Molecule ID: 56
Keyword: aspirin
User Name: user4
Date of Creation: 2024-04-27 19:27:04

PubChem

Compound Name: Aspirin
Molecular Form: C9H8O4, CH3COOC6H4COOH
Molecular weight:180.16 g/mol
CAS registration: 50-78-2;
ATC code: N - Nervous system / N02 - Analgesics / N02B - Other analgesics and antipyretics / N02BA - Salicylic acid and derivatives / N02BA01 - Acetylsalicylic acid
IUPAC name: 2-acetyloxybenzoic acid
Solubility: Solubility not found
Physical description: Physical description not found
Melting point: CAMEO Chemicals
Decomposition: Decomposition not found
Half life: The half-life of ASA in the circulation ranges from 13 - 19 minutes. Blood concentrations drop rapidly after complete absorption. The half-life of the salicylate ranges between 3.5 and 4.5 hours.
Reactivity: Reactivity not found

PubMed

Pharmacodynamics: URL: http://www.ncbi.nlm.nih.gov/pmc/articles/pmc5681618/ Paragraphs: However, guidelines regarding the usage of aspirin to prevent preeclampsia differ considerably from one country to another. Screening modalities, target population, and aspirin dosage are still a matter of debate. In this review, we report the pharmacodynamics of aspirin, its main effects according to dosage and gestational age, and the evidence-based indications for primary and secondary prevention of preeclampsia.

Overview of Efficacy: URL: http://www.ncbi.nlm.nih.gov/pmc/articles/pmc8677993/ Paragraphs: Patients experiencing acute ischemic stroke or transient ischemic attack are commonly treated with clopidogrel and/or aspirin (mono- and dual-antiplatelet therapy) to minimize the risk for recurrent stroke. Updated data from systematic studies can be used to guide practice. The present study aimed to compare findings from systematic reviews and meta-analyses addressing the efficacy and safety of clopidogrel or aspirin – alone or in combination – in patients experiencing acute ischemic stroke or transient ischemic attack.. The highest standard of evidence used to support therapeutic efficacy and safety is from systematic analyses and meta-analysis of randomized controlled trials (RCTs). Due to the increasing number of systematic reviews and meta-analyses, it is necessary to combine various analyses into overviews to provide clinicians with readily accessible knowledge.. The present review summarizes findings from systematic studies and meta-analyses addressing the efficacy and safety of clopidogrel or aspirin alone (monotherapy) or combinations (i.e., DAPT) for patients experiencing AIS or TIA.. Systematic reviews and meta-analyses that examined clopidogrel and/or aspirin for individuals experiencing acute AIS or TIA, published between 2010 and 2021, were included. Reviews including patients with AIS from all causes (including >50% carotid stenosis and large artery disease) were also included. A combination of major ischemic events, such as ischemic stroke, myocardial infarction (MI), or death, was the primary efficacy endpoint. Safety outcomes, reported as intracranial bleeding and major bleeding, were also considered.. Two authors searched for systematic studies and meta-analyses in the Cochrane Library, PubMed, Ovid, Scopus, EBSCO, and CINAHL databases published from inception to 2020 using the following keywords “Clopidogrel,” “Aspirin,” “Acute ischemic stroke,” “TIA,” “Dual-therapy,” “Mono-therapy,” “Efficacy,” and “safety.” For inclusion, all studies and

evaluations of the clinical effects of DAPT were included. Based on the inclusion criteria described above, two authors assessed eligibility. Furthermore, two authors performed an unbiased quality assessment of the systematic reviews using the Risk of Bias in Systematic reviews tool and A Measurement Tool to Assess Systematic Reviews 2.. Efficacy and safety.. In the present overview of systematic reviews addressing the efficacy and safety outcomes of clopidogrel or aspirin alone (monotherapy) or combination (i.e., DAPT) for patients with ischemic stroke/TIA, we assessed seven systematic reviews encompassing 54 RCTs and four retrospective cohort studies including 133,502 patients. Overall, we revealed a large body of scientific data supporting DAPT to be superior to monotherapy in preventing recurrent stroke (ischemic and hemorrhagic) in patients experiencing ischemic stroke/TIA.. The time to initiation of DAPT after an ischemic stroke or TIA and the duration of therapy are the most important factors determining the efficacy of treatment. Rahman et al reported that to achieve maximum efficacy, DAPT should be initiated within 12 to 24 h after minor ischemic stroke (NIHSS < 3) or TIA, and the duration of therapy should be <1 month.[14] Hao et al suggested that DAPT administered within 24 h following a high-risk TIA or minor ischemic stroke decreased the risk for a future stroke by approximately 2%, with minimal significant side effects.[17]. How to cite this article: Yang Y, Huang Z, Zhang X. Efficacy and safety of clopidogrel and/or aspirin for ischemic stroke/transient ischemic attack: an overview of systematic reviews and meta-analysis. Medicine. 2021;100:50(e27804).

Pharmacodynamics Drug Interaction:

Clinical Studies: URL: http://www.ncbi.nlm.nih.gov/pmc/articles/pmc4837230/ Paragraphs: Design Systematic review and meta-analysis of cohort studies.. Eligibility criteria for selecting studies Cohort studies with ≥1000 participants that evaluated the risk of pre-eclampsia in relation to a common and generally accepted clinical risk factor assessed at ≤16 weeks' gestation.. Data extraction Two independent reviewers extracted data from included studies. A pooled event rate and pooled relative risk for pre-eclampsia were calculated for each of 14 risk factors.. Results There were 25 356 688 pregnancies among 92 studies. The pooled relative risk for each risk factor significantly exceeded 1.0, except for prior intrauterine growth restriction. Women with antiphospholipid antibody syndrome had the highest pooled rate of pre-eclampsia (17.3%, 95% confidence interval 6.8% to 31.4%). Those with prior pre-eclampsia had the greatest pooled relative risk (8.4, 7.1 to 9.9). Chronic hypertension ranked second, both in terms of its pooled rate (16.0%, 12.6% to 19.7%) and pooled relative risk (5.1, 4.0 to 6.5) of pre-eclampsia.. Many randomized controlled trials of aspirin prophylaxis did not describe the criteria they used to define a woman as high risk, and others used abnormal findings on uterine artery Doppler ultrasonography, which has limited sensitivity, is rarely done before 16 weeks, and has limited availability among midwives and family practitioners.15 Other studies have proposed several risk factors to characterize women at high risk of pre-eclampsia, including nulliparity, older age, chronic hypertension, and prepregnancy diabetes mellitus.15 16 Yet again, the absolute and relative importance of one risk factor over another has not been systematically assessed.. Given the limitations and variability in the current criteria used to identify women at high risk of pre-eclampsia, there is a need for a clear, concise, and evidence based list of indicators to estimate a woman's risk. These indicators should consider events in any previous pregnancy as well as current pregnancy factors that can be efficiently gathered at an early prenatal visit. To generate this list, we completed a meta-analysis of large cohort studies of one or more risk factors for pre-eclampsia.. We also limited our selection to large sample cohort studies because they tend to be more representative of the general population than small single centre studies and they have sufficient statistical power to assess less prevalent, but potentially important, risk factors.21. Two authors (EB and KM), both of whom are medical students, screened studies and abstracted data. EB screened all citations retrieved from the database searches, and both authors evaluated the eligibility of the full text articles. Disagreements were resolved by discussion or in consultation with a third author (JGR). If two published studies evaluated the same cohort of women, we included the study with the largest number of women or the greatest number of relevant outcomes. Study authors were not contacted.. For each risk factor, we first calculated the pooled pre-eclampsia event rate in the exposed and unexposed groups, using an arcsine

