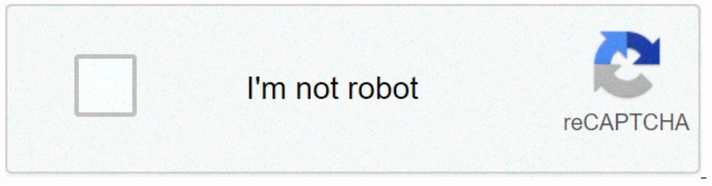

Continue

Treatment guidelines for upper gi bleed

Diagnosis and management of non-variceal upper gastrointestinal bleeding: European Society of Gastrointestinal Endoscopy (ESGE) Guideline. Goutnek IM, Dumonceau JM, Kuipers EJ, Lanas A, Sanders DS, Kurien M, Rotondano G, Hucl T, Dinis-Ribeiro M, Marmo R, Racz I, Arezzo A, Hoffmann RT, Lesur G, de Franchis R, Aabakken L, Veitch A, Radaelli F, Salgueiro P, Cardoso R, Maia L, Zullo A, Cipolletta L, Hassan C. Gralnek IM, et al. Endos. 2015 Oct;47(10):a1-46. doi: 10.1055/s-0034-1393172. Epub 2015 Sep 29. Endoscopy. 2015. PMID: 26417980 This policy covers how bleeding in the upper gastrointestinal area can be effectively managed in adults and adolescents aged 16 and over. It aims to identify which diagnostic and therapeutic steps are useful so that hospitals can develop a structure in which clinical teams can provide an optimal service for people developing this condition. In August 2016, we added a footnote to Recommendation 1.7.1 that approved proton pump inhibitors and H2 receptor antagonists for use and classified as off-label. Recommendations This directive contains recommendations on: who is it for? Health professions People over 16 years of age with acute gastrointestinal bleeding in the upper gastrointestinal area and their families and caregivers Is this policy up to date? We reviewed this directive in November 2018. We have not found any new evidence to affect the recommendations of this directive. Guideline Development Process How we develop NICE guidelines This policy was formerly referred to as acute upper gastrointestinal bleeding: management. The recommendations in this guideline represent the view of NICE, which was found after careful consideration of the available evidence. Professionals and practitioners are expected to take full account of this Directive in the exercise of their judgment, together with the individual needs, preferences and values of their patients or of the people who use their services. It is not mandatory to apply the recommendations and the Guideline does not override the responsibility to take decisions appropriate to the circumstances of the individual in consultation with them and their families and carers or guardians. Any problems (undesirable events) related to a medicinal product or medical device used for treatment or in a procedure should be reported to the Medicines and Healthcare Products Regulatory Authority using the Yellow Card Scheme. Local commissioners and healthcare providers are responsible for ensuring that the directive can be applied when individual professionals and people using services wish to use it. They should do so within the framework of local and national priorities for the financing of develop services and in the light of their obligations, take due account of the need to eliminate unlawful discrimination, promote equal opportunities and reduce health inequalities. Nothing in this directive should be interpreted in a way that would be incompatible with compliance with those obligations. Commissioners and providers have a responsibility, responsibility, clean health and care system and should assess and reduce the environmental impact of implementing the NICE recommendations wherever possible. Acute bleeding in the upper gastrointestinal area (UGIB) is common, but the annual incidence has decreased: from 78 to 61 cases in 100,000 people between 2001 and 2009 in a survey (1). Nevertheless, the 30-day mortality rate remains high at up to 11% (2). The most recent guidelines for the management of UGIB were published primarily between 2010 and 2015, among others from our group (2003, with an update in 2010) (3, 4), the American College of Gastroenterology (2012) (5), the American Society for Gastrointestinal Endoscopy (2012) (6), the National Institute for Health and Care Excellence (NICE) (in 2012) (7) and the European Society of Gastrointestinal Endoscopy (in 2015) (8). More recently, the guidelines of the Asia-Pacific Working Group 2018 have been updated (9). The management of UGIB has evolved with new endoscopic techniques, and the pharmacological landscape has changed. Anticoagulants or platelet therapy, including combination therapy, is becoming more common, significantly increasing the risk of UGIB (10). Therefore, the International Consensus Group agreed that an update of the recommendations for the management of UGIB (4) from 2010 is warranted. Similar to the 2003 (3) and 2010 (4) guidelines, this update focuses on diereanimation and risk assessment; pre-endoscopic, endoscopic and pharmacological conduction; and secondary prophylaxis for recurrent UGIB. Specific PICO issues (patient population, intervention, comparator and outcome) were developed by the Kochairs (A.N.B. and M.B.), the Steering Committee (L.L., M.A., J.S. and E.J.K.) and the METHODologists of GRADE (Grading of Recommendations Assessment, Development and Evaluation) (F.T. and G.I.L.) The sources included the basis of evidence of previous guidelines (3, 4) and English-language literature research by MEDLINE, EMBASE (Elsevier), the Cochrane Database of Systematic Reviews (Wiley) and the Cochrane Central Register of Controlled Trials (Wiley), conducted by the editorial board of the Cochrane Upper Gastrointestinal and Pancreatic Diseases Group at McMaster University. Initial searches were carried out from the foundation of the database until 2 April 2018, with additional, focused searches until mid-May 2018. Important search terms and details of the search strategies are listed in Supplement 1. Conference abstracts, case reports and animal testing were excluded. Teams of reviewers (A.B., M.B., X.C., L.L., G.I.L. and F.T.) presented titles and abstracts in two-demund productions and independently of each other and received complete texts of potentially relevant studies. The examiners also scanned bibliographies of retrieved Reviews. The Kochairs, the Steering Committee and the Methodologies then selected the studies that are relevant to each PICO issue. Discrepancies in inclusion have been highlighted by Modified version of AMSTAR-2 (A Measurement Tool to Assess Systematic Reviews) (11) was used as a decision-making tool to evaluate the methodological quality of existing systematic reviews. As a base source, we have selected the most up-to-date of the well-executed, relevant systematic evaluations. Selected assessments were used in whole or in part (with only some of the following components: studies, study characteristics, numerical data extractions, forest areas or risk-of-bias tables) and were updated or improved as needed by adding new studies, removing inappropriate studies or further evaluating the quality of the studies included (supplement Annex 2). The methodologies (F.T. and G.I.L.) assessed the risk of bias, indirectness, inconsistency, inaccuracy and other limitations (including publication biases) of the evidence using the GRADE approach (12). The overall quality of the evidence (QoE) was rated as very low, low, moderate or high for each recommendation. For each PICO question, evidence profiles (GRADE tables) were created that contained clear descriptions of benefits and damage, as well as a QoE assessment for individual results. The profiles, systematic checks and meta-analyses were made available to the voting participants 1 week before the consensus meeting (Supplement 2). A declaration (A1) met the best practice criteria (13). The Consensus Group agreed that this recommendation was clinically obvious and that the collection and analysis of evidence was unnecessary. Participants in the multidisciplinary consensus group came from 11 countries and included gastroenterologists, a cardiologist, a hematologist, a radiologist, a surgeon and an emergency physician. Up to 20 voting participants participated in the meeting for each statement (numbers varied, mainly due to travel difficulties), 2 non-voting GRADE methodologies and one non-voting moderator (J.K.M). The Kochairs, other members of the Steering Committee and Methodologies compiled a list of new and old statements presented to the group via an anonymous, web-based consensus platform (ECD Solutions). By conference call, the members of the Steering Committee agreed on the explanations justifying inclusion in the Guideline by focusing on priority areas. With a modified Delphi procedure (14), all voting participants have modified and completed the new statements. After examining the evidence profiles, participants anonymously voted on their degree of agreement or rejection of each statement and submitted comments. The votes were non-binding and were designed to measure the extent of the agreement and the pattern of uncertainty of evidence in order to allocate time for during the meeting. The Canadian Association of Gastroenterology (CAG) office tabulated the votes and comments and presented the group's findings. Although these were initially discussed in the form of declarative statements, they were dealt with by the methodologies before the consensus on specific PICO issues. Edited. At a two-day consensus meeting in May 2018, the Group applied the GRADE Evidence Decision Framework to move from evidence to recommendations by assessing 7 key criteria: the balance between desirable and undesirable effects, quality (safety) of evidence, variability of patients' values and preferences, resource needs, cost-effectiveness, acceptance and feasibility (supplement Annex 2) (15-17). Participants voted as yes, uncertain or no to the direction of the PICO question (for or against). Consensus for or against a particular strategy was reached when at least 75% of participants voted 'yes' or 'no'. On PICO issues on which agreement was reached, the Group then discussed the strength of the recommendation (strong vs. conditional) by taking into account the factors involved in the taking of evidence of decision-making (18). In cases of low or very low QoE, unless at least one of the other 3 factors was overwhelmingly strong, the strength of the recommendation (without voting) with the expression we suggest would be conditionally reduced. If the explanation warranted a vote and at least 75% of the participants voted strongly, the recommendation with the sentence we recommend would be described as strong. No consensus was reached on 4 PICO questions (no recommendation A to D) as less than 75% of participants voted either yes or no. No relevant statements have been developed for these questions, but the relevant evidence and discussions are briefly summarized in the text. The lead procedure was monitored by the CAG Clinical Affairs Committee to ensure methodological quality and a transparent, unbiased, evidence-based decision-making process. The recommendations are based on findings from the literature and consensus discussion and may not fully reflect product labelling for a particular country. The manuscript was originally written by the co-chairs (A.N.B. and M.B.) and the GRADE experts (F.T. and G.I.L.). It was reviewed and revised by the members of the Steering Committee (E.J.K., J.S., L.L. and M.A.) before being submitted to the full consensus group for feedback. Finally, the manuscript was published on the CAG website and members were asked by email to submit comments over a two-week period. In accordance with the CAG Directive, written information on conflicts of interest for the 24 months preceding the consensus meeting was provided by all participants and made available to the Group. The consensus meeting was financed by unrestricted, weapon-long grants to the CAG from the Institute of Nutrition, Metabolism and Diabetes of the Canadian Institutes of Health Research and the Saudi Gastroenterology Association. The CAG all aspects of the meeting; the sources of funding were not involved in or knowledgeable in any part of the process, from the development of search strings and declarations to the preparation and approval of these guidelines. Each statement is followed by probative force on the basis of GRADE analyses. GRADE analyses. a discussion of the evidence. The results of the vote are in Table 1, together with summaries of the new recommendations from this Consensus, recommendations revised from the 2003 and 2010 Guidelines (3, 4), and recommendations that remained unchanged because most of the Group felt that they did not currently require revision (3, 4). Table 1. Summary of consensus recommendations for the management of UGIB*Resuscitation should be initiated for patients with acute UGIB and hemodynamic instability. (Indicates a Good Practice statement.) Fluid resuscitation should be initiated in patients with UGIB and hemodynamic instability, as hemorrhagic shock can lead to multi-organ failure and death. The objectives of fluid resuscitation are to restore end organ perfusion and oxygenation of the tissue, while steps are taken to control bleeding. Uncertainty remains regarding the type of fluid (colloid vs. crystaloid) and the rate and timing of resuscitation (aggressive vs. restrictive). A systematic review of Cochrane with 70 randomised controlled trials found no difference in mortality between critically ill patients, the colloids (albumin or plasma protein fraction, hydroxyethyl starch, modified gelatin, dextran, colloids in hypertonic crystallooid or colloids in isotonic crystallooid) and those receiving crystallooids (normal saline, wrestling lactate or hypertonic saline) for resuscitation of fluids (19). A small randomized study conducted in patients with UGIB with hemorrhagic shock found no statistically significant difference in mortality between hypertonic saline extras and ringer lactate (relative risk [RR], 0.18 [95% CI, 0.02 to 1.41]) (20). A large study published after the systematic review, which included 2857 seriously ill patients, showed no difference in 28-day mortality between patients receiving colloids and those receiving crystalloids (21). The study showed an unexpected borderline reduction in 90-day mortality in patients receiving colloids (RR, 0.92 [CI, 0.86 to 0.99]) – a finding considered hypothesis-generating (21). Since the current findings do not show that colloids increase survival rates compared to crystalloids and because colloids are more expensive, the consensus group agreed that routine use in clinical practice is not justified (19). There is also uncertainty about the type of crystallineoid used in the resuscitation of liquids. A recent randomised study of 15,802 critically ill patients showed a slight reduction in acute renal injury (odds ratio [OR], 0.91 [CI, 0.84 to 0.99]) and possible slight reduction in hospital mortality (10.3% vs. 11.1%; P = 0.08) with symmetrical crystalloids (e.B. wrestler lactate) vs. saline (22). Animal models have shown that early aggressive resuscitation of fluids to increase blood pressure to normal can worsen blood loss, disrupt clotting and increase mortality (23, 24). The alternative is a restrictive or antihypertensive resuscitation in which fluid fluid Endpoint is smaller than Normotension. A systematic review of Cochrane included 6 randomized

trials that examined the timing and volume of fluid administration in 2128 patients with bleeding. The studies were heterogeneous in terms of patient types, clinical settings, fluid types and resuscitation protocols (25). None found restrictive resuscitation of liquids (with a delayed or smaller volume of liquids) as worse than a more aggressive fluid resuscitation (with an early or larger volume of liquid) in terms of mortality (25). Two randomized studies published since the review also found no differences in mortality between restrictive and aggressive resuscitation in patients with trauma and hemorrhagic shock (26, 27). The consensus group agreed that the evidence was insufficient to make a recommendation on restrictive resuscitation of liquids. The important problem in patients with hemorrhagic shock due to trauma or UGIB is to stop the bleeding and at the same time minimize the hemodynamic compromise. For patients with acute UGIB, we recommend using a Glasgow Blatchford score of 1 or less to identify patients who have a very low risk of bleeding or mortality and therefore may not require hospitalization or inpatient endoscopy. (GRADE: conditional recommendation, inferior evidence) In patients with acute UGIB, the consensus group could not recommend or oppose the use of the rockall pre-endoscopic prognosis scale to identify patients who have a very low risk of bleeding or mortality and therefore may not require hospitalization or inpatient endoscopy. (GRADE for PICO: Very inferior evidence) For patients with acute UGIB, we recommend not to use the AIMS65 prognosis value to identify patients who have a very low risk of bleeding or mortality and therefore may not require hospitalization or inpatient endoscopy. (GRADE: conditional recommendation, inferior evidence) Evidence profiles for the 3 most studied prognostic scores (Glasgow Blatchford [GBS], pre-endoscopic rockall and AIMS65) were considered separately. The QoE review focused on studies evaluating the use of pre-endoscopic assessment systems to identify patients at a very low risk of adverse outcomes. No randomized studies were identified that directly evaluated the clinical impact of use compared to the use of prognostic scales. Therefore, the evidence was derived from before-and-after studies (28) and diagnostic test accuracy studies that determined the replacement result of the diagnostic accuracy of the balance. A before-and-after study by Stanley and colleagues (28) evaluated a strategy to prevent the admission of emergency patients with UGIB who were predicted to have a very low risk of adverse outcomes (GBS of 0). This reduced the number of hospitalizations, and no difference in safety results was found, although the study was not driven for safety results. The relevant evidence included 2 high-quality systematic reviews and meta-analyses of diagnostic test accuracy studies (7, 29) and 2 2 Studies characterised by their quality and sample sizes (30, 31). The sensitivity of low cutoff scores for the detection of patients at high risk of adverse clinical outcomes was very good for GBS (0.99) and pre-endoscopic rockall scores (ranking, 0.93 to 0.96, but with more heterogeneity) and lower for AIMS65 (range, 0.78 to 0.82) (Annex Table 1) (7, 29-31). Annex Table 1. Pooled sensitivity and specificity of pre-endoscopic scoring systems to identify high-risk patients for adverse clinical outcomes For GBS and AIMS65, QoE was low, with evidence of indirectness, inaccuracy and inconsistency downgraded. For the pre-endoscopic Rockall score, QoE was very low, with the evidence downgraded for the same reasons and risk of distortion. The use of prognostic scales and the early discharge of low-risk patients have the potential to reduce the need for endoscopy, hospitalizations and associated costs without increasing the damage. Sensitivity in identifying high-risk patients is a critical outcome, as it is important not to mistakenly classify a high risk as low-risk when making decisions about early discharge. Specificity is less crucial because low specificity leads to more low-risk patients being admitted to hospital, but not in high-risk patients who are discharged. Patient preferences should also be taken into account; some patients prefer diagnostic safety, while others prefer not to be admitted to hospital. Other factors in taking early discharge into account include urban and rural environment, access to hospital or ambulance services, access to endoscopy a-hours and reimbursement issues. Whether the use of a prognostic scale leads to better patient outcomes than the use of a clinical judgment alone is not known. As the clinical judgment cannot be standardized, the Consensus Group agreed that the use of a prognostic assessment system would help to ensure consistent risk assessment and communication. Education is now necessary to embed an assessment tool in clinical practice (e.B. in electronic medical records). The consensus group proposes GBS as the preferred prognostic tool due to its high sensitivity (misclassification of ≤1% of high-risk patients as low-risk). The pre-endoscopic Rockall scale has good sensitivity, but can misclassify 4% to 7% of high-risk patients. In view of differing views on threshold sensitivity for discharge, the Consensus Group could not recommend or not of the pre-endoscopic Rockall score. The AIMS65 is designed to be used with high cutoff levels to identify high-risk patients (32) rather than low-risk patients for safe discharge. The consensus group suggests that YOU do not use AIMS65 in this setting, as even at low cutoff levels, about 20% of high-risk patients can be wrongly classified as low-risk. In patients with acute UGIB without underlying cardiovascular disease, we recommend giving blood transfusions to patients with hemoglobin levels of less than 80 g/L. (GRADE: conditional Inferior evidence)Evidence of a hemoglobin threshold for the efficacy and safety of red blood cell transfusions was found in a summary