldarera T, Ip EH, German CA, Taylor Y, et al. Specialty preference for cardiovascular prevention practice in the Southeast US and role of a preventive cardiologist. Postgrad Med J. 2023;100(1179):42-49. doi:10.1093/postmj/qgad082
6. Hira RS, Gosch KL, Kazi DS, Yeh RW, Kataruka A, Maddox TM, et al. Potential impact of the 2019 ACC/AHA guidelines on the primary prevention of cardiovascular disease recommendations on the inappropriate routine use of aspirin and aspirin use without a recommended indication for primary prevention of cardiovascular disease in cardiology practices: insights from the NCDR PINNACLE registry. Circ Cardiovasc Qual Outcomes. 2022;15(3):e007979. doi:10.1161/CIRCOUTCOMES.121.007979
7. Christensen MB, Jimenez-Solem E, Ernst MT, Schmidt M, Pottegård A, Grove EL. Low-dose aspirin for primary and secondary prevention of cardiovascular events in Denmark 1998-2018. Sci Rep. 2021;11(1):13603. Published 2021 Jun 30. doi:10.1038/s41598-021-93179-8
8. Ong SY, Chui P, Bhargava A, Justice A, Hauser RG. Estimating Aspirin Overuse for Primary Prevention of Atherosclerotic Cardiovascular Disease (from a Nationwide Healthcare System). Am J Cardiol. 2020;137:25-30. doi:10.1016/j.amjcard.2020.09.042
9. Vane JR, Botting RM. The mechanism of action of aspirin. Thromb Res 2003 June;110(5-6):255-258.
10. Jack DB. One hundred years of aspirin. Lancet 1997 Aug;350(9075):437-439.
11. Gibson PC. Aspirin in the treatment of vascular diseases. Lancet 1949 Dec;2(6591):1172-1174.
12. Arif H, Aggarwal S. Salicylic Acid (Aspirin). Treasure Island (FL): StatPearls [Internet]. Publishing; 2023 Jan. [Updated 2023 Jul 5]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK519032/ [Cited 30 Oct 2023]
13. Arnett DK, Blumenthal RS, Albert MA, Buroker AB, Goldberger ZD, Hahn EJ, et al. 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, 140(11), e596–e646. doi:10.1161/CIR.0000000000000678
14. Pearson TA, Blair SN, Daniels SR, Eckel RH, Fair JM, Fortmann SP, et al. AHA Guidelines for primary prevention of cardiovascular disease and stroke: 2002 update: consensus panel guide to comprehensive risk reduction for adult patients without coronary or other atherosclerotic vascular diseases. American Heart Association Science Advisory and Coordinating Committee. Circulation. 2002;106(3):388-391. doi:10.1161/01.cir.0000020190.45892.75
15. Pignone M, Alberts MJ, Colwell JA, Cushman M, Inzucchi SE, Mukherjee D, et al. Aspirin for primary prevention of cardiovascular events in people with diabetes: a position statement of the American Diabetes Association, a scientific statement of the American Heart Association, and an expert consensus document of the American College of Cardiology Foundation. Circulation. 2010;121(24):2694-2701. doi:10.1161/CIR.0b013e3181e3b133

16. Halvorsen S, Andreotti F, ten Berg JM, Cattaneo M, Coccheri S, Marchioli R, et al. Aspirin therapy in primary cardiovascular disease prevention: a position paper of the European Society of Cardiology working group on thrombosis [published correction appears in J Am Coll Cardiol. 2014 Nov 4;64(18):1970]. J Am Coll Cardiol. 2014;64(3):319-327. doi:10.1016/j.jacc.2014.03.049
17. McNeil JJ, Wolfe R, Woods RL, Tonkin AM, Donnan GA, Nelson MR, et al. Effect of aspirin on cardiovascular events and bleeding in the healthy elderly. N Engl J Med. 2018;379(16):1509-1518. doi:10.1056/NEJMoa1805819
18. Visseren FLJ, Mach F, Smulders YM, Carballo D, Koskinas KC, Bäck M, et al. 2021 ESC Guidelines on cardiovascular disease prevention in clinical practice. European heart journal, 42(34), 3227–3337. doi:10.1093/eurheartj/ehab484
19. Abdelaziz HK, Saad M, Pothineni NVK, Megaly M, Potluri R, Saleh M, et al. Aspirin for primary prevention of cardiovascular events. J Am Coll Cardiol. 2019;73(23):2915-2929. doi:10.1016/j.jacc.2019.03.501
20. Zheng SL, Roddick AJ. Association of aspirin use for primary prevention with cardiovascular events and bleeding events: a systematic review and meta-analysis JAMA, 321(3), 277–287. doi:10.1001/jama.2018.20578