transformation. As statistical heterogeneity was evident across studies, we used a DerSimonian-Laird binary random effects model to derive a pooled relative risk (RRpooled) and 95% confidence interval for each risk factor. For the calculated pooled relative risk for each risk factor, we assessed heterogeneity by I2.. where Pepooled is the number of women with a given risk factor in each study divided by the total number of women in that same study, pooled across studies using the arcsine transformation, and where RRpooled is the pooled relative risk calculated above. We used OpenMeta[Analyst] (Providence, RI) for all meta-analyses.. We performed three additional analyses that were limited to three chosen risk factors—namely prior pre-eclampsia (representing a risk factor arising in a prior pregnancy), chronic hypertension (a risk factor identified in the current pregnancy), and prepregnancy BMI >30 (a risk factor measured early in the current pregnancy). For each of these risk factors we had a sufficient number of studies to enable these further analyses. First, in a sensitivity analysis, we re-calculated the pooled relative risk using data limited to prospective studies, which tend to have more accurate ascertainment of risk factors and outcomes and also less biased effect sizes.22 Second, we constructed three funnel plots to assess publication bias.. No patients were involved in setting the research question or the outcome measures, nor were they involved in developing plans for implementation of the study. No patients were asked to advise on interpretation or writing up of results. There are no plans to disseminate the results of the research to study participants or the relevant patient community.. Fig 1 PRISMA flow diagram of selection and inclusion of studies in current meta-analysis of risk factor for pre-eclampsia. Appendix 2 shows the general study characteristics and sample characteristics of the included studies, comprising 25 356 688 pregnancies in 27 countries. There were 40 studies from Europe and 30 studies from North America. Of the 92 studies, 55 were retrospective and 37 were of a prospective cohort design. Sixty one studies used a standard clinical definition of pre-eclampsia, 16 used ICD (international classification of diseases) codes, and 15 provided no formal definition. The mean number of participants was 275 616 (SD 704 906), with a minimum of 1043 and a maximum of 4 395 968.. Fifty seven studies (62%) were limited to singleton pregnancies, while out of 92 studies, nine (9.8%) excluded stillbirths and 18 (19.6%) excluded congenital anomalies. Twenty four studies documented participant attrition, which was about 3% on average (appendix 2).. 140/90 mm Hg.71 When we examined studies of chronic hypertension, the pooled rate of pre-eclampsia was 16.0% (15.2% to 16.7%) among women with chronic hypertension in studies in which pre-eclampsia was based on a standard clinical definition, compared with 5.9% (5.7% to 6.2%) among women with chronic hypertension in studies in which pre-eclampsia was based on ICD coding. In the same studies, however, among women without hypertension, the respective pooled rates of pre-eclampsia were 3.1% (3.1% to 3.1%) and 2.7% (2.7% to 2.7%).. In the sensitivity analysis limited to prospective cohort studies, the pooled relative risk for prior pre-eclampsia (7.4, 95% confidence interval 5.9 to 9.5), chronic hypertension (5.4, 4.2 to 7.0), and prepregnancy BMI >30 (2.7, 2.5 to 2.9) did not differ appreciably from the pooled relative risk based on prospective and retrospective cohort studies together (fig 2).. Based on a body of large sample cohort studies, we estimated the contributions of several clinical risk factors to the development of pre-eclampsia, considering the absolute rate and relative risk of pre-eclampsia—metrics understood by clinicians—and also on the population attributable fraction—a metric applicable to public health initiatives at the population level. Except for a history of intrauterine growth restriction, each identified risk factor was associated with a significantly heightened risk of pre-eclampsia.. We pooled data from studies of more than 25 million women, enabling us to systematically evaluate several well defined risk factors that have been largely accepted in most clinical settings and within published clinical practice guidelines.9 10 11 Our inclusion of only large sample cohort studies helped curtail the bias potentially introduced by smaller studies21 but by no means eliminated the risk of participant selection bias. Many of the cohort studies we included were population based (appendix 2), thereby avoiding small audit based or single centre studies that could be more prone to selection bias.. When we limited our analysis to prospective cohort studies, which tend to have less selection bias, the pooled relative risks did not differ appreciably from those in the main analysis. Our determination of the risk of pre-eclampsia was better informed for some risk factors than for others (such as prior intrauterine growth restriction or systemic lupus erythematosus), which were based on only one or two contributing studies and a lower overall number of participants. Other risk factors (such as maternal age >40) were evaluated from a sufficient number