of studies comparing restrictive (70 to 80 g/L) compared to liberal (90 to 100 g/L) transfusion thresholds for patients with acute UGIB (33). In the systematic review of 5 randomised controlled trials in patients with UGIB (n = 1965), a restrictive transfusion was associated with a lower risk of overall mortality (RR, 0.65 [CI, 0.45 to 0.97]) and further bleeding (RR, 0.58 [CI, 0.40 to 0.84]) (33) (Annex Table 2). No subgroup differences were found in the risks of myocardial infarction, stroke or transient ischemic attack or acute kidney injury (33) or in the rate of surgical or radiological interventions between the two strategies (34, 35). These data have been downgraded due to the serious risk of bias and serious indirectness. However, the QoE for the superiority of the restrictive transfusion strategy is (less indirect) than the QoE for certain transfusion thresholds. Annex Table 2. Pooled relative and absolute risks of adverse outcomes. After restrictive or liberal RBC transfusion thresholds in patients with UGIBTwo further systematic reviews and meta-analysis, the supporting data on patients in different clinical environments (cardiac surgery, orthopaedic surgery, vascular surgery, acute blood loss or trauma, critical care, acute myocardial infarction and haematological cancer) including UGIB, found no difference in 30-day mortality, re-bleeding, heart events, myocardial infarction or stroke between the two strategies in the combined patient groups (36, 37). The data indicate that a restrictive transfusion strategy is beneficial in patients with UGIB (33) and is not associated with adverse events (36, 37). The restrictive threshold led to a decrease in the proportion of patients exposed to transfusions (36, 37) and the average number of transfunded units (33). A study evaluating direct and indirect costs reported that the total cost per red blood cell in 2008 was about US 760 US dollars (38). Although the cost per unit can vary widely per institution, a restrictive strategy is probably the most cost-effective. Only 3 randomised studies provided mortality data in the UGIB-specific review, with 2 high-quality studies providing 98.2% of the weight in metaanalysis (33). A single-centre study showed a reduction in mortality and bleeding with a haemoglobin threshold of 70 g/L compared to 90 g/L (35), while a randomised cluster study did not mortality or bleeding with a threshold of 80 g/L compared to 100 g/L (34). Although they are not hemoglobin thresholds, 1 study in UGIB patients with hemodynamic instability found no difference in mortality between early and delayed blood transfusion; However, the study was understated (RR, 5.4 [CI, 0.3 to 107.1]) (39). Factors that may influence the timing of transfusions are the availability of vein puncture personnel, vein puncture personnel, assessments, time of blood typing, availability of units, hemodilution factors and degree of hemodynamic stability. In addition, some patients may have underlying, undiagnosed cardiovascular disease, potentially putting them at higher risk of negative outcomes. Therefore, the consensus group suggested that a more conservative hemoglobin threshold of 80 g/L with a target of more than 80 g/L is cautious. The threshold recommendation does not apply to patients with exsanguinating bleeding. When adjusting the acute blood loss, hemoglobin levels can initially remain unchanged from the baseline due to plasma equilibrium times. In such situations, transfusion should not only be dictated by the current hemoglobin level, but should take into account the predicted decrease in hemoglobin and the clinical status of the patient. In patients with acute UGIB and underlying cardiovascular disease, we recommend giving blood transfusions at a higher hemoglobin threshold than in patients without cardiovascular disease. (GRADE: conditional recommendation, very inferior evidence) Two meta-analyses, 1 in patients with UGIB (33) and 1 in patients with cardiovascular disease in different clinical environments (40), included an analysis of 1 randomized study (34) that provided subgroup data on patients with and without cardiovascular disease. This small, undermotorized study (34) found no significant difference between liberal (hemoglobin threshold, 100 g/L) and more restrictive (hemoglobin threshold, 80 g/L) Transfusion in relation to mortality (RR, 4.10 [CI, 0.86 to 19.47]) (40) or further bleeding in adults with or without ischaemic heart disease (RR, 0.50 [CI, 0.23 to 1.12] and RR, 0.69 [CI, 0.13 to 3.77]) (33). This study was downgraded due to serious risk of bias (lack of glare, possible selection bias) and very serious inaccuracy (very small sample size). A re-analysis of the overall data from the meta-analysis of 11 studies in patients with cardiovascular disease (40) showed no significant differences between the liberal (90 to 113 g/L) and the restrictive (70 to 97 g/l) strategies in relation to 30-day mortality (RR, 0.87 [CI, 0.67 to 1.13]) or acute pulmonary edema (RR, 1.58 [CI, 0.55 to 4.53]), however, found a reduced risk of cardiovascular events (RR, 0.56 [CI, 0.37 to 0.85]) with the liberal transfusion strategy. This analysis has been downgraded due to the serious risk of bias, very serious indirectness and serious inaccuracy. Due to the different results of the studies and the meta-analyses, several sensitivity analyses were carried out. Although the results became less accurate, the direction of action did not change. The data that a more liberal hemoglobin threshold for transfusions may be associated with a lower risk of cardiovascular events in patients with cardiovascular disease. This is based on data from studies in different clinical environments with heterogeneous patient subgroups (e.B. patients with coronary syndromes, ischemic heart disease, heart disease, peripheral vascular disease or stroke or those with only cardiovascular risk factors such as high blood pressure and diabetes). The impact of liberal and restrictive transfusion strategies may vary between different subgroups. In addition, different definitions were used for the restrictive and liberal groups, including hemoglobin levels and the presence of anemia, and hemoglobin cutoff levels varied. Based on these limited data, the consensus group proposed to consider a higher hemoglobin threshold in patients with cardiovascular disease than in patients without cardiovascular disease (<80 g/L; statement A4). The group did not recommend a specific cutoff and explained that a cutoff would depend on other factors, including the clinical status of the patient, the nature and severity of cardiovascular disease and the severity of bleeding. NICE's guidelines recommend a higher degree of transfusion for patients with cardiovascular disease than for patients without cardiovascular disease, while AABB (formerly known as the American Association of Blood Banks) (41) recommends a hemoglobin threshold of 80 g/L for patients with cardiovascular disease, compared to 70 g/L for patients without cardiovascular disease. Again, this statement does not apply to patients with exsanguinating bleeding who may need a more liberal transfusion. In patients with acute UGIB who receive anticoagulants (vitamin K antagonists, direct oral anticoagulants), we recommend not to delay endoscopy (with or without endoscopic hemostatic therapy). (GRADE: conditional recommendation, very inferior evidence) No systematic reviews, randomised or observational studies were found specifically to treat the timing of endoscopy as the primary outcome in patients receiving anticoagulants. A retrospective cohort study in patients with acute UGIB (47%) or lower gastrointestinal bleeding compared 157 patients with anticoagulants with 157 matching control participants (42). An internationally normalized ratio (INR) of more than 2.5 was observed in 22.9% of patients receiving anticoagulants, compared to 6.4% of the participants. No statistically significant differences in bleeding rates were observed (13.4% vs. 15.9%; P = 0.52) or thromboembolism (5.7% vs. 3.2%; P = 0.68) between the anticoagulant and control groups. In patients receiving anticoagulants, early endoscopy (<24 hours after commencement) was not associated with bleeding (OR, 0.7 [CI, 0.3 to 1.8]), thromboembolic events (OR, 0.5 [CI, 0.1 to 2.1]) or endoscopic side effects (0%) Connected. Bleeding was also not associated with an INR of 2.5 or higher (OR, 0.7 [CI, 0.2 to 2.3]). In for this, thromboembolism was probably associated with an INR of 2.5 or more (OR, 7.3 [CI, 1.5 to 35.3]) and the use of a reversing agent (OR, 4.1 [CI, 1.0 to 16.5]) (42) due to a rapid correction of INR peridoscopeic (43, 44). No differences in denbleeding or thromboembolism risks were found between patients receiving direct oral anticoagulants (DOACs) and patients receiving warfarin. However, Use of warfarin had a greater need for transfusion (4.3 ± 5.9 units vs. 2.2 ± 3.1 units; P = 0.046). The perienoscopic use of a reversing agent (vitamin K) was associated with a higher risk of thromboembolism, but not with re-bleeding, while a coagulant-inhibiting interruption did not affect the risk for both outcomes. The results of anticoagulant use in patients with UGIB were not reported separately, but UGIB was associated with a higher rate of endoscopic therapy and transfusions compared to lower gastrointestinal bleeding, suggesting that the combined results may not be fully generalizable for patients with UGIB (42). This study was downgraded due to serious indirectness and inaccuracy. For patients receiving anticoagulants, the 2010 UGIB guidelines suggested correcting coagulopathy but not delaying endoscopy (4). This recommendation was made on the basis of cohort studies suggesting that early endoscopy (≤24 hours) in patients using anticoagulants can be safely performed after partial correction of inR without increasing bleeding rates compared to people who do not use anticoagulants (45, 46). In the study by Nagata and colleagues (42), an antigernant interruption had no effect on risks and no increased risk was found in patients with an INR of 2.5 or more. The consensus group cannot specify an INR boundary level that should encourage a correction of the INR. Although the available new data was limited, the introduction of the DOACs prompted the update of this recommendation. Nagata and colleagues (42) found that patients who received DOACs had less need for transfusion than patients who received warfarin. The DOACs have a short half-life – 8 to 12 hours – and their anticoagulant effect dissolves faster than warfarin. Sekehrmittel are now available, although criteria for their use in patients with UGIB are not yet defined and availability may be limited in some areas. Whether the type or extent of anticoagulation would affect the type of endoscopic hemothmatic therapy was not discussed. Other guidelines recommend the administration of vitamin K, supplemented with intravenous prothrombin complex concentrate (PCC), with the use of fresh frozen plasma only when PCC is not available (8, 9, 47). Four-factor PCC has shown efficacy in correcting INR (43, 44), as well as targeted anticoagulane reversing agents (48, 49). Some data indicate a higher risk of thrombosis with rapid reversal of anticoagulation (42, 48), but this goes beyond the scope of these guidelines. The Consensus Group agreed that the degree of coagulopathy should be assessed objectively before therapeutic decisions are made. The coagulation agent, the physiology of the patient and the adherence to therapy by the patient can affect the anticoagulation. Due to the recognized benefits of early endoscopy (declaration B3), coagulopathy should be treated as necessary, but endoscopy should not be delayed. For patients with acute UGIB, we recommend early endoscopy (within 24 hours of presentation). (CLASS: (CLASS: Recommendation, very inferior evidence)Evidence for early endoscopy was evaluated separately for patients at low and high risk of adverse outcomes (death, bleeding) (supplement Annex 2). Low-risk patients: Two systematic reviews (4, 50) including 3 randomized trials (51-53) evaluated the time of endoscopy in patients with UGIB. Two of the studies included low-risk patients who were randomly assigned to early endoscopy (within 1 to 2 hours vs. 1 to 2 days [52] or within 6 hours vs. 48 hours [53]). In both studies, no differences in mortality or bleeding were found between the groups (52, 53), but one study found that early endoscopy reduced the length of stay and the cost of care (52). The QoE was downgraded due to a serious risk of bias, indirectness and very serious inaccuracy. Observational studies have been seriously confused by the severity of bleeding and comorbidity, which may affect the results in favor of or against early endoscopy. Three retrospective cohort studies contained data reported exclusively or separately on low-risk patients who were adjusted for disruptive factors (54-56). In one study, urgent endoscopy was a predictor of negative outcomes (composite of death; Bleeding; and surgical, radiological or endoscopic intervention) in low-risk patients with UGIB (adjusted OR, 0.71 per 6 hours [CI, 0.55 to 0.91]) (54). The definition of low-risk risk in this study was a GBS less than 12, rather than the more common GBS of 2 or less. In another study using the same criterion, the time to endoscopy was not associated with mortality in the hospital (55). In the largest study, low-risk endoscopy was associated with lower hospital mortality within 24 hours (OR, 0.48 [CI, 0.24 to 0.97]), but not again bleeding, compared to later endoscopy (56). The QoE was downgraded due to a serious risk of bias and indirectness. High-risk patients: See text under No recommendation B. Safety concerns regarding early endoscopy, including the potential for insufficient resuscitation before surgery and the need to perform endoscopy outside of working hours when there are fewer endoscopy resources available, must be weighed against the potential for worse outcomes due to persistent bleeding. Since such concerns are less of a problem in low-risk patients than in high-risk patients, the decision to perform early endoscopy in low-risk patients is mainly due to cost and length of stay. The in 2010, most patients with acute UGIB (4) recommended early endoscopy (within 24 hours of presentation). This recommendation was based on data suggesting that early endoscopy enabled safe discharge of low-risk patients, improved outcomes for high-risk patients, and reduced resource consumption (4). Although the data were very low, they support the conclusion that early endoscopy can be carried out safely for low-risk patients and can reduce resource consumption. In order to reduce hospital stays and costs, the endosco-piste's recommendations for the early discharge of low-risk patients must be In the study, in which early endoscopy did not reduce resource consumption, only 21% of eligible patients were discharged prematurely (53). Early endoscopy can also lead to more high-risk endoscopic stigmas that would have dissolved spontaneously (52, 53), which can compensate for hospitalization benefits. The availability of endoscopy resources is an important aspect. A meta-analysis of 20 cohort studies found that patients with UGIB who were hospitalized outside of working hours were less likely to undergo endoscopy within 24 hours and had higher mortality rates (57). This was not the case in hospitals with formal endoscopy services. Based on the available data, the consensus group proposed to perform endoscopy within 24 hours of presentation for both low-risk and high-risk patients. For high-risk patients, see the discussion under No Recommendation B. In patients with acute UGIB at high risk of bleeding or mortality, the consensus group could not recommend or against performing endoscopy within 12 hours, compared to subsequent endoscopy. (GRADE for PICO: Very inferior evidence) No randomized study evaluated the timing of endoscopy specifically in high-risk patients with UGIB. A study in patients with stomach ulcers, including a high proportion of high-risk patients (44% with shock), found no difference in mortality with endoscopy before or after 12 hours (Annex Table 3) (51). The QoE was downgraded due to a serious risk of bias and indirectness and very serious inaccuracy. Annex Table 3. Summary of adjusted results from studies evaluating the timing of endoscopy in high-risk patients with UGIB or DeathSeven observational studies in high-risk patients with UGIB were evaluated (54-56, 58-61); however, only 2 provided adjusted mortality results (Annex Table 3) (56, 58). One study showed a reduction in mortality with very early endoscopy (<6 hours)= compared= with= later= endoscopy= (=>6 to ≤48 hours) (58). A large cohort study suggested that in hemodynamically unstable patients, very early endoscopy (≤6 hours) may increase the risk of mortality, while early endoscopy between 6 and 24 hours may reduce the risk of mortality compared to endoscopy outside this period (56). This data has been downgraded due to a serious risk of bias, inconsistency and inaccuracy. Unadjusted results from observational studies were not taken into account for this guideline. Such results are in conflict and difficult to interpret, as the impact of the bidirectional. More severe bleeding or comorbid diseases are associated with poorer results and represent a clear propensity for faster endoscopy; However, if the severity is too high, endoscopy may be delayed. Statement B3 recommends endoscopy within 24 hours for patients with UGIB. Whether high-risk patients would benefit from a very early endoscopy (within 12 hours) remains to be seen. Although active bleeding is associated with a poor prognosis, </6> </6> unstable may have more negative consequences during endoscopy. Therefore, very early endoscopy may be associated with a paradoxical negative effect in high-risk patients (56). Due to conflicting data, very different patient populations (e.B. age, bleeding severity, comorbid conditions or hemodynamic instability) and the potential for damage, the consensus group concluded that there is insufficient data to recommend a more urgent recommendation for or against endoscopy than the 24-hour window in high-risk patients. Practitioners are reminded that in patients with suspected variceal bleeding, existing recommendations suggest an endoscopy within 12 hours of presentation (62, 63). For patients with acute bleeding ulcers with high-risk stigma, we recommend endoscopic therapy with thermocoagulation or sclerisant injection. (GRADE: strong recommendation, inferior evidence) For patients with acute bleeding ulcers with high-risk stigma, we recommend endoscopic therapy with (by the scope) clips. (GRADE: conditional recommendation, very inferior evidence) Systematic reviews and meta-analysis have evaluated the role of endoscopic therapy in patients with UGIB (64-67). One review examined only epinephrine injection alone and in combination (66), while another was reported suboptimally (67). For this directive, the evidence was derived mainly from the evaluations updated in 2009 by Laine and McQuaid (64) and Barkun and colleagues (65), updated with new literature research from 2006 to 2018. No new randomized studies were found for comparing endoscopic treatment without endoscopic treatment; therefore, these analyses remain unchanged (64, 65). Compared to pharmacotherapy or without treatment, reduced thermocoagulation (heating probe or bipolar electrocoagulation) or sclerosant injection of mortality and bleeding (64, 65). No randomized studies comparing hemoclips without treatment have been found. The QoE was downgraded due to the risk of bias (mainly lack of glare). The QoE for efficacy was moderately combined for all therapies and for sclerisant injection; QoE was low due to thermocoagulation and was further downgraded due to inaccuracy. For comparisons of different active treatments, the meta-analysis of Barkun and colleagues (65) was updated with 3 new studies (68-70) (supplement 2). No differences in thermocoagulation, sclerisant injection, hemoclips and combination therapies were observed in mortality or bleeding (64, 65). The meta-analysis of data from 2 studies showed that hemoclips of epinephrine injection alone were superior in terms of bleeding (RR, 0.17 [CI, 0.05 to 0.55]), but not (RR, 2.15 [CI, 0.59 to 7.78]) (68, 71). Endoscopic hemostatic therapy has been well documented to improve results. The consensus group agreed with previous statements that endoscopic therapy is indicated in patients with high-risk stigma (active bleeding, visible vessel) and in patients with a high-risk stigma (The debate on the best method continues. Sclerosant therapy is less commonly used in clinical practice, but remains a viable option. The lack of routine PPI therapy and the ever-changing prevalence of Helicobacter pylori may influence the results of older studies. The group decided not to engage with other endoscopic mechanical techniques, such as .B over-the-scope clips. On the basis of