21. Mahmoud AN, Gad MM, Elgendy AY, Elgendy IY, Bavry AA. Efficacy and safety of aspirin for primary prevention of cardiovascular events: a meta-analysis and trial sequential analysis of randomized controlled trials. Eur Heart J. 2019;40(7):607-617. doi:10.1093/eurheartj/ehy813
22. Davidson KW, Barry MJ, Mangione CM, Cabana M, Chelmow D, Coker TR, et al. Aspirin use to prevent cardiovascular disease: US preventive services task force recommendation statement. JAMA 2022 Apr;327(16):1577-1584. doi:10.1001/jama.2022.4983
23. ASCEND Study Collaborative Group, Bowman L, Mafham M, Wallendszus K, Stevens W, Buck G, Barton J, et al. Effects of aspirin for primary prevention in persons with diabetes mellitus. N Engl J Med. 2018;379(16):1529-1539. doi:10.1056/NEJMoa1804988
24. American diabetes association professional practice committee (2022). 10. Cardiovascular disease and risk management: standards of medical care in diabetes-2022. Diabetes care, 45(Suppl 1), S144–S174. doi:10.2337/dc22-S010
25. Belch J, MacCuish A, Campbell I, Cobbe S, Taylor R, Prescott R, et al. The prevention of progression of arterial disease and diabetes (POPADAD) trial: factorial randomised placebo controlled trial of aspirin and antioxidants in patients with diabetes and asymptomatic peripheral arterial disease. BMJ. 2008;337:a1840. Published 2008 Oct 16. doi:10.1136/bmj.a1840
26. De Berardis G, Sacco M, Strippoli GF, Pellegrini F, Graziano G, Tognoni G, et al. Aspirin for primary prevention of cardiovascular events in people with diabetes: meta-analysis of randomised controlled trials [published correction appears in BMJ. 2010;340:c374]. BMJ. 2009;339:b4531. Published 2009 Nov 6. doi:10.1136/bmj.b4531
27. Türkiye Endokrinoloji ve Metabolizma Derneği. Diabetes Mellitus ve Komplikasyonlarının Tanı, Tedavi ve İzlem Kılavuzu 2022. (Türkiye Endokrinoloji ve Metabolizma Derneği, Ed.) (15. baskı). Ankara: Türkiye Endokrinoloji ve Metabolizma Derneği. Retrieved from https://file.temd.org.tr/Uploads/publications/guides/documents/diabetesmellitus_2022.pdf [Cited 30 Oct 2023] [In Turkish]
28. Guo C, Ma W, Drew DA, et al. Aspirin use and risk of colorectal cancer among older adults. JAMA Oncol 2021 Jan.;7(3):428–435.
29. Guirguis-Blake JM, Evans CV, Perdue LA, Bean SI, Senger CA. Aspirin use to prevent cardiovascular disease and colorectal cancer: updated evidence report and systematic review for the US preventive services task force. JAMA 2022 April;327(16):1585–1597.
30. Shah D, Di Re A, Toh JWT. Aspirin chemoprevention in colorectal cancer: network meta-analysis of low, moderate, and high doses. Br J Surg 2023 Jul; znad231. doi:10.1093/bjs/znad231
31. Monahan KJ, Bradshaw N, Dolwani S, Desouza B, Dunlop MG, East JE, et al. Guidelines for the management of hereditary colorectal cancer from the British Society of Gastroenterology (BSG)/Association of Coloproctology of Great Britain and Ireland (ACPGBI)/UK Cancer Genetics Group (UKCGG). Gut 2020 Mar;69(3):411–444.
32. Seppälä TT, Latchford A, Negoi I, Sampaio Soares A, Jimenez-Rodriguez R, Sánchez-Guillén L et al. European Guidelines from the EHTG and ESCP for Lynch syndrome: an updated third edition of the Mallorca guidelines based on gene and gender. Br J Surg 2021 May;108:484–498.
33. Beavers CJ, Rodgers JE, Bagnola AJ, Beckie TM, Campia U, Di Palo KE, et al. Cardio-Oncology Drug Interactions: A scientific statement from the American Heart Association. Circulation 2022 April;145(15):e811-e838. doi:10.1161/CIR.0000000000001056
34. ACOG committee opinion no. 743 summary: low-dose aspirin use during pregnancy. Obstet Gynecol 2018 Jul;132(1):254-256.
35. Davidson KW, Barry MJ, Mangione CM, Cabana M, Caughey AB, Davis EM, et al. Aspirin use to prevent preeclampsia and related morbidity and mortality: US preventive services task force recommendation statement. JAMA 2021 Sep;326(12):1186-1191.
36. Miser WF. Appropriate aspirin use for primary prevention of cardiovascular disease. Am Fam Physician 2011 Jun;83(12):1380-1386.