of studies and pregnancies but still surpassed the threshold number needed to prevent of 250.. By restricting our analyses to studies examining risk factors determined in early pregnancy, we focused on risk factors that could lead to a timely intervention, such as aspirin prophylaxis.6 7 8 We generated reliable and consistent results across studies, as most were completed in the past two decades within Western countries, and about two thirds used a standard clinical definition of pre-eclampsia. This was evidenced by a 2.7% weighted mean event rate for all risk factors across all unexposed groups, a figure close to that estimated within Western countries.118 Certainly in low income countries, where the rate of pre-eclampsia tends to be higher1 2 and the prevalence of risk factors might differ, less can be said about the behavior of the currently evaluated risk factors for pre-eclampsia.. As a limitation, 15 out of 92 studies did not provide a formal definition of pre-eclampsia, our main outcome. When the outcome was based on a standard clinical definition, the rate of pre-eclampsia was much higher than rates based on ICD coding, as noted for women with chronic hypertension and women with a BMI ≥30. Another inconsistency was in the differing definitions of certain risk factors. “Renal disease,” for example, ranged from mild to severe loss of renal function. Similarly, the definition of chronic hypertension or antiphospholipid antibody syndrome varied by study or era, or both.. Notwithstanding that limitation, antiphospholipid antibody syndrome and chronic hypertension were apparent individual risk factors for pre-eclampsia, and chronic kidney disease was likely the same. Certainly, varying definitions of a given risk factor and/or pre-eclampsia could produce heterogeneity in our associated risk estimates. Moreover, as several of our included large population based cohort studies relied on ICD coding for risk factors and pre-eclampsia, their influence would be expected to underestimate the pooled pre-eclampsia event rates or the pooled relative risk for a given risk factor and pre-eclampsia.. We observed a high level of heterogeneity for the pooled relative risk values. Some degree of heterogeneity is to be expected, however, and could actually increase the generalizability of a meta-analysis over single studies.121. In meta-analyses of observational studies, variation can be caused by measurement bias, selection bias, confounding, and differences in effect modification.122 While only 24 of 92 studies described participant attrition, the average rate was just 3%, suggesting that attrition is uncommon in obstetrical studies, where the duration of follow-up is typically under 40 weeks. In our analyses, we used bivariate data to calculate the pooled event rates, pooled relative risk, and population attributable fraction.. Even for the risk factor of prior pre-eclampsia, cohort studies have observed a sensitivity of 73-87% and a specificity greater than 95% for recalling the condition at some later period.124 While this offers some degree of re-assurance that our current analytical approach provided precise and unbiased estimates of the rate of pre-eclampsia, a meta-analysis of individual patient data from cohort studies and randomized clinical trials (for example, of aspirin prophylaxis13) could assess the veracity of this statement.. Appendix 2: Study and participant characteristics for all 92 included cohort studies

Overview of Safety: URL: http://www.ncbi.nlm.nih.gov/pmc/articles/pmc8677993/ Paragraphs: Patients experiencing acute ischemic stroke or transient ischemic attack are commonly treated with clopidogrel and/or aspirin (mono- and dual-antiplatelet therapy) to minimize the risk for recurrent stroke. Updated data from systematic studies can be used to guide practice. The present study aimed to compare findings from systematic reviews and meta-analyses addressing the efficacy and safety of clopidogrel or aspirin – alone or in combination – in patients experiencing acute ischemic stroke or transient ischemic attack.. Acute ischemic stroke (AIS) is characterized by a lack of neurological control caused by a rapid loss of blood supply to part(s) of the brain.[1,2] Recurrent stroke often occurs a few days or weeks after initial AIS or transient ischemic attack (TIA), which emphasizes the importance of therapies aimed at preventing stroke reoccurrence.[1,3] Treatment strategies for AIS include thrombolytic, antiplatelet and anticoagulant, neuroprotective therapies, and endovascular treatment techniques. The most common therapy is dual antiplatelet therapy (DAPT; e.g., clopidogrel plus aspirin).[4–7] Numerous studies investigating the effectiveness and safety of DAPT and monotherapy have been conducted in the past 10 years.[8–12]. The highest standard of evidence used to support therapeutic efficacy and safety is from systematic analyses and meta-analysis of randomized controlled trials (RCTs). Due to the increasing number of systematic reviews and meta-analyses, it is necessary to combine various analyses into overviews to provide clinicians with readily accessible knowledge.. The

present review summarizes findings from systematic studies and meta-analyses addressing the efficacy and safety of clopidogrel or aspirin alone (monotherapy) or combinations (i.e., DAPT) for patients experiencing AIS or TIA.. Systematic reviews and meta-analyses that examined clopidogrel and/or aspirin for individuals experiencing acute AIS or TIA, published between 2010 and 2021, were included. Reviews including patients with AIS from all causes (including >50% carotid stenosis and large artery disease) were also included. A combination of major ischemic events, such as ischemic stroke, myocardial infarction (MI), or death, was the primary efficacy endpoint. Safety outcomes, reported as intracranial bleeding and major bleeding, were also considered.. Two authors searched for systematic studies and meta-analyses in the Cochrane Library, PubMed, Ovid, Scopus, EBSCO, and CINAHL databases published from inception to 2020 using the following keywords “Clopidogrel,” “Aspirin,” “Acute ischemic stroke,” “TIA,” “Dual-therapy,” “Mono-therapy,” “Efficacy,” and “safety.” For inclusion, all studies and evaluations of the clinical effects of DAPT were included. Based on the inclusion criteria described above, two authors assessed eligibility. Furthermore, two authors performed an unbiased quality assessment of the systematic reviews using the Risk of Bias in Systematic reviews tool and A Measurement Tool to Assess Systematic Reviews 2.. Efficacy and safety.. In the present overview of systematic reviews addressing the efficacy and safety outcomes of clopidogrel or aspirin alone (monotherapy) or combination (i.e., DAPT) for patients with ischemic stroke/TIA, we assessed seven systematic reviews encompassing 54 RCTs and four retrospective cohort studies including 133,502 patients. Overall, we revealed a large body of scientific data supporting DAPT to be superior to monotherapy in preventing recurrent stroke (ischemic and hemorrhagic) in patients experiencing ischemic stroke/TIA.. The time to initiation of DAPT after an ischemic stroke or TIA and the duration of therapy are the most important factors determining the efficacy of treatment. Rahman et al reported that to achieve maximum efficacy, DAPT should be initiated within 12 to 24 h after minor ischemic stroke (NIHSS < 3) or TIA, and the duration of therapy should be <1 month.[14] Hao et al suggested that DAPT administered within 24 h following a high-risk TIA or minor ischemic stroke decreased the risk for a future stroke by approximately 2%, with minimal significant side effects.[17]. How to cite this article: Yang Y, Huang Z, Zhang X. Efficacy and safety of clopidogrel and/or aspirin for ischemic stroke/transient ischemic attack: an overview of systematic reviews and meta-analysis. Medicine. 2021;100:50(e27804).