the available data, a strong recommendation was made for thermocoagulation or sclerosant injections, while hemoclips were proposed (conditional recommendation). However, the data have generally shown no superiority of a method, and each can be useful depending on the location of the bleeding source and patient characteristics. In patients with actively bleeding ulcers, we recommend using TC-325 as a temporary therapy to stop bleeding when conventional endoscopic therapies are not available or fail. (GRADE: conditional recommendation, very inferior evidence) In patients with actively bleeding ulcers, we recommend using TC-325 as a single therapeutic strategy compared to conventional endoscopic therapy (clips alone, thermocoagulation alone or combination therapy). (GRADE: conditional recommendation, very inferior evidence) Evidence of the efficacy of TC-325 (hemostatic powder spray) was found in a small undermotorized study (72) and observational studies (73, 74). The study randomly assigned 20 patients and found no statistically significant differences in initial hemostasis (90% vs. 100%). or re-bleeding (33% vs. 10%) with TC-325 monotherapy compared to a conventional combination sendoscopic technique (epinephrine injection with hemoclip or heating probe application) (72). Of 8 patients with actively bleeding (spurring or wetting) ulcers, 4 out of 5 in the TC-325 group had a successful initial hemostasis, but 3 had re-bleeding. In contrast, all 3 in the conventional treatment group achieved an initial hemostasis and no containment. A systematic review of the observational data showed an immediate haemostase rate of 90%, but very high bleeding rates (72-hours, 19%; 7-days, 22%) 86 patients with ulcers treated with TC-325 (73). Bleeding rates (72 hours and 7 days) were highest in patients with active bleeding (spur, 40% and 60%; oozing, 13% and 16%). Another large prospective cohort study included 202 patients with bleeding treated with TC-325; the rate of initial hemostasis was 97%, with bleeding rates on day 8 and 30 being 27% and 34% respectively (74). The evidence was based on the serious risk of bias (lack of glare) and very serious inaccuracy (small sample sizes) small total number of events). The success of TC-325 hemostatic powder spray seems to depend on the cause of bleeding and whether the powder is used alone or in combination with other hemostatic therapy. The powder adheres only to actively bleeding lesions (73), its residence time is 24 hours or less (75), and it does not induce tissue healing (73). TC-325 use in UGIB UGIB associated with a low complication rate, although rare cases of perforation and temporary bile closure have been reported (73, 76). Additional experience is required to more clearly define the security profile. Decision modeling suggests that a conventional therapy strategy, followed by TC-325, improved efficacy and was more cost-effective than conventional therapy alone or TC-325 in most non-variceal UGIB (77) patient populations alone. TC-325 followed by conventional therapy was the most effective strategy for non-ulcer high-risk bleeding lesions with low risk of delayed bleeding. Based on the mechanism of action of TC-325 and clinical evidence, the consensus group concluded that TC-325 monotherapy may not adequately treat ulcers with high-risk stigma, but may be useful as a temporary measure to stop bleeding and that an endoscopy at second sight or a second hemostatic technique should be used. In patients with acute bleeding ulcers who underwent endoscopic therapy, the consensus group could not recommend or against doppler endoscopic probe (DEP), unlike no DEP, to assess the need for further endoscopic therapy. (GRADE for PICO: Very inferior evidence) Two randomized trials compared DEP-guided and conventional endoscopic treatment in patients with acute UGIB (78, 79). In a 1997 study by Kohler and colleagues (78), all patients had stomach ulcers, but active bleeding lesions were ruled out. The endoscopic treatment was led by Doppler findings, injection therapy alone was applied and the enddoscopy in the second glance was performed for all patients. In a 2017 study by Jensen and colleagues (79), most of the 148 patients with severe non-variceal UGIB (85%) were stomach bleeding (active bleeding, visible vessel, liable clot or flat spot). A meta-analysis of these two studies (78, 79) was carried out for this guideline (supplement Annex 2). At the personal meeting, however, it was decided to focus the evidence profiles on the study by Jensen and colleagues who reported data for patients with high-risk lesions (active bleeding, visible vessel) or liable clots. Data for patients with low-risk lesions (flat spots) were considered indirect as these lesions are not routinely subjected to endoscopic therapy. In the study by Jensen and colleagues (79), DEP reduced the bleeding of all lesions (RR, 0.42 [CI, 0.20 to 0.90]), but not in high-risk lesions (RR, 0.50 [CI, 0.24 to 1.08]). Overall, the QoE was suspended due to the risk of bias, (population and intervention) and inaccuracy (moderate sample size). Further studies are needed to determine whether DEP would be useful for guiding endoscopic treatment decisions before or after initial therapy or in both settings. One study found only a 58% match between DEP and findings in indexendoscopy (78). DeP is used to determine the need for additional therapy, DEP would be an add-on test with conventional endoscopic treatment for high-risk lesions, which would incur additional costs. Would. DEP technology. A cost minimization analysis showed that DEP-controlled combination sendoscopic therapy was cost-effective only for the management of high-risk patients compared to combination therapy (80). The Consensus Group concluded that data indicating efficacy for DEP are very limited and that a lack of availability and expertise in many centres influence splendidly. The group generally agreed that while a recommendation for or against DEP to manage UGIB is premature, it has the potential to change the usual approach to visually assessing the risk of bleeding in assessing the necessity and adequacy of endoscopic hemostase. For patients with bleeding ulcers with high-risk stigma who have undergone successful endoscopic therapy, we recommend the use of PPI therapy via an intravenous strain, followed by a continuous intravenous infusion (unlike no treatment or H2 receptor antagonist). (GRADE: strong recommendation, according to quality certificates) In patients with bleeding ulcers with high-risk stigma who have undergone successful endoscopic therapy, the consensus group could not recommend or against non-high-dose PPI therapy (unlike no treatment or H2 receptor antagonist). (GRADE for PICO: Very inferior evidence) Two Cochrane assessments of PPIs in UGIB have been updated for this policy (81, 82). The first (81) involving 24 studies comparing PPIs with placebo or H2 receptor antagonists (H2RAs) was updated with a further 14 randomized trials. Of these, 12 contained data on patients with high-risk stigma (active bleeding, visible vessel) or adhering clot who had undergone appropriate endoscopic therapy. There was a moderate QoE that PPI therapy reduced mortality risk compared to no PPI or H2RAs (OR, 0.56 [CI, 0.34 to 0.94]) and a high QoE that reduced the risk of bleeding (OR, 0.43 [CI, 0.29 to 0.63]) (Table 2). Evidence of mortality has been downgraded due to the serious risk of bias (mainly due to lack of glare in some studies). Table 2. Pooled ORs and absolute risks of adverse outcomes, According to the PPI regimen, in patients with high-risk stigmas who had endoscopic therapyThe second meta-analysis (82), which included 22 studies comparing different PPI therapies, was updated with a further 18 studies. Of these, 25 high-dose PPIs (defined as 80 mg intravenous bolus followed by 72 hours of continuous intravenous infusion of 8 mg/h) with non-high-dose PPIs, and 17 contained data on patients with high-risk stigmata or adherent clots that were endoscopic had been subjected to. No differences in the risk of mortality or bleeding were found between high-dose and non-high-dose PPIs (low and moderate QoE) or between high-dose and oral PPIs (very low and low QoE) (Table 2). Indirect comparisons between high-dose PPI values and no treatment or H2RAs, as well as between non-high-dose PPIs and no treatment or H2RAs, showed a very low QoE for the superiority of high-dose PPI therapy (update of [81]). Moderate QoE supported the of non-high-dose PPIs compared to no PPI for the result of re-bleeding, but the QoE for mortality was low. The evidence was downgraded, mainly due to inaccuracy and risk of bias for some comparisons. Side effects have been poorly reported in most studies. Overall, no consistent signal of a difference between PPI therapy and placebo or H2RAs, between high-dose and non-high-dose PPI therapies, or between intravenous and oral PPI therapy was found. The exception was an increased risk of thrombophlebitis with PPIs, which are administered intravenously compared to oral. High-dose PPI therapy (i.e. an 80 mg intravenous bolus followed by 72 hours of continuous intravenous infusion of 82 hours) reduces bleeding and mortality. Since non-high-dose therapy was associated with a reduction in bleeding but not with mortality compared to no PPI therapy, a majority of the consensus group did not support the recommendation of non-high-dose PPI therapy. The Consensus Group is not confident that the accuracy of the estimates of the absolute differences between high- and non-high-dose PPI therapy in terms of mortality and bleeding is sufficient to consider the two therapies equivalent. Studies on non-high-dose PPI therapy are complicated by various dosing regimens and methods of administration, including continuous intravenous infusion, intravenous bolus and oral therapies. Cost-effectiveness studies have shown that high-dose intravenous PPIs after successful endoscopic hemostasis improve results with a modest increase in costs compared to non-high-dose intravenous or oral PPI strategies (83-86). In addition, the incremental cost of various PPI therapies (continuous or intermittent, before or after endoscopic therapy) is modest compared to the total cost per patient. The consensus group concluded that the evidence supports a strong recommendation for high-dose PPIs for patients with bleeding ulcers with high-risk stigmata (active bleeding or visible vessel) who had successful endoscopic therapy. The recommendation for patients with adhering clots remains unchanged (declaration B6) and includes endoscopic therapy or consideration of PPI therapy alone (Table 1). Given the proven benefits of bleeding outcomes and the fact that the cost and availability of intravenous formulations may be problems in some areas, the Consensus Group also did not recommend the use of lower PPI doses. For patients with high-risk ulcer bleeding (i.e. an ulcer requiring endoscopic therapy), 3 days of high-dose PPI therapy), we recommend using twice daily oral PPI (vs. once daily) 14 days, followed by once daily. (GRADE: conditional recommendation, very inferior evidence) One study included patients at high risk of bleeding (Rockall scores ≥6) who had undergone successful endoscopic therapy and received high-dose PPI therapy for 3 days (intravenous esomeprazole, 80 mg load dose followed by a continuous 8 mg/h infusion) (87). The patients were randomly oral esomeprazole, 40 mg, either once or twice daily for 11 days (days 3 to 14). All patients received an additional 2 weeks of PPI therapy once a day. A reduction was observed in derbleeding (RR, 0.37 [CI, 0.19 to 0.73]), but not in mortality rates (RR, 0.38 [CI, 0.10 to 1.38]) with twice-daily PPIs compared to once-daily PPIs. The QoE was downgraded due to the risk of bias and inaccuracy. Based on the data suggesting superiority over the standard dose for bleeding, the consensus group proposed the use of twice-daily ppIs to complete 2 weeks of PPI therapy after 3 days of high-dose therapy. No updates to the 2010 International UGIB Guidelines (4). In patients with previous ulcer bleeding who receive cardiovascular prophylaxis with single or dual antiplatelet therapy, we recommend the use of PPI therapy compared to no PPI therapy. (GRADE: conditional recommendation, inferior evidence) Single-antiplatelet therapy: Evidence of the role of PPI therapy in patients receiving antiplatelet therapy with a single agent was available in 5 randomized trials (88-92) comparing PPIs with no PPI in patients who needed continued platelet therapy. Due to the heterogeneity in draft studies and comparison groups, a meta-analysis of all 5 studies was not carried out. All five tests were carried out in Hong Kong. A history of H pylori infection and eradication treatment was common. One study found that PPIs were more effective than placebo in reducing recurrent complications (bleeding, perforation and obstruction) (RR, 0.11 [CI, 0.01 to 0.84]) in patients with previous ulcer complications who had successful H-pylori eradication and required continued platelet therapy (acetylsalicylic acid [ASA]) (88). A meta-analysis of 2 studies showed that PPI plus ASA reduced bleeding rates compared to clopidogrel alone (RR, 0.07 [CI, 0.01 to 0.34]) in patients with previous ASA-associated ulcer hemorrhage who did not have H-pylori infection or had successfully eradicated it (90, 91). In patients with previous ASA-associated ulcer bleeding, studies found no difference between PPIs and eradication treatment in patients with H-pylori infection (89) or between PPIs and H2RAs in patients without H-pylori infection or those who had H-pylori infection eradicated (92). Two studies found no differences in mortality rates between PPIs and placebo groups (88) or between PPIs plus ASA versus clopidogrel (89). The evidence has been downgraded, mainly due to very serious inaccuracy (small studies, very low number of events). Dual antiplatelet therapy (DAPT): No randomised assessed the use of PPIs in patients with DAPT patients with a history of ulcer bleeding. Two systematic checks were found in patients receiving DAPT after percutaneous coronary intervention or in the presence of coronary heart disease (93, 94). The reporting and methodological quality of both assessments were suboptimal, with studies that were ineligible (e.B. due to patients who did not receive DAPT, incorrect comparisons or or counting). A meta-analysis carried out for this Directive included 4 randomised studies (n = 4805) comparing PPIs with no PPI therapy in patients receiving prophylactic DAPT (ASA and clopidogrel). The largest study was international (95), while the other 3 were conducted in China (96-98). Meta-analysis showed a reduction in gastrointestinal bleeding risk with PPI therapy compared to placebo (n = 4 studies; RR, 0.25 [CI, 0.14 to 0.45]) and no impact on mortality (n = 3 studies; RR, 1.02 [CI, 0.68 to 1.54]) or myocardial infarction risk (n = 2 studies; RR, 0.96 [CI, 0.51 to 1.81]). No studies were found to evaluate ASA in combination with other platelet drugs such as prasugrel or ticagrelor. The evidence was downgraded to a high or unclear risk of bias in Chinese studies and to serious indirectness in all 4 studies (most patients had no history of ulcer bleeding). The evidence consistently supports benefit with PPI therapy in patients with previous ulcer bleeding who continue single- or dual-anti-platelet therapy and suggests that PPI therapy is superior to clopidogrel only in patients receiving ASA. Most patients in these studies had H-pylori infection prior to PPI therapy, and in one study, eradication treatment alone was just as effective as PPI therapy (89). Observational data suggest that the risk of ulcer bleeding in patients receiving low-dose ASA can be reduced in patients who had eradicated H-pylori infection compared to patients who were never infected (99). PPI therapy is expected to be beneficial in populations with lower rates of H-pylori infections, although the extent of the effect may be reduced. The consensus group suggested that eradication therapy alone could be sufficient to reduce the risk of bleeding for some patients with H-pylori infection, with only incremental benefits associated with additional PPI therapy. Although various adverse events have been reported with THE PPI therapy (Declaration E5), the systematic review and meta-analysis for this guideline did not reveal an increased risk of myocardial infarction in patients receiving DAPT. Based on evidence, the consensus group proposes PPI therapy to prevent bleeding in most patients who require one- or two-anti-platelet therapy for a duration consistent with the ongoing need for platelet therapy. In patients with previous ulcerbleeding who require continued cardiovascular prophylaxis with anticoagulande therapy (vitamin K antagonists, DOACs), we recommend the use of PPI therapy compared to none (GRADE: conditional recommendation, very inferior evidence) Compared to no PPI therapy, the use of PPIs in patients receiving anticoagulant therapy was associated with a reduced risk of bleeding in 2 large cohort studies (100, 101), but not in 3 case-control studies (102-104). Most patients involved in these studies had no history of ulcer bleeding. In a small case-control study in patients with uGIB history, this was the Patients receiving warfarin plus PPIs (RR, 1.93 [CI, 0.23 to 16.28]) compared to patients who did not receive warfarin (103). In contrast, one of the cohort studies observed the greatest risk reduction with PPI therapy compared to no PPI therapy in patients with a history of stomach ulcers or gastrointestinal bleeding (adjusted incidence rate ratio, 0.14 [CI, 0.06 to 0.30]) (101). None of the studies included assessed mortality. The evidence was downgraded due to indirectness (most patients had no previous ulcer bleeding). A history of ulcer bleeding is associated with an increased risk of bleeding, and although anticoagulants do not cause ulcer bleeding, they increase the risk of bleeding from areas that have mucoagula fractures. Meta-analysis of mainly observational studies has suggested possible links between PPI therapy and side effects, including community-acquired pneumonia, hip fracture, colorectal cancer, chronic kidney disease, community-acquired enteric infection and Clostridium difficile infection (105-109). An analysis of factors such as consistency, specificity, temporality and biological plausibility, as well as confusing factors, showed that the evidence of causality is very weak (110). The Consensus Group concluded that in high-risk patients with a persistent need for anticoagulants, the results suggest that the benefits of secondary prophylaxis outweigh the risks. The unproven potential and rare safety concerns should not prevent treatment of patients at risk of life-threatening consequences. Although UGIB management has improved significantly over the last two decades, areas where more data are needed remain (Annex Table 4). In particular, further studies are needed to define the benefits of specific prognostic scales, the role of restrictive versus liberal transfusion practice in patients with UGIB and cardiovascular disease, optimal PPI therapies, optimal endoscopic hemostatic therapies, and the role of PPIs in patients receiving antithrombotic therapy. Planned analyses of the COMPASS study (Cardiovascular Outcomes for People Using Anticoagulation Strategies) can clarify the efficacy and safety of PPIs compared to no PPI in patients receiving anticoagulant therapy (111). Annex Table 4. Areas of foresightSeveral relevant articles that were not available at the time of this consensus have been published since the completion of the literature research (as of May 2018). This includes a large randomized trial in patients with cardiovascular disease that compared the efficacy and safety of DOACs or ASAs with or without PPI therapy (112, 113). Studies have examined PPIs compared to H2RAs for recurrent UGIB (114) as well as endoscopic therapy with hedemic powder and hemoclips (115, 116). In addition, the use of DEP for the management of hemostasis was further investigated (117). Although a discussion about over-the-scope clips for recurring stomach ulcers is the framework of this data (118). These are just a few examples of new or ongoing studies that have the potential to affect clinical practice, but they cannot. The Consensus Group cannot comment on the results of these studies because no systematic literature research has been carried out and the GRADE approach has not been applied. It is currently planned to develop a user-friendly clinical algorithm for UGIB management, slide presentations, short videos and CAG podcasts. The guidelines and supporting materials are distributed to all participating societies and regions through places such as symposia meetings or workshops at social meetings. Important recommendations are published on the websites of the company and the government. Finally, we expect these guidelines to continue to be updated as new data becomes available.