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Benefits/Risks: URL: http://www.ncbi.nlm.nih.gov/pmc/articles/pmc7140149/ Paragraphs: In combination with aspirin, clopidogrel is often used as part of dual antiplatelet therapy (DAPT) for the secondary prevention of ACS. Although newer, more potent P2Y12 inhibitors (prasugrel and ticagrelor) show a greater reduction in ischemic risk compared with clopidogrel in randomized trials of ACS patients, these newer P2Y12 inhibitors are often associated with an increased risk of bleeding. Deescalation of DAPT by switching from prasugrel or ticagrelor to clopidogrel may be required in some patients with ACS.. Furthermore, real-world studies of ACS patients have not confirmed the benefits of the newer P2Y12 inhibitors over clopidogrel. In patients with very high-risk TIA or stroke, short-term DAPT with clopidogrel plus aspirin for 21–28 days, followed by clopidogrel monotherapy for up to 90 days, is recommended. Clopidogrel monotherapy may also be used in patients with symptomatic PAD. In conclusion, there is strong evidence supporting the use of clopidogrel antiplatelet therapy in several clinical settings, which emphasizes the importance of this medication in clinical practice.. There has been an increase in the incidence and prevalence of cardiovascular disease (CVD) in the past few decades, including acute coronary syndrome (ACS), which has become a leading cause of mortality and morbidity worldwide [1–5]. The number of CVD-related deaths has increased by 12.5% during the past decade, accounting for approximately one-third of all deaths globally, mainly because of population growth and aging [3]. Patients with ACS have an increased risk of new ischemic events [6, 7], and ischemic heart disease and stroke are main contributors to global CVD burden [3].. In patients with CVD, platelet activation is triggered by an injured or dysfunctional vascular endothelium, which leads to platelet aggregation and subsequent pathologic thrombus formation and ischemic events [8]. Hence, antiplatelet therapy is the mainstay of the treatment and secondary prevention of CVD. The first

medication used as an antiplatelet agent was aspirin, a competitive cyclooxygenase inhibitor that reduces thromboxane A2 synthesis and inhibits platelet aggregation. The addition of a P2Y12 inhibitor as a second antiplatelet agent provides further suppression of platelet function through a complementary pathway and has shown significant benefits in reducing ischemic complications in patients with CVD.. Prasugrel and ticagrelor are third-generation P2Y12 inhibitors that were developed to address the slow onset and heterogeneous platelet inhibitory properties of clopidogrel. In patients with ACS, randomized controlled trials (RCTs) showed a greater reduction in recurrent ischemic events with these novel agents compared with clopidogrel [14–17]. However, the newer P2Y12 inhibitors were associated with an increased risk of nonfatal bleeding complications, thus limiting the benefit.. Over the past few years, several interesting questions concerning the use of P2Y12 inhibitors have emerged. Firstly, clopidogrel was included as the comparator agent in RCTs of ticagrelor and prasugrel [14–17], and although most patients with ACS receive ticagrelor or prasugrel, clopidogrel is still widely prescribed [18]. Secondly, the use of newer generation P2Y12 inhibitors is associated with increased costs and a higher risk of bleeding [16, 17, 19–21], as well as nonbleeding adverse effects (e.g., dyspnea with ticagrelor use). [22]. Hence, deescalation in antiplatelet therapy (i.e., switching from the newer more potent P2Y12 inhibitors to clopidogrel) has become part of stage-adapted therapy [23]. Lastly, real-world studies have not confirmed the benefits of the newer P2Y12 inhibitors over clopidogrel with regard to efficacy and safety. For example, the CHANGE DAPT study in ACS patients treated by percutaneous coronary intervention (PCI) showed that DAPT with ticagrelor was associated with an increased risk of adverse clinical and cerebral events compared with clopidogrel. In the last few years, thrombotic complications have decreased with the use of latest generation drug-eluting stents (DESs) and more potent P2Y12 inhibitors, while awareness of the impact of bleeding complications for adverse outcomes, including mortality, has increased [26]. As a result, reducing the risk of bleeding has become one of the major goals of DAPT, and guidelines recommend that the choice of treatment should consider the benefit-risk balance between the risk of ischemic and bleeding events [23].. The need for an optimal balance between ischemic benefit and bleeding risk, as well as reducing the risk of nonbleeding adverse effects as ticagrelor-related dyspnea, or/and the costs associated with long-term use of the newer P2Y12 inhibitors, has led to the development of DAPT “deescalation” (i.e., the switching from a more potent to a less potent P2Y12 inhibitor, usually clopidogrel) [23].. Deescalation has emerged as a medium- to long-term bleeding reduction strategy in patients after PCI, when thrombotic risk decreases but the bleeding risk persists, and in patients deemed unsuitable for long-term potent and more expensive antiplatelet agents (e.g., those with high bleeding risk or low socioeconomic status), and clinical trials have assessed the benefits of DAPT deescalation in patients with ACS [27, 28].. Platelet function testing (PFT) may be used to assess an individual's response to antiplatelet therapy [29, 30]. On-treatment high platelet reactivity (HPR) has been associated with an increased risk of cardiovascular events, including stent thrombosis, while low platelet reactivity (LPR) may lead to an enhanced response to P2Y12 inhibitors and an increased bleeding risk [29–31]. In the ARMYDA-2 study, PFT was used to assess whether a 600 mg loading dose of clopidogrel would achieve more rapid maximal platelet inhibition than a 300 mg loading dose, with a final goal of providing tailored antiplatelet therapy based on PFT results. RCTs assessing the clinical benefit of PFT to adjust antiplatelet therapy during or early after PCI, including GRAVITAS [34], TRIGGER-PCI [35], ARCTIC [36], and ANTARCTIC [37], have failed to demonstrate the clinical benefits of PFT. One reason for the failure of these studies may be that patients with HPR were randomized to clopidogrel continuation or switching to a more potent P2Y12 inhibitor, despite the fact that previous studies had already demonstrated that the positive predictive value of HPR for recurrent ischemic events is low (<60%).. The previous version of the European guidelines on myocardial revascularization recommended limiting the use of PFT or genetic testing to specific high-risk patients (e.g., those with a history of stent thrombosis, compliance issues, suspected resistance, or a high bleeding risk) [38]. However, given the increased bleeding risk with newer antiplatelet agents and their associated adverse effect that may lead to discontinuation, RCTs have investigated alternative deescalation strategies that may include a role for PFT.. [27]. Other limitations of TOPIC included its single-center and open-label design, the limited sample size, the number of patients lost to follow-up or crossing over to the other treatment arm exceeding the total number of events for many of the individual endpoints, a low-risk patient profile, no