References1. Laine L , Yang H , Chang SC , et al. Trends in hospitalizations and deaths due to GI complications in the United States from 2001 to 2009. At J Gastroenterol. 2012;107:1190-5; Quiz 1196. [PMID: 22688850] doi:10.1038/ajg.2012.168 CrossrefMedlineGoogle Scholar2. Rosenstock SJ , M' ller MH , Larsson H , et al. Improving the quality of care for stomach ulcers: Nationwide cohort study with 13,498 consecutive patients in the Danish Clinical Register of Emergency Surgery. At J Gastroenterol. 2013;108:1449-57. [PMID: 23732464] doi:10.1038/ajg.2013.162 CrossrefMedlineGoogle Scholar3. Barkun A , Bardou M and Marshall JK ; Nonvariceal Upper GI Bleeding Consensus Conference Group. Consensus recommendations for the treatment of patients with non-variceal upper gastrointestinal bleeding. Ann Intern Med. 2003;139:843-57 LinkGoogle Scholar4. Barkun AN , Bardou M , Kuipers EJ , et al. International Consensus Upper Gastrointestinal Bleeding Conference Group. International consensus recommendations for the management of patients with non-variceal upper gastrointestinal bleeding. Ann Intern Med. 2010;152:101-13 doi:10.7326/0003-4819-152-2-20100190-00009 LinkGoogle Scholar5. Laine L and Jensen DM . Treatment of patients with ulcer bleeding. At J Gastroenterol. 2012;107:345-60; Quiz 361. [PMID: 22310222] doi:10.1038/ajg.2011.480 CrossrefMedlineGoogle Scholar6. Hwang JH , Fisher DA , Ben-Menachem T , et al. Standards of Practice Committee of the American Society for Gastrointestinal Endoscopy. The role of endoscopy in the treatment of acute non-variceal upper GI bleeding. Gastrointestinal endosc. 2012;75:1132-8. [PMID: 22624808] doi:10.1016/j.gie.2012.02.033 CrossrefMedlineGoogle Scholar7. National Institute for Health and Care Excellence. Acute upper gastrointestinal bleeding: Management (NICE clinical guideline 141), 2012. Last updated: November 2018. Access to www.nice.org.uk/guidance/cg141 on August 12, 2019. Google Scholar8. Goutnek IM , Dumonceau JM , Kuipers EJ , et al. Diagnosis and of non-variceal upper gastrointestinal bleeding: European Society of Gastrointestinal Endoscopy (ESGE) Directive. Endoscopy. 2015;47:a1-46. [PMID: [PMID: doi:10.1055/s-0034-1393172 CrossrefMedlineGoogle Scholar9. Sung jj , Chiu PW , Chan FKL , et al. Asia Pacific Working Group Consensus on non-variceal upper gastrointestinal bleeding: an update 2018. Good. 2018;67:1757-1768. [PMID: 29691276] doi:10.1136/gutjnl-2018-316276 CrossrefMedlineGoogle Scholar10. Abraham NS , Hartman C , Richardson P , et al. Risk of lower and upper gastrointestinal bleeding, transfusions and hospitalizations with complex antithrombotic therapy in elderly patients. Circulation. 2013;128:1869-77. [PMID: 24025594] doi:10.1161/CIRCULATIONAHA.113.004747 CrossrefMedlineGoogle Scholar11. Shea BJ , Reeves BC , Wells G , et al. AMSTAR 2: a critical evaluation tool for systematic reviews involving randomized or non-randomized trials of health interventions or both. Bmj. 2017;358:j4008. [PMID: 28935701] doi:10.1136/bmj.j4008 CrossrefMedlineGoogle Scholar12. Guyatt GH , Oxman AD , Vist GE , et al. GRADE Working Group. GRADE: a looming consensus on the quality of evidence and the strength of the recommendations. Bmj. 2008;336:924-6. [PMID: 18436948] doi:10.1136/bmj.39489.470347.AD CrossrefMedlineGoogle Scholar13. Guyatt GH , Schünemann HJ , Djulbegovic B , et al. Guideline Panels should not GRADE Good Practice Statements . J Clin Epidemiol. 2015;68:597-600. [PMID: 25660962] doi:10.1016/j.jclinepi.2014.12.011 CrossrefMedlineGoogle Scholar14. Dalkey N . An experimental study of group opinion: the Delphi method. Futures. 1969;1:408-26. CrossrefGoogle Scholar15. Schünemann HJ , Mustafa R , Brozek J , et al. GRADE Working Group. GRADE Guidelines: 16th GRADE Evidence for Decision Frameworks for Clinical Practice and Healthcare Trials. J Clin Epidemiol. 2016;76:89-98. [PMID: 26931285] doi:10.1016/j.jclinepi.2016.01.032 CrossrefMedlineGoogle Scholar16. Alonso-Coello P , Oxman AD , Moberg J , et al. GRADE Working Group. GRADE Evidence to Decision (EtD) framework: a systematic and transparent approach to making well-informed healthcare decisions. 2: Guidelines for clinical practice. Bmj. 2016;353:i2089. [PMID: 27365494] doi:10.1136/bmj.i2089 CrossrefMedlineGoogle Scholar17. Alonso-Coello P , Schünemann HJ , Moberg J , et al. GRADE Working Group. GRADE Evidence to Decision (EtD) framework: a systematic and transparent approach to making well-informed healthcare decisions. 1: Introduction. Bmj. 2016;353:i2016. [PMID: 27353417] doi:10.1136/bmj.i2016

CrossrefMedlineGoogle Scholar18. Guyatt GH , Oxman AD , Kunz R , et al. GRADE Working Group. From proof to recommendations. Bmj. 2008;336:1049-51. [PMID: 18467413] doi:10.1136/bmj.39493.646875.AE CrossrefMedlineGoogle Scholar19. Perel P , Roberts I and Ker K . Colloids versus crystalloids for fluid resuscitation in critically ill patients. Cochrane Database Syst Rev. 2013 CD000567. [PMID: 23450531] doi:10.1002/14651858.CD000567.pub6 CrossrefMedlineGoogle Chavez-Negrete A , Majluf Cruz S , Frati Munari A , et al. Treatment of hemorrhagic shock with intraosseous or intravenous intravenous hypertonic saline-dextran solution. Eur Surg Res. 1991;23:123-9. [PMID: 1718756] CrossrefMedlineGoogle Scholar21. Annane D , Siami S , Jaber S , et al. CRISTAL Investigators. Effects of resuscitation of fluids with colloids vs. crystallooids on mortality in critically ill patients with hypovolemic shock: the randomized CRISTAL study. Jama. 2013;310:1809-17. [PMID: 24108515] doi:10.1001/jama.2013.280502 CrossrefMedlineGoogle Scholar22. Semler MW , Self WH , Wanderer JP , et al. SMART Investigators and the Pragmatic Critical Care Research Group. Balanced crystalloids versus saline in seriously ill adults. N Engl J Med. 2018;378:829-839. [PMID: 29485925] doi:10.1056/NEJMoa1711584 CrossrefMedlineGoogle Scholar23. Kowalenko T , Stern S , Dronen S , et al. Improved result with hypotensive resuscitation of an uncontrolled hemorrhagic shock in a pig model. J Trauma. 1992;33:349-53; Discussion 361-2. [PMID: 1404501] CrossrefMedlineGoogle Scholar24. Stern SA , Dronen SC , Birrer P , et al. Effects of blood pressure on the volume of bleeding and survival in a near-fatal bleeding model with a vascular injury. Ann Emerg Med. 1993;22:155-63. [PMID: 8427424] CrossrefMedlineGoogle Scholar25. Kwan I , Bunn F , Chinnock P , et al. Time and volume of fluid application for patients with bleeding. Cochrane Database Syst Rev. 2014 CD002245. [PMID: 24599652] doi:10.1002/14651858.CD002245.pub2 CrossrefMedlineGoogle Scholar26. Schreiber MA , Meier EN , Tisherman SA , et al. ROC Investigators. A controlled resuscitation strategy is feasible and safe in antihypertensive trauma patients: results of a prospective randomized pilot study. J Trauma Acute Care Surg., 2015;78:687-95; Discussion 695-7. [PMID: 25807399] doi:10.1097/TA.00000000000000600 CrossrefMedlineGoogle Scholar27. Carrick MM , Morrison CA , Tapia NM , et al. Intraoperative hypotensive resuscitation for patients undergoing laparotomy or thoracotomy due to trauma: premature termination of a randomized prospective clinical trial. J Trauma Acute Care Surg. 2016;80:886-96. [PMID: 27015578] doi:10.1097/TA.000000000001044CrossrefMedlineGoogle Scholar28. Stanley AJ , Ashley D , Dalton HR , et al. Outpatient management of patients with low-risk upper gastrointestinal bleeding: multicentre validation and prospective evaluation. Lancet. 2009;373:42-7. [PMID: 19091393] doi:10.1016/S0140-6736(08)61769-9 CrossrefMedlineGoogle Scholar29. Ramaekers R , Mukarram M , Smith CA , et al. The predictive value of preendoscopic risk values for predicting negative outcomes in patients in the emergency room with upper gastrointestinal bleeding: a systematic review. Acad Emerg Med. 2016;23:1218-1227. [PMID: 27640399] doi:10.1111/acem.13101 CrossrefMedlineGoogle Scholar30. Laursen SB , Dalton HR , Murray IA , et al. Upper Gastrointestinal Hemorrhage International Performance of the new thresholds of Glasgow Blatchford score in the management of patients with upper gastrointestinal bleeding. Clin Gastroenterol Hepatol. Hepatol. [PMID: 25058843] doi:10.1016/j.cgh.2014.07.023 CrossrefMedlineGoogle Scholar31. Stanley AJ , Laine L , Dalton HR , et al. International Gastrointestinal Bleeding Consortium. Comparison of risk assessment systems for patients with upper gastrointestinal bleeding: international multicentre prospectus study. Bmj. 2017;356:i6432. [PMID: 28053181] doi:10.1136/bmj.i6432 CrossrefMedlineGoogle Scholar32. Saltzman JR , Tobacco YP , Hyett BH , et al. A simple risk value accurately predicts mortality in the hospital, the length of stay and the cost of acute bleeding in the upper GI. Gastrointestinal endosc. 2011;74:1215-24. [PMID: 21907980] doi:10.1016/j.gie.2011.06.024 CrossrefMedlineGoogle Scholar33. Odutayo A , Desborough MJ , Trivella M , et al. Restrictive versus liberal blood transfusion in gastrointestinal bleeding: a systematic review and metaanalysis of randomized controlled trials. Lancet Gastroenterol Hepatol. 2017;2:354-360. [PMID: 28397699] doi:10.1016/S2468-1253(17)30054-7 CrossrefMedlineGoogle Scholar34. Jairath V , Kahan BC , Gray A , et al. Restrictive versus liberal blood transfusion in acute upper gastrointestinal bleeding (TRIGGER): a pragmatic, open, clusterrandomized feasibility study. Lancet. 2015;386:137-44. [PMID: 25956718] doi:10.1016/S0140-6736(14)61999-1 CrossrefMedlineGoogle Scholar35. Villanueva C , Colomo A , Bosch A , et al. Transfusion strategies for acute upper gastrointestinal bleeding. N Engl J Med. 2013;368:11-21. [PMID: 23281973] doi:10.1056/NEJMoa1211801 CrossrefMedlineGoogle Scholar36. Carson JL , Stanworth SJ , Roubinian N , et al. Transfusion thresholds and other strategies for controlling the allogeneic transfusion of red blood cells. Cochrane Database Syst Rev. 2016;10:CD002042. [PMID: 27731885] MedlineGoogle Scholar37. Holst LB , Petersen MW , Haase N , et al. Restrictive versus liberal transfusion strategy for red blood cell transfusion: systematic review of randomized studies with meta-analysis and process study analysis. Bmj. 2015;350:h1354. [PMID: 25805204] doi:10.1136/bmj.h1354 CrossrefMedlineGoogle Scholar38. Shander A , Hofmann A , Ozawa S , et al. Activity-based costs of blood transfusions in surgical patients in four hospitals. Transfusion. 2010;50:753-65. [PMID: 20003061] doi:10.1111/j.1537-2995.2009.02518.x CrossrefMedlineGoogle Scholar39. Blair SD , Janvrin SB , McCollum CN , et al. Effect of early blood transfusion on gastrointestinal bleeding. Br J Surg. 1986;73:783-5. [PMID: 3533203] CrossrefMedlineGoogle Scholar40. Abererty AB , O'Donnell R , Brunskill S , et al. Effects of restrictive versus liberal transfusion strategies on the results of patients with cardiovascular disease in non-cardiac surgery: systematic review and meta-analysis. Bmj. 2016;352:i1351. [PMID: 27026510] doi:10.1136/bmj.i1351 CrossrefMedlineGoogle Scholar41. Carson JL , Guyatt G , Heddle NM , et al. Clinical Practice Guidelines from AABB: Transfusion thresholds and storage of red blood cells. Jama. 2016;316:2025-2035. [PMID: [PMID: doi:10.1001/jama.2016.9185 CrossrefMedlineGoogle Scholar42. Nagata N , Sakurai T , Moriyasu S , et al. Effects of INR monitoring, reversing agent use, heparin bridging, and anticoagulant interruption on rebleeding and thromboembolism in acute gastrointestinal bleeding. PLoS One. 2017;12:e0183423. [PMID: 28863196] doi:10.1371/journal.pone.0183423 CrossrefMedlineGoogle Scholar43. Goldstein JN , Refaai MA , Milling TJ Jr , et al. Four-factor prothrombin complex concentrate versus plasma for rapid vitamin K antagonist reversal in patients requiring urgent surgical or invasive procedures: a phase 3b, open label, non-inferiority, randomized trial. Lancet. 2015;385:2077-87. [PMID: 25728933] doi:10.1016/S0140-6736(14)61685-8 CrossrefMedlineGoogle Scholar44. Sarode R , Milling TJ Jr , Refaai MA , et al. Efficacy and safety of a 4-factor prothrombin complex focus on vitamin K antagonists with major bleeding in patients: a randomized, plasma-controlled Phase IIIb study. Circulation. 2013;128:1234-43. [PMID: 23935011] doi:10.1161/CIRCULATIONAHA.113.002283 CrossrefMedlineGoogle Scholar45. Choudari CP, Rajgopal C and Palmer KR. Acute gastrointestinal bleeding in anticoagulated patients: diagnoses and response to endoscopic treatment. Well. 1994;35:464-6. [PMID: 8174982] CrossrefMedlineGoogle Scholar46. Thomopoulos KC , Mimidis KP , Theocharis GJ , et al. Acute upper gastrointestinal bleeding in patients on long-term oral anticoagulation therapy: endoscopic findings, clinical management and outcome. World J Gastroenterol. 2005;11:1365-8. [PMID: 15761977] CrossrefMedlineGoogle Scholar47. National Institute for Health and Care Excellence. Blood transfusion (NICE clinical lineline 24), 2015. Last updated: November 2015. Access to www.nice.org.uk/guidance/ng24 on August 12, 2019. Google Scholar48. Connolly SJ , Milling TJ Jr , Eikelboom JW , et al. ANNEXA-4 Investigators. Andexanet alfa for acute major bleeding associated with factor Xa inhibitors. N Engl J Med. 2016;375:1131-41. [PMID: 27573206] doi:10.1056/NEJMoa1607887 CrossrefMedlineGoogle Scholar49. Pollack CV Jr , Reilly PA , van Ryn J , et al. Idarucizumab for Dabigatran Reversal - complete cohort analysis. N Engl J Med. 2017;377:431-441. [PMID: 28693366] doi:10.1056/NEJMoa1707278 CrossrefMedlineGoogle Scholar50. Mirror BM, Vakil NB and Ofman JJ. Endoscopy for acute non-variceal upper gastrointestinal tractbleeding: Is it better earlier? A systematic review. Arch Intern Med. 2001;161:1393-404. [PMID: 11386888] CrossrefMedlineGoogle Scholar51. Lin HJ , Wang K , Perng CL , et al. Early or delayed endoscopy for patients with gastric ulcer bleeding. A prospective randomized trial. J Clin Gastroenterol. 1996;22:267-71. [PMID: 8771420] CrossrefMedlineGoogle Scholar52. Lee JG , Turnipseed S , Romano PS , et al. The triage based on endoscopy reduces the and the cost of treating bleeding with upper GI: a randomized controlled trial. Gastrointestinal endosc. 1999;50:755-61. [PMID: [PMID: CrossrefMedlineGoogle Scholar53. Bjorkman DJ , Zaman A , Fennerty MB , et al. Urgent vs. elective endoscopy for acute non-variceal upper-GI bleeding: an effectiveness study. Gastrointestinal endosc. 2004;60:1-8. [PMID: 15229417] MedlineGoogle Scholar54. Kumar NL , Cohen AJ , Nayor J , et al. The timing of upper endoscopy affects outcomes in patients with acute nonvariceal upper GI bleeding. Gastrointestinal endosc. 2017;85:945-952. [PMID: 27693643] doi:10.1016/j.gie.2016.09.029 CrossrefMedlineGoogle Scholar55. Lim LG , Ho KY , Chan YH , et al. Urgent endoscopy is associated with lower mortality in high-risk but not low-risk non-variceal gastrointestinal bleeding. Endoscopy. 2011;43:300-6. [PMID: 21360421] doi:10.1055/s-0030-1256110 CrossrefMedlineGoogle Scholar56. Laursen SB , Leontiadis GI , Stanley AJ , et al. Relationship between the time of endoscopy and mortality in patients with gastric ulcer bleeding: a nationwide cohort study. Gastrointestinal endosc. 2017;85:936-944. [PMID: 27623102] doi:10.1016/j.gie.2016.08.049 CrossrefMedlineGoogle Scholar57. Xia XF , Chiu PWY , Tsoi KKF , et al. The effect of extra-hour hospital admission on mortality and clinical outcomes in patients with upper gastrointestinal bleeding: a systematic review and meta-analysis of 20 cohorts. United European Gastroenterol J. 2018;6:367-381. [PMID: 29774150] doi:10.1177/2050640617732651 CrossrefMedlineGoogle Scholar58. Cho SH , Lee YS , Kim YJ , et al. Results and role of urgent endoscopy in high-risk patients with acute non-variceal gastrointestinal bleeding. Clin Gastroenterol Hepatol. 2018;16:370-377. [PMID: 28634135] doi:10.1016/j.cgh.2017.06.029 CrossrefMedlineGoogle Scholar59. Ahn DW , Park YS , Lee SH , et al. Clinical result of acute nonvariceal upper gastrointestinal bleeding after hours: the role of urgent endoscopy. Korean J Intern Med. 2016;31:470-8. [PMID: 27048253] doi:10.3904/kjim.2014.099 CrossrefMedlineGoogle Scholar60. Targownik LE , Murthy S , Keyvani L , et al. The role of rapid endoscopy for high-risk patients with acute non-variceal upper gastrointestinal bleeding. May J Gastroenterol. 2007;21:425-9. [PMID: 17637943] CrossrefMedlineGoogle Scholar61. Tai CM , Huang SP , Wang HP , et al. High-risk ED patients with non-variceal upper gastrointestinal bleeding undergoing emergency or urgent endoscopy: a retrospective analysis. Am J Emerg Med. 2007;25:273-8. [PMID: 17349900] CrossrefMedlineGoogle Scholar62. Garcia-Tsao G , Sanyal AJ , Grace ND , et al. Practice Guidelines Committee of American Association for Study of Liver Diseases. Prevention and treatment of gastroesophageal variceals and variceal bleeding in cirrhosis. At J Gastroenterol. 2007;102:2086-102. [PMID: 17727436] CrossrefMedlineGoogle Scholar63. de Franchis R ; Baveno V Faculty. Revision of the consensus in the portal Report of the Baveno V ConsensusWorkshop on the methodology of diagnosis and therapy for portal hypertension. J Hepatol. 2010;53:762-8. [PMID: 20638742] 20638742] CrossrefMedlineGoogle Scholar64. Laine L and McQuaid KR . Endoscopic therapy for blood ulcers: an evidence-based approach based on meta-analysis of randomized controlled trials. Clin Gastroenterol Hepatol. 2009;7:33-47; Quiz 1-2. [PMID: 18986845] doi:10.1016/j.cgh.2008.08.016 CrossrefMedlineGoogle Scholar65. Barkun AN , Martel M , Toubouti Y , et al. Endoscopic hemostasis in stomach ulcer bleeding in patients with high-risk lesions: a series of meta-analyses. Gastrointestinal endosc. 2009;69:786-99. [PMID: 19152905] doi:10.1016/j.gie.2008.05.031 CrossrefMedlineGoogle Scholar66. Vergara M , Bennett C , Calvet X , et al. Epinephrine injection versus adrenaline injection and a second endoscopic method for high-risk bleeding ulcers. Cochrane Database Syst Rev. 2014 CD005584. [PMID: 25308912] doi:10.1002/14651858.CD005584.pub3 CrossrefMedlineGoogle Scholar67. Baracat F , Moura E , Bernardo W , et al. Endoscopic hemostasis in gastric ulcers: systematic review and meta-analysis of randomized controlled studies. Surg Endosc. 2016;30:2155-68. [PMID: 26487199] doi:10.1007/s00464-015-4542-x CrossrefMedlineGoogle Scholar68. Ljubicic N , Budimir I , Biscanin A , et al. Endoclips vs large or small volume epinephrine in stomach ulcer recurrent bleeding. World J Gastroenterol. 2012;18:2219-24. [PMID: 22611315] doi:10.3748/wjg.v18.i18.2219 CrossrefMedlineGoogle Scholar69. Cui J , Huang LY , Liu YX , et al. Efficacy of endoscopic therapy in gastrointestinal bleeding from the lesion of dieulafoy. World J Gastroenterol. 2011;17:1368-72. [PMID: 21455339] doi:10.3748/wjg.v17.i10.1368 CrossrefMedlineGoogle Scholar70. Grgov S , Radovanovic-Dinic B and Tasic T . Could the use of epinephrine improve the hemostatic efficacy of hemoclips in bleeding stomach ulcers? A prospective randomized trial. Vojnosanit Pregl. 2013;70:824-9. [PMID: 24266309] CrossrefMedlineGoogle Scholar71. Chung IK , Ham JS , Kim HS , et al. Comparison of the hemostatic efficacy of the endoscopic hemoclip method with hypertonic saline epinephrine injection and a combination of the two for the treatment of bleeding stomach ulcers. Gastrointestinal endosc. 