data on MI without revascularization, and the study being underpowered for stent thrombosis. Despite these limitations, TOPIC was the first RCT to evaluate a deescalation strategy not guided by PFT. Furthermore, there was no significant difference in ischemic complications at 1 year with prasugrel or ticagrelor versus clopidogrel, resulting in a net clinical benefit in favor of switching to clopidogrel-based DAPT. In the TROPICAL-ACS study, PFT-guided DAPT deescalation (early switch from prasugrel to clopidogrel) was noninferior to prasugrel at 1 year with regard to the risk of cardiovascular death, myocardial infarction (MI), or stroke (referred to hereafter as major adverse cardiovascular events (MACEs)) after PCI for ACS [28]. This study was important as it represented a comparison of no PFT (newer P2Y12 inhibitor) versus a PFT-guided strategy. However, some limitations of TROPICAL-ACS were the fact that 40% of patients in the deescalation group required escalation back to prasugrel (thereby nullifying any bleeding advantage) and that it is difficult to replicate this study in clinical practice, as there were two therapeutic changes in 2 weeks.. Furthermore, no clopidogrel loading dose was used, no mention of transition events is provided, a higher than expected proportion of patients on prasugrel had HPR (15%), and data according to the type of antiplatelet therapy in the PFT-guided arm were not available [28]. Evidence was provided for considering HPR a modifiable risk factor, with HPR on prasugrel being associated with an increased risk for ischemic events and LPR being an independent predictor of bleeding both with prasugrel and with clopidogrel.. A recent RCT has investigated the benefits of genotype-guided selection of antiplatelet therapy in patients undergoing primary PCI with stent implantation (n = 2488) [40]. In this study, patients were assigned to receive P2Y12 inhibitor therapy based on early CYP2C19 genetic testing (genotype-guided group) or either ticagrelor or prasugrel (standard-treatment group). Over 12 months, genotype-guided therapy was noninferior to standard therapy with regard to the combined net adverse clinical outcome of death from any cause, MI, definite stent thrombosis, stroke, or PLATO major bleeding (5.1% versus 5.9%; 95% CI, −2.0 to 0.7; $P < 0.001$ for noninferiority).. However, the risk of the primary bleeding outcome was significantly reduced with genotype-guided therapy versus standard treatment (9.8% versus 12.5%; hazard ratio (HR), 0.78; 95% CI, 0.61 to 0.98; P=0.04). Of note, CYP2C19 genotyping in this study was performed using central laboratory assays or an on-site point-of-care device [40], which represent quick and easy methods for genotype-guided selection of oral P2Y12 inhibitors [41]. Furthermore, a personalized pharmacogenomic approach to selecting antiplatelet therapy for patients with ACS on the basis of a patient's genetic (such as CYP2C19) and clinical characteristics may reduce ischemic and bleeding events [42].. In addition, ethnic and racial variability in drug metabolism is also known to contribute to the polymorphic expression of metabolizing enzymes [41]. The benefits of testing CYP2C19 polymorphisms before prescribing clopidogrel in patients treated with drug-eluting stent implantation after PCI have been suggested by some studies, mainly in Asian populations [43]. However, genetic polymorphisms can explain only 12% of clopidogrel response variability [44], as suggested by the suboptimal concordance between the genotype and the phenotype ARCTIC-Gene substudy [45].. In a real-world study of Italian patients with ACS and diabetes (n = 559), DAPT was prescribed at hospital discharge in 88% of the patients (39%, 38%, and 23% received clopidogrel, ticagrelor, and prasugrel, respectively) [46]. The authors concluded that this confirmed the “paradox” of using a less effective drug to treat sicker patients in this high-risk population [46]. However, the features of increased ischemic risk may also predict a higher bleeding risk, which may also explain the prevalent use of clopidogrel.. The presence of diabetes has been shown to increase the risk of ischemic events but also significantly increases the risk of bleeding complications. Thus, data from this real-world study suggest that physicians use “very early deescalation” by prescribing at hospital discharge the medication they consider the best option to manage the thrombosis-bleeding risk trade-off in these high-risk patients.. Bleeding risk is of particular concern in elderly patients, who represent a large proportion of patients with ACS; however, this patient population was underrepresented in the PLATO and TRITON trials [16, 17]. In the recently presented POPular AGE study of patients aged ≥70 years with NSTE-ACS, after 12 months, treatment adherence was 76% with clopidogrel versus 51% with ticagrelor [47]. The most common reasons for discontinuation of ticagrelor were bleeding, initiation of oral anticoagulation, and dyspnea.. The relative risk of major or minor bleeding was significantly reduced by 26% with clopidogrel, with PLATO major bleeding reported in 4.4% of patients with clopidogrel versus 8% with ticagrelor or prasugrel. The net clinical benefit (defined as the composite of

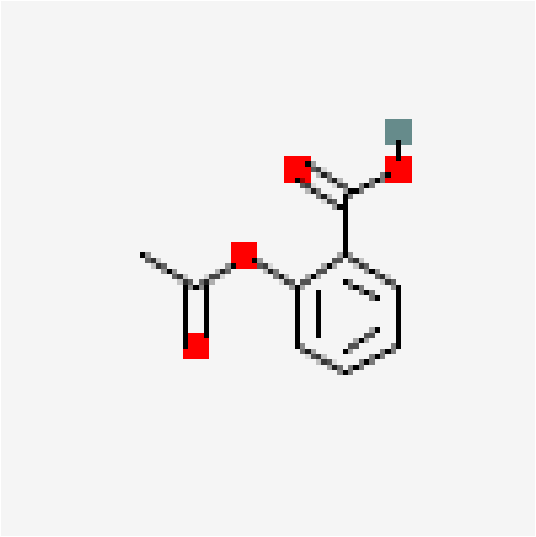
all-cause mortality, MI, stroke, or PLATO major or minor bleeding) showed an absolute risk difference of 3.4% in favor of clopidogrel, which did not reach the prespecified cutoff for noninferiority [47]. Similarly, the Elderly ACS 2 trial in patients aged >74 years with ACS undergoing PCI was prematurely terminated after a planned interim analysis found no significant difference between reduced-dose prasugrel and standard-dose clopidogrel with regard to the primary endpoint (composite of death, MI, disabling stroke, or rehospitalization for cardiovascular causes or bleeding). The GRAPE registry study investigated the long-term efficacy and safety of clopidogrel, prasugrel, and ticagrelor in real-world acute ACS patients who underwent PCI [53]. After 1 year of follow-up, the rate of MACEs was lower with prasugrel versus clopidogrel (4.4% versus 10.1%; HR, 0.53; 95% CI, 0.30 to 0.91) but was similar with ticagrelor and clopidogrel (6.8% versus 10.1%; HR, 0.78; 95% CI, 0.54 to 1.12). Compared with clopidogrel, the risk of any type of BARC-classified bleeding was higher with prasugrel (HR, 1.61; 95% CI, 1.33 to 1.95) and ticagrelor (HR, 1.81; 95% CI, 1.55 to 2.10).. An adjusted comparison showed no difference in any outcomes between prasugrel- and ticagrelor-treated patients. This study concluded that, in PCI-treated patients with ACS, prasugrel showed better anti-ischemic benefits over clopidogrel, although the use of prasugrel and ticagrelor was associated with an increased risk of bleeding events [53].. Of note, differences in baseline patient characteristics between the three P2Y12 inhibitor groups should be considered when interpreting the results of the GRAPE registry study [53]. Risk factors for ischemic or bleeding complications were more common among patients in the clopidogrel group than those receiving prasugrel or ticagrelor (i.e., they were older, higher proportions were female, and they had a history of hypertension, prior stroke, or impaired renal function) [53]. Similar patient selection biases were previously reported in real-world studies comparing clopidogrel with other P2Y12 inhibitors [54–56].. Furthermore, in the SWEDEHEART registry study of ACS patients treated with or without PCI, mortality rates were lower with ticagrelor versus clopidogrel, but significantly more patients on ticagrelor were treated with PCI and ticagrelor was preferentially used in patients with a low risk of bleeding and death (as indicated by lower CRUSADE and GRACE scores, respectively) [57, 58].. Current guidelines recommend the use of ticagrelor over clopidogrel in patients with ACS, mainly based on the results of the randomized PLATO trial [17]. In PLATO, ticagrelor significantly reduced the risk of MACEs by 16% at 12 months compared with clopidogrel (HR, 0.84; 95% CI, 0.77 to 0.92; $P < 0.001$) but was associated with an increased rate of noncoronary artery bypass graft-related major bleeding (4.5% versus 3.8%; P=0.03) [17].. The real-world CHANGE DAPT study evaluated the safety and efficacy of a ticagrelor- versus clopidogrel-based DAPT regimen in ACS patients treated with newer generation DESs [24]. In propensity score-adjusted multivariate analysis, ticagrelor was associated with an increased risk of the composite endpoint of net adverse clinical and cerebral events (defined as all-cause death, any MI, stroke, or major bleeding; HR, 1.75; 95% CI, 1.20 to 2.55; P=0.003) and major bleeding (HR, 2.75; 95% CI, 1.34 to 5.61; P=0.01) compared with clopidogrel [24].. These results are consistent with those of the GRAPE registry [53]. Moreover, in CHANGE DAPT, the increased bleeding risk with ticagrelor was observed despite more transradial procedures, more pump inhibitor use, and less glycoprotein IIb/IIIa inhibitor use, factors which may reduce periprocedural bleeding [24]. These data are also consistent with the TOPIC trial, in which switching from prasugrel or ticagrelor to clopidogrel 1 month after PCI was not associated with significant changes in ischemic outcomes but resulted in fewer bleeding events [27].. A characteristic of TIA and minor ischemic strokes is a rapid recovery from the symptoms of cerebral ischemia [67, 68]. This rapid clinical recovery may indicate the presence of at-risk ischemic tissue, a pathophysiologic trait that may be responsible for greater instability [68, 69]. Therefore, although TIA and minor stroke do not cause disabling symptoms, they often precede a more severe, disabling stroke, or other vascular events [70, 71]. A systematic review and meta-analysis found that the risk of stroke was 17% in the 90 days following a TIA. [71], and in a population-based database study, the combined risk of stroke, MI, or death was 22% over a 1-year follow-up after TIA [72]. A more recent TIA registry study showed that the risk of recurrent TIA or stroke remained similar over 1–5 years after the index event [73].. Early initiation of antiplatelet treatment is recommended for patients with noncardioembolic stroke or TIA to prevent recurrent stroke or cardiovascular events. In the population-based EXPRESS study, early treatment after TIA was associated with an 80% reduction in the 90-day risk of recurrent stroke [74]. In another study, the early risk of recurrent stroke was significantly lower in patients who received rapid TIA assessment and

treatment compared with standard care (9.7% versus 4.7%; P=0.05). Aspirin is the most common antiplatelet agent used to treat patients with a history of TIA or stroke as it reduces the risk of stroke recurrence. RCTs have demonstrated that DAPT may also be effective in these patients [76–79]. However, until recently, Italian guidelines stated that DAPT has to be considered only for selected high-risk TIA and minor stroke patients and for a short period (2-3 weeks) after stroke onset [80].. In the MATCH trial of 7,599 patients with a recent history of TIA or stroke, aspirin plus clopidogrel did not significantly reduce the risk of the composite primary endpoint of ischemic stroke, MI, worsening of peripheral arterial disease, vascular death, or rehospitalization for acute ischemia compared with placebo plus clopidogrel over 18 months (relative risk reduction, 6.4%; 95% CI, −4.6 to 20.4; P=0.244) [78]. However, the incidence of life-threatening bleeding was higher with aspirin plus clopidogrel versus clopidogrel alone (2.6% versus 1.3%; difference, 1.3%; 95% CI, 0.6 to 1.9; P < 0.0001).. Therefore, this study showed that adding aspirin to clopidogrel in high-risk patients did not significantly reduce major vascular events and was associated with an increased risk of major bleeding [78]. Moreover, bleeding complications remained constant over the study duration, which may suggest that there is a time margin after which the risk of bleeding might outweigh any ischemic benefit.. In the CHANCE trial of 5,170 Chinese patients with nondisabling ischemic stroke or TIA, clopidogrel plus aspirin for 21 days followed by clopidogrel alone for 69 days (DAPT) reduced the risk of recurrent ischemic and hemorrhagic stroke compared with aspirin alone by 32% (8.2% versus 11.7%; HR, 0.68; 95% CI, 0.57 to 0.81; P < 0.001) [81]. DAPT was associated with similar rates of moderate or severe bleeding (0.3% in each group; P=0.73) or hemorrhagic stroke (0.3% in each group; P=0.98) versus aspirin alone [81].. Interestingly, the clopidogrel plus aspirin group continued to have a significantly lower risk of stroke after 1 year of follow-up (HR, 0.78; 95% CI, 0.65 to 0.93; P=0.006) [82]. These findings indicate that DAPT with aspirin plus clopidogrel, initiated within 24 hours of the index event, is superior to aspirin alone for preventing the risk of stroke, without increasing the risks of hemorrhage in patients with TIA or minor stroke [81].. The generalizability of the CHANCE results may be questioned as the study was conducted entirely in China, in a population with a higher incidence of large-artery intracranial atherosclerosis than in other countries. In addition, CHANCE screened 41,561 patients with stroke or TIA to find 5,170 (12.4%) appropriate subjects to enroll, and patients with major ischemic stroke, who are at risk for hemorrhagic transformation, were excluded [81]. Finally, the results of this trial cannot be generalized beyond 90 days after the index event because thereafter the cumulative risk of bleeding with clopidogrel plus aspirin compared with aspirin alone offsets the benefits, as shown in earlier studies [77, 78, 83].. The POINT trial compared the safety and efficacy of clopidogrel plus aspirin versus aspirin alone in a non-Chinese population of 4,881 patients with nondisabling ischemic stroke or TIA [84]. Within 12 hours of symptom onset, patients were randomized to receive either clopidogrel (600 mg loading dose followed by 75 mg daily) plus aspirin (50–325 mg daily) or aspirin alone for 90 days. Clopidogrel plus aspirin was associated with a significantly lower risk of major ischemic events (ischemic stroke, MI, or ischemic vascular death) compared with aspirin alone (5.0% versus 6.5%; HR, 0.75; 95% CI, 0.59 to 0.95; P=0.02) and a higher risk of major hemorrhage at 90 days (0.9% versus 0.4%; HR, 2.32; 95% CI, 1.10 to 4.87; P=0.02). [84]. This higher risk of major hemorrhage was likely related to the longer duration of clopidogrel plus aspirin therapy and the high initial loading dose of clopidogrel (600 mg) used in the POINT trial. Notably, the findings of POINT confirm and expand the results of the CHANCE trial, supporting the hypothesis that the effective use of DAPT for early secondary stroke prevention is related to ethnicity [84].. These results, coupled with the findings of the CHANCE trial, indicate that the optimal duration of DAPT (clopidogrel plus aspirin) is 21–28 days. Moreover, the results of CHANCE suggest that, after the first phase of DAPT (22–90 days), clopidogrel alone is more effective than aspirin alone when compared from days 22 to 90, without an increased risk of bleeding [81]. A recent metaregression of 11 RCTs and 24,175 patients showed that the greatest benefit of DAPT in terms of prevention of recurrent stroke was observed in patients with a more elevated risk profile at baseline, increased stroke severity, or concurrent carotid artery disease and in patients who received early initiation of DAPT for ≤3 months. When considering the effect of newer P2Y12 inhibitors, the SOCRATES trial found that ticagrelor was not superior to aspirin in reducing the risk of stroke, MI, or death at 90 days in patients with acute ischemic stroke or TIA [87]. Although there was no significant difference in the rate of serious adverse events between groups, permanent