1999;49:13-8. [PMID: 9869717] CrossrefMedlineGoogle Scholar72. Kwek BEA , Ang TL , Ong PLJ , et al. TC-325 versus the conventional combined technique for endoscopic treatment of stomach ulcers with high-risk bleeding stigma: A randomized pilot study. J Dig Dis. 2017;18:323-329. [PMID: 28485544] doi:10.1111/1751-2980.12481 CrossrefMedlineGoogle Scholar73. Chen YI and Barkun AN . Hemostatic powder in gastrointestinal bleeding: a systematic check. Gastrointest Endosc Clin N Am. 2015;25:535-52. [PMID: 26142037] doi:10.1016/j.giec.2015.02.008 CrossrefMedlineGoogle Scholar74. Haddara S , Jacques J , Lecleire S , et al. A novel haemostatic powder for upper gastrointestinal bleeding: a multicentre study (the Endoscopy. 2016;48:1084-1095. [PMID: 27760437] CrossrefMedlineGoogle Scholar75. Chen YI , Barkun A and Nolan S . Hemostatic Powder Powder in the treatment of upper and lower gastrointestinal bleeding: a two-year experience at a single institution. Endoscopy. 2015;47:167-71. [PMID: 25264762] doi:10.1055/s-0034-1378098 CrossrefMedlineGoogle Scholar76. Hagel AF , Albrecht H , Nägel A , et al. The use of hemospray in gastrointestinal bleeding during emergency endoscopy. Gastroenterol Res Pract. 2017;2017:3083481. [PMID: 28232848] doi:10.1155/2017/3083481 CrossrefMedlineGoogle Scholar77. Barkun AN , Adam V , Lu Y , et al. The use of hemospray improves the cost-benefit ratio in the treatment of upper gastrointestinal nonvariceal bleeding. J Clin Gastroenterol. 2018;52:36-44. [PMID: 27749635] doi:10.1097/MCG.000000000000709 CrossrefMedlineGoogle Scholar78. Kohler B , Maier M , Benz C , et al. Acute ulcer bleeding. A prospective randomized study comparing Doppler and Forrest classifications in endoscopic diagnosis and therapy. Dig Dis Sci. 1997;42:1370-4. [PMID: 9246030] CrossrefMedlineGoogle Scholar79. Jensen DM, Kovacs TOG, Ohning GV, et al. Doppler endoscopic probe monitoring blood flow improves risk layering and results of patients with severe nonvariceal upper gastrointestinal bleeding. Gastroenterology. 2017;152:1310-1318. [PMID: 28167214] doi:10.1053/j.gastro.2017.01.042 CrossrefMedlineGoogle Scholar80. Chen VK and Wong RC . Endoscopic Doppler ultrasound versus endoscopic stigma-controlled management of acute stomach ulcer bleeding: a multi-model cost analysis. Dig Dis Sci. 2007;52:149-60. [PMID: 17109216] CrossrefMedlineGoogle Scholar81. Leontiadis GI , Sharma VK and Howden CW . Proton pump inhibitor treatment for acute stomach ulcer bleeding. Cochrane Database Syst Rev. 2006 CD002094. [PMID: 16437441] MedlineGoogle Scholar82. Neumann I , Letelier LM , Rada G , et al. Comparison of different therapies of proton pump inhibitors for acute stomach ulcer bleeding. Cochrane Database Syst Rev. 2013 CD007999. [PMID: 23760821] doi:10.1002/14651858.CD007999.pub2 CrossrefMedlineGoogle Scholar83. Leontiadis GI , Sreedharan A , Dorward S , et al. Systematic review of the clinical efficacy and cost-effectiveness of proton pump inhibitors in acute upper gastrointestinal bleeding. Health Technol review. 2007;11:iii-iv, 1-164. [PMID: 18021578] CrossrefMedlineGoogle Scholar84. Barkun AN , Adam V , Sung JJ , et al. Cost-effectiveness of high-dose intravenous esomeprazole for gastric ulcer bleeding. Pharmaco-economicity. 2010;28:217-30. [PMID: 20151726] doi:10.2165/11531480-000000000-00000CrossrefMedlineGoogle Scholar85. Al-Sabah S , Barkun AN , Herba K , et al. Cost-effectiveness of proton pump inhibition before endoscopy in gastrointestinal bleeding in the upper gastrointestinal area. Clin Gastroenterol Hepatol. 2008;6:418-25. [PMID: 18304891] doi:10.1016/j.cgh.2007.12.037 CrossrefMedlineGoogle Scholar86. Lu Y , Adam V , Pond V , et al. The timing or the of intravenous proton pump inhibitors in acute gastrointestinal bleeding in the upper gastrointestinal area has little effect on costs. At J Gastroenterol. 2016;111:1389-1398. 2016;111:1389-1398. 27140030] doi:10.1038/ajg.2016.157 CrossrefMedlineGoogle Scholar87. Cheng HC , Wu CT , Chang WL , et al. Double oral esomeprazole after a 3-day intravenous esomeprazole infusion reduces recurrent stomach ulcer bleeding in high-risk patients: a randomized controlled trial. Well. 2014;63:1864-72. [PMID: 24658598] doi:10.1136/gutjnl-2013-306531 CrossrefMedlineGoogle Scholar88. Lai KC , Lam SK , Chu KM , et al. Lansoprazole for the prevention of recurrences of ulcer complications with long-term use of low-dose aspirin. N Engl J Med. 2002;346:2033-8. [PMID: 12087138] CrossrefMedlineGoogle Scholar89. Chan FK , Chung SC , Suen BY , et al. Prevent recurrent upper gastrointestinal bleeding in patients with Helicobacter pylori infection who take low-dose aspirin or naproxen. N Engl J Med. 2001;344:967-73. [PMID: 11274623] CrossrefMedlineGoogle Scholar90. Chan FK , Ching JY , Hung LC , et al. Clopidogrel versus aspirin and esomeprazole for the prevention of recurrent ulceration. N Engl J Med. 2005;352:238-44. [PMID: 15659723] CrossrefMedlineGoogle Scholar91. Lai KC , Chu KM , Hui WM , et al. Esomeprazole with aspirin versus clopidogrel for the prevention of recurrent gastrointestinal ulcer complications. Clin Gastroenterol Hepatol. 2006;4:860-5. [PMID: 16797240] CrossrefMedlineGoogle Scholar92. Chan FK , Kyaw M , Tanigawa T , et al. Similar efficacy of proton pump inhibitors vs. H2 receptor antagonists in reducing the risk of upper gastrointestinal bleeding or ulcers in high-risk users of low-dose aspirin. Gastroenterology. 2017;152:105-110. [PMID: 27641510] doi:10.1053/j.gastro.2016.09.006 CrossrefMedlineGoogle Scholar93. Khan MY , Siddiqui WJ , Alvarez C , et al. Reduction of postpercutaneous coronary intervention angina in addition to gastrointestinal events in patients with combined proton pump inhibitors and dual platelet therapy: systematic review and meta-analysis. Eur J Gastroenterol Hepatol. 2018;30:847-853. [PMID: 29596078] doi:10.1097/MEG.00000000000001125 CrossrefMedlineGoogle Scholar94. Hu W , Tong J , Kuang X , et al. Influence of proton pump inhibitors on clinical results in coronary heart disease receiving aspirin and clopidogrel: a meta-analysis. Medicine (Baltimore). 2018;97:e9638. [PMID: 29504996] doi:10.1097/MD.000000000009638 CrossrefMedlineGoogle Scholar95. Bhatt DL , Cryer BL , Contant CF , et al. COGENT Investigators. Clopidogrel with or without omeprazole in coronary heart disease. N Engl J Med. 2010;363:1909-17. [PMID: 20925534] doi:10.1056/NEJMoa1007964 CrossrefMedlineGoogle Scholar96. Wei P , Zhang YG , Ling L , et al. Effects of short-term use of pantoprazole in combination with aspirin and clopidogrel in the treatment of acute STEMI. Exp Ther Med. 2016;12:2861-2864. [PMID: 27882086] CrossrefMedlineGoogle Scholar97. Ren YH , Zhao M , Chen YD , et al. affects the efficacy of clopidogrel, but not ischaemic events in patients with acute coronary syndrome undergoing elective percutaneous coronary intervention. Chin Med J J 2011;124:856-61. [PMID: 21518592] MedlineGoogle Scholar98. Wu H , Jing Q , Wang J , et al. Pantoprazole for the prevention of gastrointestinal bleeding in high-risk patients with acute coronary syndromes. J Crit Care. 2011;26:434. [PMID: 21273036] doi:10.1016/j.jcrc.2010.12.007 CrossrefMedlineGoogle Scholar99. Chan FK , Ching JY , Suen BY , et al. Effects of Helicobacter pylori infection on the long-term risk of stomach ulcer bleeding in low-dose aspirin users. Gastroenterology. 2013;144:528-35. [PMID: 23333655] doi:10.1053/j.gastro.2012.12.038 CrossrefMedlineGoogle Scholar100. Ray WA , Chung CP , Murray KT , et al. Association of proton pump inhibitors with reduced risk of warfarin-related severe gastrointestinal bleeding. Gastroenterology. 2016;151:1105-1112. [PMID: 27639805] doi:10.1053/j.gastro.2016.08.054 CrossrefMedlineGoogle Scholar101. Chan EW , Lau WC , Leung WK , et al. Prevention of dabigatran-related gastrointestinal bleeding with gastroprotective agents: a population-based study. Gastroenterology. 2015;149:586-95. [PMID: 25960019] doi:10.1053/j.gastro.2015.05.002 CrossrefMedlineGoogle Scholar102. Lin KJ , Hernéndez-D'az S , and Garcéa Rodriguez LA . Acid suppressants reduce the risk of gastrointestinal bleeding in patients with antithrombotic or anti-inflammatory therapy. Gastroenterology. 2011;141:71-9. [PMID: 21458456] doi:10.1053/j.gastro.2011.03.049 CrossrefMedlineGoogle Scholar103. Massa Gonzalez EL and Garcéa Rodriguez LA . Proton pump inhibitors reduce the long-term risk of recurrent gastrointestinal bleeding in the upper gastrointestinal area: an observational study. Aliment Pharmacol Ther. 2008;28:629-37. [PMID: 18616644] doi:10.1111/j.1365-2036.2008.03780.x CrossrefMedlineGoogle Scholar104. Lanas A , Garcia-Rodriguez LA and Arroyo MT ; Investigator of the Asociacion Espaéola de Gastroenterologa (AEG). Effect of anti-sectolet drugs and nitrates on the risk of ulcer bleeding associated with nonsteroidal anti-inflammatory drugs, platelet preservatives and anticoagulants. At J Gastroenterol. 2007;102:507-15. [PMID: 17338735] CrossrefMedlineGoogle Scholar105. Islam MM , Poly TN , Walther BA , et al. Negative results of the long-term use of proton pump inhibitors: a systematic review and metaanalysis. Eur J Gastroenterol Hepatol. 2018;30:1395-1405. [PMID: 30028775] doi:10.1097/MEG.000000000000011198 CrossrefMedlineGoogle Scholar106. Hussain S , Siddiqui AN , Habib A , et al. Use and risk of hip fracture by proton pump inhibitors: systematic verification and meta-analysis. Rheumatol Int. 2018;38:1999-2014. [PMID: 30159775] doi:10.1007/s00296-018-4142-x CrossrefMedlineGoogle Scholar107. Nochaiwong S , Ruengorn C , Awiphan R , et al. The relationship between the use of proton pump inhibitors and the risk of negative renal outcomes: systematic review and meta-analysis. Nephrol Dial Transplant. [PMID: 28339835] doi:10.1093/ndt/gfw470 CrossrefMedlineGoogle Scholar108. Hafiz RA , Wong C , Paynter S , et al. The risk of enteric infection in the proton proton acquired by the Community Inhibitor therapy: systematic review and meta-analysis. Ann Pharmacother. 2018;52:613-622. [PMID: 29457492] doi:10.1177/1060028018760569 CrossrefMedlineGoogle Scholar109. Cao F , Chen CX , Wang M , et al. Updated meta-analysis of controlled observational studies: proton pump inhibitors and risk of Clostridium difficile infection. J Hosp Infection. 2018;98:4-13. [PMID: 28842261] doi:10.1016/j.jhin.2017.08.017 CrossrefMedlineGoogle Scholar110. Vaezi MF, Yang YX and Howden CW. Complications of proton pump inhibitor therapy. Gastroenterology. 2017;153:35-48. [PMID: 28528705] doi:10.1053/j.gastro.2017.04.047 CrossrefMedlineGoogle Scholar111. Bosch J , Eikelboom JW , Connolly SJ , et al. Reason, design and basic characteristics of participants in the cardiovascular results for people with anticoagulation strategies (COMPASS) study. Can J Cardiol. 2017;33:1027-1035. [PMID: 28754388] doi:10.1016/j.cjca.2017.06.001 CrossrefMedlineGoogle Scholar112. Moayyedi P , Eikelboom JW , Bosch J , et al. COMPASS Investigators. Pantoprazole to prevent gastroduodenal events in patients receiving rivaroxaban and/or aspirin in a randomized, double-blind, placebo-controlled study. Gastroenterology. 2019;157:403-412. [PMID: 31054846] doi:10.1053/j.gastro.2019.04.041 CrossrefMedlineGoogle Scholar113. Moayyedi P , Eikelboom JW , Bosch J , et al. COMPASS Investigators. Safety of proton pump inhibitors based on a large, multi-year, randomized trial in patients receiving rivaroxaban or aspirin. Gastroenterology. 2019;157:682-691. [PMID: 31152740] doi:10.1053/j.gastro.2019.05.056 CrossrefMedlineGoogle Scholar114. Wong GLH , Lau LHS , Ching JYL , et al. Prevention of recurrent idiopathic gastroduodenal ulceration: a double-blind, randomized study. Well. 2019. [PMID: 31229990] doi:10.1136/gutjnl-2019-318715 CrossrefMedlineGoogle Scholar115. Baracat FI , de Moura DTH , Brunaldi VO , et al. Randomized controlled study of hemostatic powder versus endoscopic clipping for non-variceal upper gastrointestinal bleeding. Surg Endosc. [PMID: 30927124] doi:10.1007/s00464-019-06769-z CrossrefMedlineGoogle Scholar116. Toka B , Eminler AT , Karacaer C , et al. Comparison of monopolar hemostatic pliers with soft clotting with hemoclip for gastric ulcers: a randomized study (with video). Gastrointestinal endosc. 2019;89:792-802. [PMID: 30342026] doi:10.1016/j.gie.2018.10.011 CrossrefMedlineGoogle Scholar117. Kantowski M , Schoepfer AM , Settmacher U , et al. Evaluation of the endoscopic doppler for the conduct of hemostasis in case of bleeding with high risk from stomach ulcers. Scand J Gastroenterol. 2018;53:1311-1318. [PMID: 30394134] doi:10.1080/00365521.2018.1509121 CrossrefMedlineGoogle Scholar118. Schmidt A , Gölder S , Goetz M , et al. Over-the-scope clips are more effective than standard endoscopic therapy for patients with Blutungen von Magengeschwüren. Gastroenterology. 2018;155:674-686. [PMID: 29803838] doi:10.1053/j.gastro.2018.05.037 CrossrefMedlineGoogle ScholarPage 2Pharmacy 2Pharmacy Managers are involved in administering prescription drugs to more than 266 million Americans in private and public health plans, making them the main buyers of prescription drugs in the United States. Some industry estimates show that the tools that PBMs use, such as negotiating rebates and rebates from drugmakers, encouraging generic consumption, and offering alternative pharmacy channels, could lead to savings of 654 billion dollars between 2016 and 2025, including 350 billion dollars in commercial plans and more than 250 billion dollars in Medicare Part D prescription drug plans (3). Analysts report that the total value of the pharmaceutical manufacturers' price concessions in 2017 was USD 127 billion (4). Pharmacy service managers claim that they save consumers an average of USD 941 per year (5). Despite the potential cost savings, PBMs face increased scrutiny in the face of rising drug prices. There is little transparency in THE PBMs, and the contracts negotiated between health plans and PBM for fees, and the proportion of a discount withheld by the PBM, are considered confidential. Prescription drug prices have risen by more than 10% per year for each of the top 20 brand-name drugs prescribed to seniors, and PBMs are negotiating discounts on these higher prices (6). Pharmaceutical companies claim to be raising prices to pay for the discounts demanded by the PBMs, but PBM refutes this (7). Over the last decade, PBMs have seen higher revenues as list prices for medicines, especially high-priced specialty medicines, have continued to rise. Operating profit of the 3 PBMs with the largest market share increased from 3.4 billion U.S. dollars in 2007 to 12.4 billion U.S. dollars in 2016 (8). The recent consolidation of the PBM market has given the few large PBMs greater leverage and bargaining power. Although there are about 60 PBMs operating in the United States, the consolidation has resulted in 3 of them (CVS Caremark, OptumRx and Express Scripts) accounting for up to 85% of the market share (9). Two mergers between PBM and health insurers have raised concerns among providers, patients and other stakeholders that increased market concentration as a result of the mergers could lead to reduced competition and higher prices for patients. The first merger concerned Cigna's acquisition of Express Scripts and was approved by the Ministry of Justice in September 2018 (10). The second concerned cvS Health, which Aetna acquired as CVS tried to expand its MinuteClinic model and provide additional medical services at its sites (11). The American Medical vehemently opposed the merger, pointing to the potential for less competition in the market and higher prices for consumers (12). On 10 October 2018, the Ministry of Justice approved the merger on the condition that CVS divest Aetna's medicare Part D business (13). As the market continues to consolidate, companies like Amazon are looking for the possibility of by selling prescription medicines and medical devices directly to consumers, convinced that eliminating the middleman will lead to cost savings. Some insurance companies have decided to end their relationship with PBMs indefinitely and create their own internal PBMs. In 2017, For example, Anthem announced that it would end its relationship with Express Scripts and develop its own pharmacy benefit management arm called IngenioRx by 2020 (14). In the US pharmaceutical market, where consumer competition and consumer choice are cornerstones of a healthy market system, consolidation that limits these factors can create scenarios in which PBMs are not motivated to negotiate with manufacturers to keep drug costs low. In addition, PBMs have been criticized for clawbacks that occur when patient payments or coinsurance are set at a rate higher than the cost of the drug for the insurer. A recent study showed that patients were overpaid for their prescriptions by at least 2.00 23 percent of the time in 2013, with an average overpayment of USD 7.69 and a total overpayment of USD 135 million (15). Increased visibility and criticism of PBMs, including class-action lawsuits, have been filed against PBMs alleging illegal pricing systems, violations of anti-kickback statutes, and other misconduct (16). Between 2017 and 2018, 27 states enacted laws that would prohibit gag clauses from preventing pharmacists from telling consumers when they can get their drugs at a lower price if they pay for the drug instead of through their insurance plan. In addition, some states have introduced or passed laws requiring PBM to disclose business relationships with pharmacies and health plans. In total, there are 191 PBMs legislation in 46 countries, which includes various provisions to improve transparency, pricing and licensing (17). The Pharmacy Benefits Manager & Records Act was enacted on July 10, 2017 and prohibits gagging clauses for pharmacists that prevent them from passing on certain information to a person who buys a drug, such as the availability of other, more cost-effective drugs. The bill also prohibits a healthcare company or PBM from requiring a person to pay an amount for a covered prescription greater than the lowest of the applicable supplement; the amount of damage allowed (the amount pledged by the health provider or THE PBM to pay the pharmacy); or the amount a person would pay for the drug if they did not have an insurance plan, benefits or discounts. Finally, the draft law authorises the to check the contracts of pharmacy services for your compliance and to react to infringements by invalidating contracts containing unfair commercial practices (18). Maine passed two bills that seek to fix potential problems related to PBM. The Clean Claims Submitted by Pharmacies Act prohibits a Insurance institution or [PBM] from the collection of a co-payment or other fee exceeding the claim costs of a prescription drug and prohibits a carrier or [PBM] from penalising a pharmacy provider for providing information (gag clause) related to the cost of a participant a-pocket or the clinical efficacy of a prescription or alternative medicinal product (19). The Maximum Allowable Cost Pricing Lists Act sets requirements for maximum allowable costs (MAC) price lists used by [PBMs], requires [PBMs] to provide information about these prices and the methods used to plan this pricing for sponsors, a complaint procedure for pharmacies for disputes related to maximum allowable cost prices, and provides for financial penalties for violations (20). In addition, the state passed a law on maximum allowable price lists used by pharmacy benefit managers who charge prescription drug costs from PBMs to plan sponsors of the maximum allowable price list (20). In 2017, North Dakota passed two bills to provide for a comprehensive reform of PBM operations in the state. This included prohibiting PBMs from charging pharmacies certain fees, including by point of sale (also known as direct or indirect compensation fees); the obligation of PBMs to share the amount reimbursed to a pharmacy for a prescription; Prohibition of gag clauses; prohibits PBM from imposing accreditation standards on pharmacies that go beyond the federal and state licensing requirements to enter their networks; and the introduction of conflict of interest provisions (21). The Pharmaceutical Care Management Association challenged the laws in court, claiming that they were anticipated by the Federal Employee Retirement Income Security Act of 1974. In November 2017, a judge in the U.S. District Court for the District of North Dakota found that neither the law related to plans under the Employee Retirement Income Security Act nor was related to the law that would succeed on merit, and rejected the Pharmaceutical Care Management Association's request for injunction. The court ultimately ruled that neither the Employee Retirement Income Security Act of 1974 nor Medicare prejudged state laws, and that they can be enforced in their entirety, with the exception of the Plan Disclosure Provision (22).1. ACP supports improved transparency, standards, and regulation for pharmacy benefit managers (PBMs), including a ban on gag clauses that prevent pharmacies from sharing price information with consumers. ACP supports strict oversight and mergers and consolidation on the PBM market. The continued lack of transparency on the part of PBMs and insurers can hinder the view of patients, doctors, and others on the drug supply chain and make it difficult to determine whether a particular company is unreasonably driving up drug prices. This lack of transparency can also prevent the identify of viable policy solutions and further delays. Comes. this would help curb spending on prescription drugs. Although there have been many calls for transparency from pharmaceutical companies and greater support for transparency in healthcare in general, all stakeholders must commit to improving transparency as the healthcare industry works towards creating an innovative but sustainable market for prescription drugs. The Trump administration included PBM transparency in its draft drug pricing, American Patients First, and asked for information on how to improve transparency about PBMs and the prices that patients pay at the pharmacy (23). The National Academy for State Health Policy drafted a model law on PBMs, which consists of various provisions of the proposed and enacted state legislation, including licensing, fiduciary liability, a ban on gagging clauses, limiting the cost of patients a-pocket, conflicts of interest, consumer protection, discount transparency, and restrictions on PBM requirements for pharmacies (24). The aim of the law was to bring more transparency and better business practices to a traditionally furtive industry. Banning gag clauses that prevent pharmacists from informing patients when cheaper alternatives are available, such as.B paying cash for a prescription rather than going through insurance coverage, is a sensible move that has won bipartisan support. Recently, the Centers for Medicare & Medicaid Services sent a letter to Medicare Sub-D Plan administrators, declaring that such clauses are unacceptable and run counter to our efforts to promote transparency in drug prices and lower drug prices (25). The consolidation of the PBM market raises concerns about possible antitrust problems and has proven to be a price increase for patients (26). Although there are many smaller regional PBMs, the large national PBMs, which account for most of the market share, continue to be equipped with pharmaceutical companies. More broadly, agreements between PBMs, insurers or other companies should be subject to a rigorous review of both potential antitrust issues and implications for other aspects of the pharmaceutical supply chain, such as the entry of generics and biosimilars.2. ACP supports the availability of accurate, comprehensible, and actionable information about the price of prescription drugs. The ACP urges health plans to provide doctors and patients with this information at the time of prescribing in order to ensure sound decision-making on clinically appropriate and facilitate care. Patients are being urged to take more responsibility for their health care, as they shoulder greater cost-sharing through highly deductible health plans and co-insurance. Therefore, they are more likely to talk to their doctors about the cost of certain treatments. However, doctors often do not have the information to communicate with patients who ask for prescription drugs, and A survey showed that while most doctors said that costs should be taken into account in their decision-making, they have limited knowledge of cost estimates (27). One study found that doctors correctly estimated the price of a prescription drug less than half the time (28). Providing cost and pricing information to doctors can be associated with positive results. One study found that the use of an electronic drug reference database containing information on patient drug coverage led to the prescription of different medicines, increased the likelihood of prescribing generics and led to a shorter time for prescribing new generics (29). Studies have also shown that the disclosure of forms and drug costs to providers is associated with smaller increases in total drug costs; However, this cannot lead to lower out-of-pocket costs or higher drug use (30). Further studies are needed to determine how to maximize potential cost savings. It is also important that the information provided is accurate, up-to-date and actionable. A review of formula accuracy in electronic medical records found that 95.3% of the time for Medicaid patients were accurate for the reviewed family medical records, but only 78.2% of the time for people with private insurance (31). As the health system has shifted to a higher value on quality, not on the quantity of care, consumers have a greater responsibility for the cost of health goods and services and have become more involved in their care. Despite this emphasis on the consumer, doctors and other healthcare professionals account for a significant proportion of health spending (32). Although the pursuit of better engagement among payers, doctors and patients has recently been a priority, there are still large gaps and additional efforts are needed to make progress (32). Health plans should explore strategies such as.B, value-based insurance design, which has been shown to improve drug liability and reduce costs for patients. Additional studies on value-based insurance design are needed to determine the best design to optimize quality and improve cost savings (33).3. ACP believes that health plans, PBMs, and drugmakers should report to the Department of Health and Human Services the amount paid for prescription drugs, the total amount of discounts, and non-proprietary pricing information, and make publicly available. Each disclosure mandate should be that negotiated rebates are de-identified with certain companies and that confidential information that could be considered as trade secrets or could lead to price increases. There is a great deal of interest from policymakers and the public in greater transparency in pricing and payment for prescription drugs. Legislation at the federal level would bring additional transparency to the PBM by that a certain amount of rebates is passed on to insurers and consumers. The Creating Transparency to Have Drug Rebates Unlocked Act, introduced in the Senate, would address a lack of transparency in PBMs, especially Medicare. It would require the PBM to repay the total amount of rebates they receive from pharmaceutical companies and how much of those rebates will be repaid to Medicare beneficiaries. The revelations would be posted on the Website of the Centers for Medicare & Medicaid Services. After the PbM expires, a minimum percentage of rebates would be passed on to a health plan with the aim of reducing premiums or other cost sharing. The cost-sharing for part D beneficiaries would be based on the negotiated price of medicinal products as opposed to the list price and would bring greater benefits (34). Reporting rebates could help address a problem in Medicare Part D, where plan sponsors underestimate the amount of rebates they receive. A report by the inspector general found that in 2008, the plan sponsors underestimated their planned offers by 69% of the time, resulting in higher premiums for beneficiaries (35). The main concern about such mandates is that the disclosure of price or rebate information may lead to tacit collusion between manufacturers, which may lead to higher prices (36). In addition, companies can claim that this information could be considered a trade secret. Approaches to alleviating disclosure mandate concerns include provisions that companies must disclose unless they can demonstrate that the information constitutes a trade secret, or involve other experts in a field such as researchers or patient advocates who would analyse data and release it in a way that would no longer constitute a trade secret (37). Page 3The Medicare Part D Prescription Drug Program is a voluntary benefit available to Medicare recipients when MMA was passed in 2003. In 2018, a standard Medicare Part D plan included a deductible of up to USD 405; an additional payment or co-insurance (usually for high-priced, special or non-preferred medicines) for prescriptions with an initial coverage limit of up to USD 3750; and a coverage gap (also known as the doughnut hole) in which beneficiaries pay a larger share of the cost of medicines up to USD 5000. After reaching USD 5000 in out-of-pocket costs, the beneficiaries enter the catastrophic coverage level (9). Low-income beneficiaries eligible for Medicare and Medicaid, qualified Medicare recipients, certain low-income Medicare recipients, qualified individuals, and those receiving only social security contributions are automatically entitled to the Income Support Programme (LIS) and are automatically enrolled in a prescription drug plan with premiums at or below the national average if they do not choose their own plan (9). Those in the LIS program pay nothing for prescription drugs once they have reached the catastrophic stage, while those who are not in the program have a lower level cost sharing, but are at risk for high out-of-pocket costs (10). In 2015, 9% (3.6 million) of Medicare Part D recipients had total drug spending above the threshold for catastrophic coverage, and 72% of them (2.6 million) participated in the LIS program. After 2017, Medicare spending, including prescription drug payments, should grow faster than spending on private health plans. Medicare also pays for a limited number of medications via the Part B benefit, such as drugs used with long-lasting medical equipment, injectable osteoporosis drugs, other injectable and infused medications and medications used in the outpatient environment of the hospital (which are used in patients under observational status in a hospital without being formally approved, or those used in outpatient clinics on the same day). Payments for Part B drugs are calculated as an average selling price plus 6% (ASP+6%) a formula introduced in 2006 after the adoption of the MMA. As part of the 2012 budget commitment, the Centers for Medicare & Medicaid Services (CMS) had to cut payments for Part B by about 2%, so that the current reimbursement rate is ASP+4.3%. In 2015, Medicare part-B drugs, including those administered by doctors, suppliers, and hospital outpatients, accounted for usd 25.7 billion in Medicare spending, with two-thirds (USD 17.0 billion) of part B (11) expenditure staked by doctors and suppliers. Although Part B covers a range of medicines, including some more cost-effective generics, the top 10 drugs that account for the largest share of part B spending are more expensive and typically range from between 1000 and 6000 dollars per administration (12). Most of them are biologics without biosimilar competition. Medicaid payments for outpatient prescription drugs vary from state to state, and states have flexibility over whether to offer a prescription drug program and how they manage the program, though there are federal requirements related to the federal rebate program and reimbursement plans (13). The Medicaid Drug Rebate Program (MDRP) requires drug makers to enter into a rebate agreement with the secretary of the Department of Health and Human Services (HHS) in exchange for coverage of the manufacturer's drugs through state Medicaid programs. Under the MDRP, manufacturers are required to pay states a discount for each unit of a drug that falls under a state Medicaid program. The discount is calculated by CMS and is based either on a percentage of the average manufacturer's price (AMP) of the drug or on the lowest price, wholesalers and other consumers. This allows states to offer buyers the best price and create a best-price lower limit, with no buyer able to negotiate the price of a drug that is below the Medicaid price (14). Manufacturers are responsible for providing CMS with the price of the drug (either AMP or best price) and product information, including classification as an innovator or non-innovator drug. With a few exceptions, manufacturers of usually branded name) drugs are obliged to pay a discount of either 23.1% of amp per unit or the difference between the AMP and the best price, while discounts for non-innovator (generic) drugs amount to 13% of the AMP per unit (15). As part of the Bipartisan Budget Act of 2015, manufacturers are required to offer additional discounts if the AMP of a drug exceeds the inflation rate (16). Although much of the public controversy over the prices of Sovaldi (sofosbuvir), Daraprim (pyrimethamine) and the EpiPen and EpiPen Jr-Epinephrine injectors has died, federal measures to reduce the price or cost of prescription drugs have been primarily incremental, and additional reforms by policymakers are needed to reduce the cost of insulin, antibiotics and other common prescription drugs. , which have experienced large price increases that can make them prohibitively expensive for patients. The Bipartisan Budget Act of 2018 included two proposals related to drug costs: one to close the Medicare Part D coverage gap in 2019, a year earlier than planned, and the other to avoid the exclusion of biosimilars in the coverage gap rebate program. At the state level, significant activities have been achieved to combat high drug prices, with a focus on transparency, the prevention of price fixing and legislation related to pharmacy service managers. A bill passed in Maryland would have required the state Medicaid agency to notify the attorney general of an excessive price increase for a major generic or an unpatented brand-name drug, with fines of up to 10,000 U.S. dollars for violations (17). That law was overturned by the Fourth Court of Appeal on the ground that it had infringed constitutional rights in connection with interstate trade (18). Several bills have been introduced in Congress proposing solutions that include drug importation, intellectual property protection, and the establishment of an interagency committee to review drug prices (19). The House and Senate held 25 hearings between the 114th and 115th Congress, which are relevant to drug pricing, namely price jumps or price spikes, investments in biomedical innovation, and the reauthorization of the Prescription Drug User Fee Act (20). President Trump has made reducing the cost of prescription drugs a central aspect of his 2016 campaign, and his administration has explored ways to make the cost of prescription drugs affordable for Americans. The administration has proposed several regulations to address the problem of price transparency and drug payment in government programs. White House proposals, including the budget proposal for the 2019 financial year; the Council of Economic Advisers; and hhS companies have focused on reducing costs for patients, such as.B by passing on the rebates negotiated by pharmacy service managers to Medicare Part D beneficiaries at the pharmacy counter. In May 2018, President Trump introduced American Patients First, a set of policy priorities. Priorities. Proposed measures that HHS could take to reduce spending on medicines in four key policy areas and reduce the list price for medicines: improved competition, better negotiation, incentives for lower list prices and lower out-of-pocket costs (21). Immediate action includes measures to promote biologics and prevent the playmaking of the regulatory process, experiment with value-based purchasing in federal programs, and develop proposals to stop price increases in the private market resulting from Medicaid or the Patient Protection and Affordable Care Act. The government strongly opposed foreign governments, which it said were taking advantage of U.S. innovation by undervaluing drugs, an idea also discussed in the White House Council of Economic Advisers White Paper on biopharmaceutical pricing reform, reflected in the government's early announcement on the proposed regulation of an international price index for certain Medicare Part B drugs. The Council of Economic Advisers proposed to pursue an improved trade policy or policy linking public refunds in the United States to prices paid by foreign governments (22). However, it is unclear how these and other proposals will be implemented or enforced.1. ACP supports