discontinuation was more common with ticagrelor, mainly due to dyspnea (a known adverse effect of ticagrelor [17, 88]) [87]. Interestingly, in a meta-analysis of 12 RCTs of aspirin versus control in the secondary prevention after TIA or ischemic stroke (n = 15,778), aspirin reduced the 6-week risk of recurrent ischemic stroke by 58% (HR, 0.42; 95% CI, 0.32 to 0.55; P < 0.0001) and disabling or fatal ischemic stroke by 71% (HR, 0.29; 95% CI, 0.20 to 0.42; P < 0.0001), but these benefits diminished with longer term use [89].. These data support the need for more intensive antiplatelet therapy (DAPT) in the early postevent period, when the ischemic risk is higher, and less intensive treatment thereafter to minimize the risk of bleeding complications.. The 2018 American Heart Association/American Stroke Association guidelines recommend the use of DAPT (aspirin and clopidogrel) for 21 days in patients with minor stroke (class of recommendation IIa, level of evidence B-R) [10], and the 2018 update of the Canadian Stroke guidelines suggests DAPT with clopidogrel plus aspirin for 21–30 days followed by monotherapy with aspirin or clopidogrel alone in very high-risk patients with TIA (ABCD2 score > 4) or minor stroke of noncardioembolic origin (evidence level A). Peripheral artery disease (PAD) is characterized by the narrowing or blockage of the arteries of the lower extremities due to atherosclerosis. The term “peripheral arterial diseases” encompasses all atherosclerotic diseases in arteries other than the coronary arteries and aorta [92]. PAD is a global health issue, with high levels of associated morbidity and mortality and an estimated overall prevalence of 3–10%, and 15–20% in those aged >70 years [93]. This burden is expected to increase significantly during the next 20 years, due to population aging and changes in atherosclerosis risk factors.. The risk factors for PAD include older age, diabetes, hyperlipidemia, hypertension, smoking, and atherosclerosis at other sites [95]. PAD is usually asymptomatic in the initial clinical stage. The most common first symptom is intermittent claudication (IC), defined as lower limb pain induced by physical activity that is rapidly relieved at rest [93]. Disease progression may result in critical limb ischemia (CLI), defined as pain at rest or ischemic ulceration and gangrene [93], which is associated with severe impairment of lower limb function and a high risk of amputation, especially in patients who cannot undergo a surgical or endovascular revascularization [96].. In addition, patients with PAD typically exhibit multivessel disease and may also present with coronary artery disease (CAD) or cerebral artery disease, which further reduces their quality of life [97]. Patients with symptomatic or asymptomatic PAD have an increased risk of all-cause mortality, cardiovascular mortality, MI, and stroke, even after adjustment for conventional risk factors [92, 95].. The aim of PAD management is to alleviate symptoms and prevent disease progression and complications [92]. Medical treatment includes lifestyle modifications, such as dietary changes and increased physical activity, and risk-factor modification, such as smoking cessation and the initiation of antihypertensive and lipid-lowering drugs [92]. As cardiovascular risk factors can lead to the development of atherosclerosis and atherothrombosis due to platelet activation [98, 99], antiplatelet therapy in addition to risk-factor modification is the hallmark treatment to reduce cardiovascular events in patients with PAD. The 2017 European Society of Cardiology (ESC)/European Society for Vascular Surgery (ESVS) guidelines stated that long-term single antiplatelet therapy is recommended in symptomatic PAD patients (class of recommendation I, level of evidence A) and in all patients who have undergone revascularization (class of recommendation I, level of evidence C) [92]. In both cases, clopidogrel may be preferred over aspirin (class of recommendation IIb, level of evidence B) [92]. However, antiplatelet therapy is not routinely indicated in patients with isolated asymptomatic PAD because of a lack of proven benefit.. These recommendations are based, at least in part, on the results of the CAPRIE trial [100]. In this study of 19,185 patients with a history of MI, ischemic stroke, or symptomatic PAD, the relative risk of the primary outcome (MACEs) was significantly reduced with clopidogrel versus aspirin (5.3% versus 5.8%; relative risk reduction, 8.7%; 95% CI, 0.30 to 16.5; P=0.043) [100]. Although these results suggested that long-term clopidogrel therapy may be superior to aspirin in reducing the risk of vascular events, these benefits were marginal.. However, the benefit of clopidogrel over aspirin was mainly driven by the large effect shown in patients with PAD, raising the possibility that clopidogrel and aspirin had equivalent efficacy in patients presenting with MI. In the subgroup of patients with symptomatic PAD at baseline (n = 6,452), clopidogrel was associated with a 22% reduction versus aspirin in the relative risk of MACEs (HR, 0.78; 95% CI, 0.65 to 0.93), as well as a significant reduction in the risk of cardiovascular death (HR, 0.76; 95% CI, 0.64 to 0.91).. In the CHARISMA trial, DAPT with clopidogrel plus aspirin was not more effective than aspirin monotherapy in