the amendment of the Medicare Part D program for low-income subsidies (LIS) for cost-sharing and co-payment to encourage the use of lower-cost generic or biosimilar drugs, such as.B eliminating the cost-sharing of generics for LIS members. Twelve million Medicare Part D beneficiaries are enrolled in the LIS program. Although the use of low-cost generics by Part D beneficiaries is relatively high and continues to increase as generics become available, the overall drug use rate among LIS recipients is lower than for other Medicare recipients. The Medicare Payment Advisory Commission analyzed data on generic sands for LIS enrolments and non-LIS enrolments between 2009 and 2011, and found a rate of 74% and 79% respectively in 2011 (23). An analysis of CMS data showed a generic drug delivery rate of 79.2% among LIS participants compared to 83.1% for non-LIS participants, with consistent differences between groups of 4% or 5% between 2006 and 2012 (23). Despite the current rate of generic tax on LIS enrolments and non-LIS enrolments, additional savings are possible for Medicare and its beneficiaries. The CMS estimates that Medicare could have saved nearly 9 billion dollars if available equivalent generics had been used instead of brand-name drugs, and 3 billion dollars in to the Part D programme and its beneficiaries (24). Zero-copay generics have the strongest effect on generic drug use for both LIS recipients and non-LIS enrolments (25). Up to a total maximum of USD 5000, LIS participants will pay either USD 1.25 or USD 3.35 for generics and USD 3.70 or USD 8.35 for brand-name medicines (26). The price difference may not provide sufficient financial incentives for an LIS LIS to choose a generic drug over a brand name drug. Reducing or eliminating cost-sharing for LIS participants would not require legislative action, as this would not increase cost allocation, reduce overall costs for LIS participants and promote the use of generic sedans among them. Reducing or eliminating cost-sharing or co-payments for generics could also reduce Medicare spending on reinsurance payments, as the majority of participants who reach the catastrophic stage of coverage are in the LIS program (24). In addition to conventional generics, biosimilar cost sharing should also ensure that LIS participants have an incentive to choose lower-cost alternatives to branded biopharmaceuticals. Biosimilars have the potential to save USD 54 billion in direct expenditure on biological medicines between 2017 and 2026 (27). The U.S. Food and Drug Administration (FDA) has approved 9 biosimilars for use in the United States. However, most approved biosimilars are delayed by patent disputes or settlement agreements between biosimilar and reference product manufacturers, and only 3 biosimilars are currently marketed in the United States (28). For example, Amjevita (adalimumab-atto), a biosimilar of the blockbuster biologic Humira (adalimumab), was approved in 2016, but will not be released in the United States until 2023 (29), and a second biosimilar by Humira, Cyltezo (adalimumab-adbm), will be bound in litigation related to the large number of patents (also known as patent rebates). Despite the delay in the launch of most biosimilars, payment and cost-sharing measures for authorised indications of biosimilars should now be established in order to influence price decisions and promote the use of these medicinal products as soon as they enter the market.2. The ACP countries support annual spending caps for Medicare Part D recipients who are in the catastrophic phase of coverage. In 2016, Medicare recipients spent an average of USD 3024 on medical expenses, including USD 756 (25%). Medicare recipients can bear significant costs for prescription drugs if they take expensive specialty drugs and reach the catastrophic coverage phase. Between 2007 and 2015, the number of seniors in Medicare Part D reaching the catastrophic limit of coverage doubled to more than 1 million. In 2015, these participants paid an average of more than 3,000 dollars out of their pockets, with 1 in 10 spending at least 5,200 dollars, mainly driven by hepatitis C drugs (10). This group is likely to take higher-priced specialty drugs (defined by as a medication with a negotiated monthly price over 670 USD) for chronic diseases and can also take several medications (10). Non-LIS participants using certain specialty drugs for certain health conditions were more likely than those with other conditions to reach the catastrophic stage of coverage (31). Medicare recipients have an average per capita income of USD 13 to USD 30 050, depending on demographic characteristics. The high out-of-pocket costs associated with these specialty drugs can create barriers to access to these patients. In 2012, 96% of patients taking specialty drugs for multiple sclerosis reached the catastrophic stage of reporting, and 48% reached this stage by the end of February. In 2008, only 4% of patients taking multiple sclerosis drugs reached the catastrophic stage by the end of February (32). An analysis of specialty medicines showed that the selling price of the multiple sclerosis drug Avonex (interferon No. 1) increased by 333.5% between 2005 and 2015 (from USD 17 438 to USD 75 595) (31). Policymakers should introduce caps on prescription drug spending during the catastrophic period of coverage to protect vulnerable seniors from increased financial burdens. In other areas of Medicare, caps have been proposed; A 2016 resolution from the House Budget Committee included a Medicare proposal with a catastrophic cap on annual spending a-pocket, which it said was an important aspect of the private insurance market that is currently lacking in Medicare, which would protect the sick and poorest beneficiaries (33). Policymakers should also consider how to mitigate or minimize possible unintended consequences of a cap, such as .B reform of the structure of Medicare reinsurance subsidies, or the change in Part D's risk adjustment algorithm without imposing additional costs on beneficiaries.3. Acp supports the adoption of Medicare Part D negotiation models that would lower the price of prescription drugs for beneficiaries. While the ACP States reaffirm their support for a complete repeal of the non-interference clause, acp also supports an interim approach, such as the possibility for the Minister of Health and Human Services (HHS) to negotiate a limited number of high-priced or individual medicines.b. ACP supports a public Medicare Part D plan option that allows the HHS secretary to negotiate prices with drugmakers. Any public plan run by Medicare must meet the same requirements as private plans and comply with ACP policies on formulas. Since the introduction of MMA in 2003 (34), there has been discussion of allowing Medicare to use its purchasing power and negotiating the price of drugs in the Part D program directly with pharmaceutical manufacturers. Negotiations were considered for inclusion, but the bill ultimately included a non-interference clause that strictly prohibited HHS from entering the intervene between drug manufacturers and pharmacies and sponsors of the prescription plan and require a specific formula or [introduction] of a price structure for the reimbursement of covered Part D medicines in order to promote competition in the market (35). Opponents of repealing the non-interference clause claim that the current system is working well and that spending in the program is below the original projections. Reports from the Congressional Budget Office, which The Office of the Inspector General (OIG) and the Government Accountability Office have found that the Medicaid program, which requires mandatory federal rebates, is able to achieve lower average drug prices than those in Part D (36, 37). An assessment by the Congressional Budget Office in 2007 to repeal the non-interference clause found that there would be modest cost savings if the government were able to negotiate, and stated that the government would not be able to achieve better prices than those already negotiated without limiting the formula, similar to the Department of Veterans Affairs or under other specific circumstances. , e.B. for single medicines without market competition (38). Other estimates, however, put the potential savings much higher (up to 16 billion dollars a year) if the government were able to negotiate for Part D drugs and achieve the same prices as the Department of Veterans Affairs or Medicaid (39). Giving Medicare Part D the power to negotiate drug prices is favored by a bipartisan majority of the public, with more than 90% of Democrats, Republicans, and independents agreeing with this approach (40). The negotiating power was also endorsed in a report by the National Academies of Sciences, Engineering, and Medicine on improving the affordability of prescription drugs as part of a package of broader reforms to consolidate and use purchasing power and strengthen form design (41). The decision on how and to what extent Medicare should negotiate drug prices is complex, and policymakers have begun to examine the scope of government bargaining power. In one proposal, the researchers presented three key questions to be taken into account when evaluating negotiating proposals for Part D: what drugs HHS would have to negotiate, whether HHS could negotiate both price and formula design, and whether the negotiated terms would apply to all Part D plans (42). A proposal that emerged during the Obama administration would allow HHS to negotiate a limited amount of cost and biological drugs (43). Senator Bernie Sanders' Medicare for All Act would give the federal government monopsony power to negotiate prescription drug prices with pharmaceutical manufacturers (44). The ACP countries have long pursued policies to support Medicare's ability to use its purchasing power and negotiate drug prices directly with manufacturers, and continue to support the repeal of the non-interference clause. Although negotiations alone may not be enough to curb drug prices, this approach would allow the government to To reduce the cost of the Medicare program, while allowing plan sponsors to retain the power to negotiate for the vast majority of drugs covered by the program. Without repeal, the non-interference clause should be amended to allow the government to negotiate on high-cost drugs, in which Medicare has significant financial interests. Another proposal is the creation of a public option plan, Part D, in which the HHS negotiates drug prices within the plan and has authority over the prescription in addition to private plans. This type of plan would work in the same way as private plans, but would allow the government to exclude certain drugs from the formula as long as they meet the minimum benefits required by other plans, and in a way that is consistent with ACP policy on formulas. An examination of the potential impact of such a plan revealed some competitive advantages (45). This approach may be limited in scope, as it would only benefit those who choose the plan, and potential exclusions in forms can cause problems related to the Medicare safety net (46). A public plan approach should be tested before a comprehensive rollout.4. ACP supports efforts to minimize the financial impact on the federal government of the misclassification of prescription drugs in the Medicaid Drug Rebate Program (MDRP). The Centers for Medicare & Medicaid Services should determine which legal authorities are necessary to ensure compliance with the MDRP, and Congress should pass legislation to grant such agencies. Misclassifications in the MDRP can increase the share of spending on prescription drugs and divert funds from other programs and services. In response to a request from Congress, the OIG conducted a study on misclassifications in the MDRP and found that manufacturers may have misclassified 885 of the 30,000 drugs in the program (47). Ten misclassifications between 2012 and 2016 may have cost Medicaid '1.3 billion in lost base and inflation-adjusted rebates, and four manufacturers were associated with more than half of the misclassifications (47). Two drugs, the EpiPen and EpiPen Jr autoinjectors, were improperly classified as generics for the purposes of the program, although they did not have an FDA-approved equivalent. The maker of the EpiPen, Mylan, recently entered into a settlement agreement with the Department of Justice to settle claims related to the False Claims Act for knowingly misclassifying the EpiPen to avoid rebates (48). The False Claims Act is used to prosecute cases in which the federal government has been defrauded by a private party. Outside of the prosecution under the False Claims Act, the OIG alleges that HHS does not have explicit legal authority to require manufacturers to modify data that has been misclassified, and oversight of the program was weak. The OIG recommends that CMS pursue a means of Correcting inaccurate classification data reported to the Medicaid rebate program, and suggests that CMS could seek legislative authority to force manufacturers to provide accurate data or improve up-to-date data (47). The chairmen of the Congressional Committee recently sent a letter to cmS Administrator Seema Verma expressing concern about misclassifications and asking for additional information about CMS authorities and monitoring the program (49). Granting permission from CMS, CMS, Manufacturers who change classification data and support improved monitoring of the program will ensure that state Medicaid programs receive adequate discounts on prescription drugs and minimize potential disruptions to access to drugs among Medicaid recipients.5. ACP supports further investigation of payment models in federal health programs, including methods for aligning the payment of prescription drugs administered in the office, in a way that would reduce incentives to prescribe higher-priced drugs when cheaper and similarly effective drugs are available. Medicare Part B payment for a medically administered drug is tied to the price of the drug, which can help companies set high list prices for those drugs and provide a greater incentive to prescribe more expensive drugs, even if there are cheaper, similarly effective alternatives that would be tolerated by the patient. In 2016, CMS proposed tests to pay for prescription drugs in Medicare Part B in a nationwide demonstration project through the Center for Medicare & Medicaid Innovation. The project would have changed the current ASP+6% payment for Part B drugs to an ASP+2.5% payment and a flat fee in the initial phase of the project, and in the second phase would have tested value-based purchasing, such as reference prices or indication-based pricing. The project sparked public backlash, particularly from pharmaceutical companies and some medical companies, based on Medicare data suggesting that patient access under Part B would be better than the formula proposed by the demonstration. The project was officially withdrawn in July 2017 (50). The ACP comments on the proposed rule expressed concerns about the first phase of the project, in particular the financial burden that the change might have entailing for small or solo practices, and called on the CMS to reconsider the scope of the demonstration (51). Several alternatives to the ASP+ payment model have been proposed. A proposal would have shifted the payment for some drugs from Part B to Part D (52). Another called for improved ASP data reporting, changes in the payment rate for drugs paid at wholesale purchase costs, an obligation for manufacturers to pay Medicare a discount if the ASP exceeds an inflation benchmark, consolidation of billing codes and negotiations between providers and manufacturers on behalf of doctors (53). A third proposal proposed to eliminate the link between price and payment, and another advocated the establishment of two Medicare paid the lower option for a particular drug (54). These and other proposals need to be further investigated to determine whether they would really lead to cost savings, their potential impact on doctor's offices of different sizes, impact on patient access and possible unintended consequences. Demonstration projects or pilot projects resulting from proposals should be met with robust robust doctors) should be scaled appropriately and safety precautions should be in place to ensure patients' access to medicines. Page 4I served as an officer in the Marine Corps for 10 years before becoming a physician-scientist. My perspectives on military life and medicine therefore developed independently of each other. These two worlds crossed during the residency at Philadelphia Veterans Affairs (VA) Medical Center. Here my military service helped me to be a better doctor. It was there that I shared my military experience for the first time with my VA colleagues, most of whom miss the experience. Many aspects of the military seemed alien to them, despite their years of service, which cared for veterans. As a doctor and veteran, I have learned that a better understanding of ... References Page 5Admissions and search committees often include 1 or more diversity champions who focus on recruiting students, trainees, faculty and leaders of underrepresented minorities (URM) to improve diversity in medicine. It was proposed that as a best practice for URM recruitment in medical schools, institutions should use high-level URM faculties, residents and students to serve as recruiters, interviewers and members of the electoral committee on admissions committees (1). But, despite the tireless efforts of many people, progress has been slow. In addition, this practice has created the well-known minority tax, the disproportionate burden and the resulting emotional exhaustion that many URM persons ... References1. Smedley BD , Stith AY , Colburn L , et al. Institute of Medicine (USA). The Right Thing to Do, The Smart Thing to Do: Enhancing Diversity in the Health Professions: Summary of the Symposium on Diversity in Health Professions in Honor of Herbert W. Nickens, M.D. Washington, DC National Academies Pr 2001 Google Scholar2. Association of American Medical Colleges. U.S. Medical School Faculty, 2017. Complementary table C. Department chair by department, gender and race/ethnicity. 2018. Access to www.aamc.org/download/486590/data/supplementaltablec.pdf on August 18, 2019. Google Scholar3. Institute for Diversity in Health Management. Diversity and Disparities: A Benchmarking Study of U.S. Hospitals in 2015. Chicago: Institute for Diversity in Health Management; 2015. Access to www.diversityconnection.org/diversityconnection/leadership-conferences/2016%20Conference%20Docs%20and%20Images/Diverity_Disparities2016_final.pdf on August 18, 2019. Google Scholar4. Aysola J , Barg FK , Martinez AB , et al. Perception of factors associated with inclusive work and learning environments in health organizations: a qualitative narrative analysis. JAMA Netw Open. 2018;1:e181003. [PMID: 30646094] CrossrefMedlineGoogle Scholar5. Capers Q 4th , Clinchot D , McDougle L , et al. Implicit racial bias in the admission of medical schools. Acad Med. 2017;92:365-9. [PMID: 27680316] doi:10.1097/ACM.0000000000001388 CrossrefMedlineGoogle Scholar6. Devine PG , Researcher , Cox WTL , et al. Gender-based, habit-breaking intervention led to increased recruitment of female faculties in STEM departments. J Exp Soc Psychol. 