preventing the primary outcome of MACEs in patients with stable atherosclerotic disease or multiple cardiovascular risk factors (n = 15,603) [77]. A post hoc analysis of CHARISMA participants with PAD (n = 3,096) showed that the primary outcome occurred at a similar rate with clopidogrel plus aspirin versus aspirin monotherapy (7.6% versus 8.9%; HR, 0.85; 95% CI, 0.66 to 1.08; P=0.18) [101].. However, DAPT reduced the risk of other secondary endpoints, such as MI (HR, 0.63; 95% CI, 0.42 to 0.96; P=0.029) and the rate of hospitalization for ischemic events (HR, 0.81; 95% CI, 0.68 to 0.95; P=0.011). There was an increased rate of minor bleeding with clopidogrel plus aspirin versus aspirin alone (OR, 1.99; 95% CI, 1.69 to 2.34; P < 0.001), although the rates of severe, fatal, or moderate bleeding did not differ between the groups [101].. In a post hoc analysis of the PLATO trial [17], patients with coronary disease and concurrent PAD showed some ischemic benefit with ticagrelor versus clopidogrel [102], and in the PEGASUS-TIMI 54 trial of patients with prior MI (n = 21,162), those with concurrent PAD (n = 1,143) showed a significantly greater reduction in the absolute risk of MACEs with ticagrelor compared with patients without PAD [103].. Most studies investigating the effect of antiplatelet treatment in high-risk atherothrombotic diseases have focused on patients with ACS and stable CAD. The EUCLID trial was designed to evaluate antiplatelet therapies with ticagrelor versus clopidogrel in patients with symptomatic PAD (n = 13,885) [104]. In this trial, the incidence of the primary efficacy endpoint (MACEs) was similar with ticagrelor and clopidogrel (10.8% versus 10.6%; HR, 1.02; 95% CI, 0.92 to 1.13; P=0.65), and the primary safety endpoint (major bleeding) occurred in 1.6% of the patients in both groups (HR, 1.10; 95% CI, 0.84 to 1.43; P=0.49).. The incidences of acute limb ischemia and revascularization were similar between groups, whereas the relative risk of ischemic stroke was significantly reduced with ticagrelor versus clopidogrel (1.9% versus 2.4%; HR, 0.78; 95% CI, 0.62 to 0.98; P=0.03). There were fewer fatal bleeding events with ticagrelor but more discontinuations of ticagrelor than clopidogrel, including discontinuations due to bleeding [104]. Hence, despite showing some benefit in patients with PAD in earlier studies, monotherapy with ticagrelor, a more potent P2Y12 inhibitor than clopidogrel, failed to demonstrate any benefit over clopidogrel monotherapy in reducing the rate of adverse cardiovascular events in the EUCLID study and showed a similar rate of major bleeding.. Interestingly, the COMPASS trial of rivaroxaban use (with or without aspirin) in patients with stable CVD [105] may help to enlighten our understanding of the role of antiplatelet and antithrombotic strategies in patients with PAD. In COMPASS, which included patients with established CAD, PAD, or both, the primary efficacy endpoint (MACEs) occurred in 4.1% of patients in the rivaroxaban plus aspirin group, 4.9% in the rivaroxaban monotherapy group, and 5.4% in the aspirin monotherapy group, representing a 24% reduction in the relative risk of MACEs with low-dose rivaroxaban plus aspirin versus aspirin alone (HR, 0.76; 95% CI, 0.66 to 0.86; P < 0.001). [105]. Rivaroxaban plus aspirin was also associated with a reduction in all-cause mortality compared with aspirin alone (3.4% versus 4.1%; HR, 0.82; 95% CI, 0.71 to 0.96; P=0.01). In contrast, rivaroxaban alone was associated with a significant reduction in the risk of MACEs versus aspirin alone (HR, 0.90; 95% CI, 0.79 to 1.03; P=0.12). More major bleeding events were reported with either rivaroxaban plus aspirin (3.1%) or rivaroxaban monotherapy (2.8%) than with aspirin monotherapy (1.9%; P < 0.001 for both comparisons). [105]. In a prespecified analysis of patients with PAD from the COMPASS trial (n = 7,470), there were a 28% reduction in the risk of MACEs, a 46% reduction in the risk of major adverse limb events (MALEs), and a 70% reduction in the risk of major amputations with rivaroxaban plus aspirin versus aspirin alone [106]. However, increased rates of major and minor bleeding were observed with rivaroxaban plus aspirin compared with aspirin monotherapy.. Deescalation from ticagrelor or prasugrel to clopidogrel is recommended in ACS patients to obtain an optimal balance between ischemic benefit and bleeding risk and to reduce the risk of adverse effects (such as dyspnea) and/or the increased costs associated with long-term use of newer P2Y12 inhibitors. Genotype-guided DAPT deescalation may be favored. Moreover, clopidogrel may be considered the first choice of antiplatelet therapy in elderly patients with ACS. The results of real-world studies have questioned the superior efficacy of newer P2Y12 inhibitors over clopidogrel for ACS patients treated by PCI.. In patients with stroke or very high-risk TIA, intensive DAPT with aspirin plus clopidogrel should be administered for 21–28 days after the acute event, followed by less intensive treatment for up to 90 days, to minimize the risk of bleeding complications; clopidogrel is potentially more effective than aspirin as antiplatelet monotherapy. In patients with symptomatic PAD, or those who have undergone

peripheral revascularization, clopidogrel is the preferred agent for antiplatelet monotherapy based on the results of the CAPRIE and EUCLID trials.. In conclusion, given the strong evidence supporting the efficacy, safety, and cost-effectiveness of clopidogrel for antiplatelet therapy in several different clinical settings, its familiarity in the medical community, its wide availability, and low cost, clopidogrel remains an important medication in clinical practice and a mainstay of antiplatelet therapy.



Img 1: Molecule structure of aspirin (Source: PubChem)