2017;73:211-5. [PMID: 29249837] doi:10.1016/j.jesp.2017.07.002 CrossrefMedlineGoogle Scholar Page 6Disclaimer: The content of this article is solely the responsibility of the authors and does not represent the official views of the National Institutes of Health.Grant Support: The authors confirm the support of the Columbia Precision Medicine Initiative, Columbia University, New York, New York, and the National Institutes of Health (NIH), Columbia Clinical and Translational Science Award Grant UL1TR001873 from the National Center for Translational Sciences (NCATS). Dr. Bello reports on the support of the NIH/National Heart, Lung, and Blood Institute Grant K23 HL136853 and the Katz Foundation. Dr. Miller reports on nih/NCATS 5KL2TR001874, NIH/National Institute of Neurological Disorders and Stroke Grant K23NS107645, and Louis V. Gerstner, Jr. Foundation.Disclosures: Dr. Bello reports non-financial support from the American Heart Association outside of the submitted paper. Dr Miller reports on personal compensation for drug counseling related to a maternal stroke. Authors, who are not named here, have not disclosed any conflicts of interest. The disclosures can also be viewed under www.acponline.org/authors/icmje/ConflictOfInterestForms.do?msNum=M19-1601. Darren B. Taichman, MD, PhD, Executive Editor, reports that he has no financial relationships or interests to disclose. Cynthia D. Mulrow, MD, MSc, Senior Deputy Editor, reports that she has no relationships or interests to disclose. Jaya K. Rao, MD, MHS, Deputy Editor, reports that she holds shares/options to Eli Lilly and Pfizer. Catharine B. Stack, PhD, MS, Deputy Editor, Statistics, reports that it holds shares in Pfizer, Johnson & Johnson and Colgate-Palmolive. Christina C. Wee, MD, MPH, Deputy Editor, reports on employment at Beth Israel Deaconess Medical Center. Sankey V. Williams, MD, Deputy Editor, reports that he has no financial relationships or interests to disclose. Yu-Xiao Yang, MD, MSCE, Deputy Editor, reports that he has no financial ties or interest to disclose. Corresponding author: Natalie A. Bello, MD, MPH, Division of Cardiology, Columbia University Medical Center, 622 West 168th Street, PH 3-342, New York, NY 10032; Email, . Current author addresses: Dr. Bello: Division of Cardiology, Columbia University Medical Center, 622 West 168th Street, PH 3-342, New York, NY 10032.Dr. Miller: Neurological Institute of New York, 710 West 168th Street, 6th Floor, New York, NY 10032.Dr. Columbia University Irving Medical Center, 622 West 168th Street, 16-66, New York, NY 10032.Dr. Wapner: Columbia University Irving Medical Center Center 622 West 168th Street, PH-16-66D, New York, NY 10032.Author contributions: Conception and design: N.A. Bello, E.C. Miller, K.L. Cleary.Analysis and interpretation of the data: K.L. Cleary, R. Wapner.Draft article: N.A. Bello, E.C. Miller, K.L. Cleary, R. Wapner.Critical revision of the article for important intellectual content: N.A. Bello, E.C. Miller, K.L. Cleary, R. Wapner.Critical revision of the article for important intellectual content: N.A. Bello, E.C. Miller, K.L. Cleary, R. Wapner.Critical revision of the article for important intellectual content: N.A. Bello, E.C. Miller, K.L. Cleary, R. Wapner.Critical revision of the article for important intellectual content: N.A. Bello, E.C. Miller, K.L. Cleary, R. Wapner. E.C. Miller, K.L. Cleary, R. Wapner.Final approval of this article: N.A. Bello, E.C. Miller, K.L. Cleary, R. Wapner.Administrative, technical or logistical support: K.L. Cleary, R. Wapner.Collection and compilation of data: N.A. Bello.This article was published in Annals.org on October 15, 2019. Page 7Obesity is one of the most common chronic diseases that U.S. primary care physicians see, but are probably least commonly treated during routine primary care (1). Many doctors are unfamiliar with the standards of treating obesity (2), in part because they are not tested on them (3). It is clear that doctors need better education, training and tools to tackle obesity like other chronic diseases. As with other conditions that require intensive intervention, it is not necessarily the place of the internist to carry out such interventions himself. Rather, a personalized recommendation for weight loss along with a recommendation ... References1. Kraschnewski JL , Sciamanna CN , Stuckey HL , et al. A silent response to the obesity epidemic: decline in U.S. medical weight counseling. Med Care. 2013;51:186-92. [PMID: 23047128] doi:10.1097/MLR.0b013e3182726c33 CrossrefMedlineGoogle Scholar2. Turner M , Jannah N , Kahan S , et al. Current understanding of the guidelines for the treatment of obesity by healthcare professionals. Obesity (silver spring). 2018;26:665-71. [PMID: 29570250] doi:10.1002/oby.22142 CrossrefMedlineGoogle Scholar3. Kushner RF , Butsch WS , Kahan S , et al. Obesity coverage in medical approval examinations in the United States. What is being tested? Teach Learn Med. 2017;29:123-8. [PMID: 28033472] doi:10.1080/10401334.2016.1250641 CrossrefMedlineGoogle Scholar4. Bennett WL , Wang NY , Gudzune KA , et al. Satisfaction with the involvement of the primary care provider is associated with greater weight loss: results of the practice-based POWER study. Patient Educ Couns. 2015;98:1099-105. [PMID: 26026649] doi:10.1016/j.pec.2015.05.006 CrossrefMedlineGoogle Scholar5. Tsai AG and Bessesen DH . Obesity. Ann Intern Med. 2019;170:ITC33-ITC48 doi:10.7326/AITC201903050 LinkGoogle Scholar6. Conroy MB , McTigue KM , Bryce CL , et al. Effect of the electronic health protocol – based coaching on weight maintenance. A randomized study. Ann Intern Med. 2019;171:777-84. doi:10.7326/M18-3337 LinkGoogle Scholar7. Jensen MD , Ryan DH , Apovian CM , et al. American College of Cardiology/American Heart Task Force on Practice Guidelines. 2013 AHA/ACC/TOS Guideline for The Management of Overweight and Obesity in Adults: A Report by the American College of Cardiology/American Heart Association Task Force on Practice Guidelines Guidelines The Obesity Society. J Am Coll Cardiol. 2014;63:2985-3023. [PMID: 24239920] doi:10.1016/j.jacc.2013.11.004 CrossrefMedlineGoogle Scholar8. Tsai AG . Why I treat obesity. Perm J. 2019;23. [PMID: 31167707] doi:10.7812/TPP/18-240 CrossrefMedlineGoogle Scholar Page 8More than a century ago, Sigmund Freud developed a scientific approach to psychotherapy that has since evolved into several forms – none more ubiquitous than cognitive behavioral therapy (CBT) (1). Although these treatments can vary significantly in content, they share a simple overarching premise: spending time talking to patients about their inner experiences can help change thinking and behavior. The discovery of psychotropic drugs in the mid-20th century led to a parallel movement in psychiatry, in which biological interventions for the treatment of mental disorders were sought in the same way as previous efforts to identify antibiotics for the treatment of infections (2). Although both treatments have strong evidence ... References1. Churchill R , Moore TH , Caldwell D , et al. Cognitive behavioral therapies compared to other psychological therapies for depression. Cochrane Database Syst Rev. 2010. [PMID: 25411559] MedlineGoogle Scholar2. Moncrieff J . Magic balls for mental disorders: the emergence of the concept of an antipsychotic drug. J Hist Neurosci. 2013;22:30-46. [PMID: 23323530] doi:10.1080/0964704X.2012.664847 CrossrefMedlineGoogle Scholar3. Gartlehner G , Gaynes BN , Amick HR , et al. Comparative benefits and damage of antidepressants, psychological, complementary and movement treatments for severe depression. An evidence report for a clinical practice guideline from the American College of Physicians. Ann Intern Med. 2016;164:331-41 doi:10.7326/M15-1813 LinkGoogle Scholar4. Amick HR , Gartlehner G , Gaynes BN , et al. Comparative benefits and damage of second generation antidepressants and cognitive behavioural therapies in the initial treatment of severe depressive disorders: systematic review and meta-analysis. Bmj. 2015;351:h6019. [PMID: 26645251] doi:10.1136/bmj.h6019 CrossrefMedlineGoogle Scholar5. Ross EL , Vijan S , Miller EM , et al. The cost-effectiveness of cognitive behavioral therapy compared to second-generation antidepressants for the initial treatment of severe depressive disorder in the United States. A decision analysis model. Ann Intern Med. 2019;171:785-95. doi:10.7326/M18-1480 LinkGoogle Scholar6. Hollon SD , DeRubeis RJ , Fawcett J , et al. Effect of cognitive therapy with antidepressants vs. antidepressants alone on the rate of recovery in severe depressive disorders: a randomized clinical trial. JAMA Psychiatry. 2014;71:1157-64. [PMID: 25142196] doi:10.1001/jamapsychiatry.2014.1054 CrossrefMedlineGoogle Scholar7. Cuijpers P , SD , van Straten A , et al. Does cognitive behavioral therapy have a lasting effect that is better than keeping patients on continuation of pharmacotherapy? A meta-analysis. BMJ Open. 2013;3. [PMID: 23624992] doi:10.1136/bmjopen-2012-002542 doi:10.1136/bmjopen-2012-002542 Scholarship8. Dunlop BW , Kelley ME , McGrath CL , et al. Preliminary results to support insula metabolic activity as a predictor of the outcome of psychotherapy and drug treatments for depression. J Neuropsychiatry Clin Neurosci. 2015;27:237-9. [PMID: 26067435] doi:10.1176/appi.neuropsych.14030048 CrossrefMedlineGoogle Scholar9. GBD 2016 disease and injury incidence and prevalence employee. Global, regional and national incidence, prevalence and years of disability lived for 328 diseases and injuries in 195 countries, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet. 2017;390:1211-59. [PMID: 28919117] doi:10.1016/S0140-6736(17)32154-2 CrossrefMedlineGoogle Scholar10. Bachmann S . Epidemiology of suicide and psychiatric perspective. Int J Environ Res Public Health. 2018;15. [PMID: 29986446] doi:10.3390/ijerph15071425 CrossrefMedlineGoogle Scholar Page 9Decision Analysis Models should be considered as essential tools of evidence-based medicine. They provide a framework for integrating many data sources, assessing probative value, testing assumptions and scenarios, investigating uncertainties, and ultimately information about the likely value of alternative strategies to improve health. Over the years, such models have helped challenge the prevailing wisdom and brought clarity to various health policy debates – and emphasizes, for example, that prevention programs typically do not save money, and that very expensive technologies can sometimes offer value for money. If decision analysis models are useful for solving clinical and political issues, ... References1. Box GEP . Robustness in the strategy of scientific model making. In: Launer RL, Wilkinson GN, eds. Robustness in statistics. New York Academic Pr 1979 201-36. Google Scholar2. Neumann PJ , Kim DD , Trikalinos TA , et al. Future directions for cost-benefit analyses in health and medicine. Med Decis Make. 2018;38:767-777. [PMID: 30248277] doi:10.1177/0272989X18798833 CrossrefMedlineGoogle Scholar3. en Koning HJ , Meza R , Plevritis SK , et al. Benefits and damage of strategies for screening lung cancer in the field of computed tomography: a comparative modelling study for the U.S. Preventive Services Task Force. Ann Intern Med. 2014;160:311-20 doi:10.7326/M13-2316 LinkGoogle Scholar4. Palmer AJ , Si L , Tew M , et al. Computer modelling of diabetes and its transparency: a report on the eighth Mount Hood Challenge. Value health. 2018;21:724-731. [PMID: 29909878] doi:10.1016/j.jval.2018.02.002 CrossrefMedlineGoogle Scholar5. Eaton JW , Menzies NA , Stover J , et al. Health benefits, costs and cost-effectiveness of previous approvals for adult antiretroviral therapies and extended a combined analysis of 12 mathematical models. Lancet Glob Health. 2014;2:e23-34. [PMID: 25104632] doi:10.1016/S2214-109X(13)70172-4 CrossrefMedlineGoogle Scholar6. Criss SD , Cao P , Bastani M , et al. Cost-effectiveness analysis of lung cancer Lung cancer in the United States. A comparative modeling study. Ann Intern Med. 2019;171:796-804. doi:10.7326/M19-1795 LinkGoogle Scholar7. Sanders GD , Neumann PJ , Basu A , et al. Behavioural recommendations, methodological procedures and reporting on cost-benefit analyses: second panel on cost-effectiveness in health and medicine. Jama. 2016;316:1093-103. [PMID: 27623463] doi:10.1001/jama.2016.12195 CrossrefMedlineGoogle Scholar8. Kovalchik SA , Tammemagi M , Berg CD , et al. Targeting of low-dose CT screening is based on the risk of lung cancer death. N Engl J Med. 2013;369:245-254. [PMID: 23863051] doi:10.1056/NEJMoa1301851 CrossrefMedlineGoogle Scholar9. Green AK and Bach P . Model-based suitability for lung cancer screening: where theory meets practice [Editorial]. Ann Intern Med. 2018;168:223-224 doi:10.7326/M17-3316 LinkGoogle Scholar10. Kim DD , Cohen JT , Wong JB , et al. Targeted incentive programs for lung cancer screenings can improve public health and economic efficiency. Health Aff (Millwood). 2019;38:60-67. [PMID: 30615528] doi:10.1377/hlthaff.2018.05148 CrossrefMedlineGoogle Scholar Page 10Nonvariceal upper gastrointestinal bleeding (UGIB) is common, can be severe, and often requires urgent attention. In recent decades, worldwide rates of this disease have been due to strategies to prevent gastrointestinal damage from nonsteroidal anti-inflammatory drugs and aspirin, therapies for eradicating Helicobacter pylori, and a lower prevalence of H pylori infection in the population (1). During the same period, new endoscopic and pharmacological therapies improved evidence-based care for patients with non-variceal UGIB. Recently, an international multidisciplinary expert group (2) updated the International Consensus Recommendations on the Management of Patients with Nonvariceal Upper Gastrointestinal Bleeding (3). ... References1. Lanas A , Dumonceau JM , Hunting RH , et al. Non-variceal upper gastrointestinal bleeding. Nat Rev Dis Primers. 2018;4:18020. [PMID: 29671413] doi:10.1038/nrdp.2018.20 CrossrefMedlineGoogle Scholar2. Barkun AN , Almadi M , Kuipers EJ , et al. Management of non-variceal upper gastrointestinal bleeding: Key recommendations of the International Consensus Group. Ann Intern Med. 2019;171:805-22. doi:10.7326/M19-1795 LinkGoogle Scholar3. Barkun AN , Bardou M , Kuipers EJ , et al. International Consensus Upper Gastrointestinal Bleeding Conference Group. International consensus recommendations for the management of patients with non-variceal upper gastrointestinal bleeding. Ann Intern Med. 2010;152:101-13 doi:10.7326/0003-4819-152-2-20100190-00009 LinkGoogle Scholar4. Gralnek IM , Dumonceau JM , Kuipers EJ , et al. Diagnosis and management of non-variceal upper gastrointestinal bleeding: European Society of Gastrointestinal Endoscopy (ESGE) Endoskopie. 2015;47:a1-46. [PMID: 26417980] doi:10.1055/s-0034-1393172 CrossrefMedlineGoogle Scholar5. Gesungen jj , Chiu PW , Chan FKL , et al. al. Working group consensus on non-variceal upper gastrointestinal bleeding: an update 2018. Good. 2018;67:1757-1768. [PMID: 29691276] doi:10.1136/gutjnl-2018-316276 CrossrefMedlineGoogle Scholar6. Bhatt DL , Cryer BL , Contant CF , et al. COGENT Investigators. Clopidogrel with or without omeprazole in coronary heart disease. N Engl J Med. 2010;363:1909-17. [PMID: 20925534] doi:10.1056/NEJMoa1007964 CrossrefMedlineGoogle Scholar7. Goodman SG , Clare R , Pieper KS , et al. Platelet Inhibition and Patient Outcomes Trial Investigators. Association of proton pump inhibitors n.A. to cardiovascular results with clopidogrel and ticagrelor: findings from platelet inhibition and patient outcomes study. Circulation. 2012;125:978-86. [PMID: 22261200] doi:10.1161/CIRCULATIONAHA.111.032912 CrossrefMedlineGoogle Scholar8. Moayyedi P , Eikelboom JW , Bosch J , et al. COMPASS Investigators. Pantoprazole to prevent gastroduodenal events in patients receiving rivaroxaban and/or aspirin in a randomized, double-blind, placebo-controlled study. Gastroenterology. 2019;157:403-412. [PMID: 31054846] doi:10.1053/j.gastro.2019.04.041 CrossrefMedlineGoogle Scholar9. Sachar H , Vaidya K and Laine L . Intermittent vs continuous proton pump inhibitor therapy for high-risk bleeding ulcers: systematic review and meta-analysis. JAMA Intern Med. 2014;174:1755-62. [PMID: 25201154] doi:10.1001/jamainternmed.2014.4056 CrossrefMedlineGoogle Scholar10. Lanas A , Aabakken L , Fonseca J , et al. Variability in the treatment of non-variceal upper gastrointestinal bleeding in Europe: an observational study. Adv Ther. 2012;29:1026-36. [PMID: 23225523] doi:10.1007/s12325-012-0069-x CrossrefMedlineGoogle Scholar Page 11Escalating drug prices and eroding health insurance have not only contributed to significant spending on prescription drugs, but have also raised concerns about patients' ability to afford necessary medications, including such critical drugs as insulin and cancer therapies. Curbing spending on prescription drugs has become a major focus of health care institutions, political organizations, and the federal government, which has led to many congressional hearings and policy statements by specialty medical organizations whose members see the impact of non-compliance with cost-related drugs in practice. In its current strategy paper, the Health and Public Policy Committee of the American College of Physicians (ACP) ... References1. Daniel H and Bornstein SS ; Health and Public Policy Committee of the American College of Physicians. Policy recommendations for public health plans to curb the rising cost of prescription drugs: a position paper from the American College of Physicians. Ann Intern Med. doi:10.7326/M19-0013 LinkGoogle Scholar2. Medicaid Services Investment and Accountability Act of 2019, Pub. L. Nr. 116-16, 2019. Google Scholar3. Medicare Payment Advisory Commission. Bericht an den Kongress: Medicare Zahlungspolitik. 2018. 2018. 12 September 2019 in www.medpac.gov/docs/default-source/reports/mar18_medpac_entirereport_sec.pdf. Google Scholar4. Kesselheim AS , Huybrechts KF , Choudhry NK , et al. Prescription drug insurance and patient health results: a systematic review. At J Public Health. 2015;105:e17-30. [PMID: 25521879] doi:10.2105/AJPH.2014.302240 CrossrefMedlineGoogle Scholar5. Dusetzina SB , Jazowski S , Cole A , et al. Sending the wrong price signal: Why do some brand-name drugs cost Medicare recipients less than generics? Health Aff (Millwood). 2019;38:1188-94. [PMID: 31260351] doi:10.1377/hlthaff.2018.05476 CrossrefMedlineGoogle Scholar6. Moorkens E , Vulto AG , Huys I , et al. Policy on biosimilar uptake in Europe: an overview. PLoS One. 2017;12:e0190147. [PMID: 29284064] doi:10.1371/journal.pone.0190147 CrossrefMedlineGoogle Scholar7. Dusetzina SB , Keating NL and Huskamp HA . Proposals to redesign Medicare Part D – Easing the burden of rising drug prices. N Engl J Med. 2019;381:1401-4. [PMID: 31483987] doi:10.1056/NEJMp1908688CrossrefMedlineGoogle Scholar8. Cubanski J, Neuman T, True S, et al. What's the Latest on Medicare Drug Price Negotiations? San Francisco: Kaiser Family Foundation; Retrieved www.kff.org/medicare/issue-brief/whats-the-latest-on-medicare-drug-price-negotiations on September 12, 2019. Google Scholar9. Pollitz K, Neuman T, Tolbert J, et al. What role does private health insurance play today and under Medicare-for-All and other public options proposals? San Francisco: Kaiser Family Foundation; 2019. Access to www.kff.org/health-reform/issue-brief/whats-the-role-of-private-health-insurance-today-and-under-medicare-for-all-and-other-public-option-proposals on September 12, 2019. Google Scholar10. Sachs R. Administration Outlines Plan to Lower Pharmaceutical Prices in Medicare Part B. Health Affairs Blog. 26 October 2018. Access to www.healthaffairs.org/do/10.1377/hblog20181026.360332/full on September 12, 2019. Google Scholar Page 12On Being a DoctorDezember 3, 2019Author, article and disclosure Information Visual AbstractI have been swaying through the first months of the residence. It's my holiday week and I'm sick. I drive through the stages of mourning, passing quickly through denial, because I am painfully overburdened and go to anger and even jealousy of the relatively glamorous life that Andrew, my partner – who is not in medicine – leads. When I say glamorously, I mean that he often has 2-day weekends, while I spend most of my Saturdays writing discharge summaries and snorting potassium. You never get sick, I pichbege. Well, I'm always sick. Which is true, but I often forget it. Andrew wears all ... ...