



Helping hematologists conquer blood diseases worldwide



Ten Things Physicians & Patients Should Question



What is Choosing Wisely?

- Choosing Wisely is a national medical stewardship campaign led by the ABIM Foundation in collaboration with leading Specialty Societies
- The campaign challenges Medical Professional Societies to identify five tests, treatments or procedures that physicians and patients should question
- The ABIM Foundation recommends that Societies consider evidence, cost, frequency, and clinical



How These Lists Were Created

- The first ASH Choosing Wisely list was released in December, 2013, and the second in December, 2014
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How These Lists Were Created

- Systematic reviews were completed for each of the 10 shortlisted items
 - A hierarchical search strategy was used, literature searches abridged if relevant, recent, evidence-based guidelines were found
- Directed by its five guiding principles and by the systematic reviews, the Task Force selected five tests, procedures or treatments to question
- Final recommendations were reviewed for clarity and accuracy by 2-4 content experts for each item
- Final items were approved by the ASH Executive Council



Don't transfuse more than the minimum number of red blood cell (RBC) units necessary to relieve symptoms of anemia or to return a patient to a safe hemoglobin range (7 to 8 g/dL in stable, non-cardiac inpatients).

- A large body of evidence demonstrates that liberal RBC transfusion strategies do not benefit patients
- Thus, liberal transfusion should be avoided in most clinical settings
- Transfusion of RBC is associated with a risk of adverse events, is expensive at approximately \$200-300 per unit, and is a limited resource

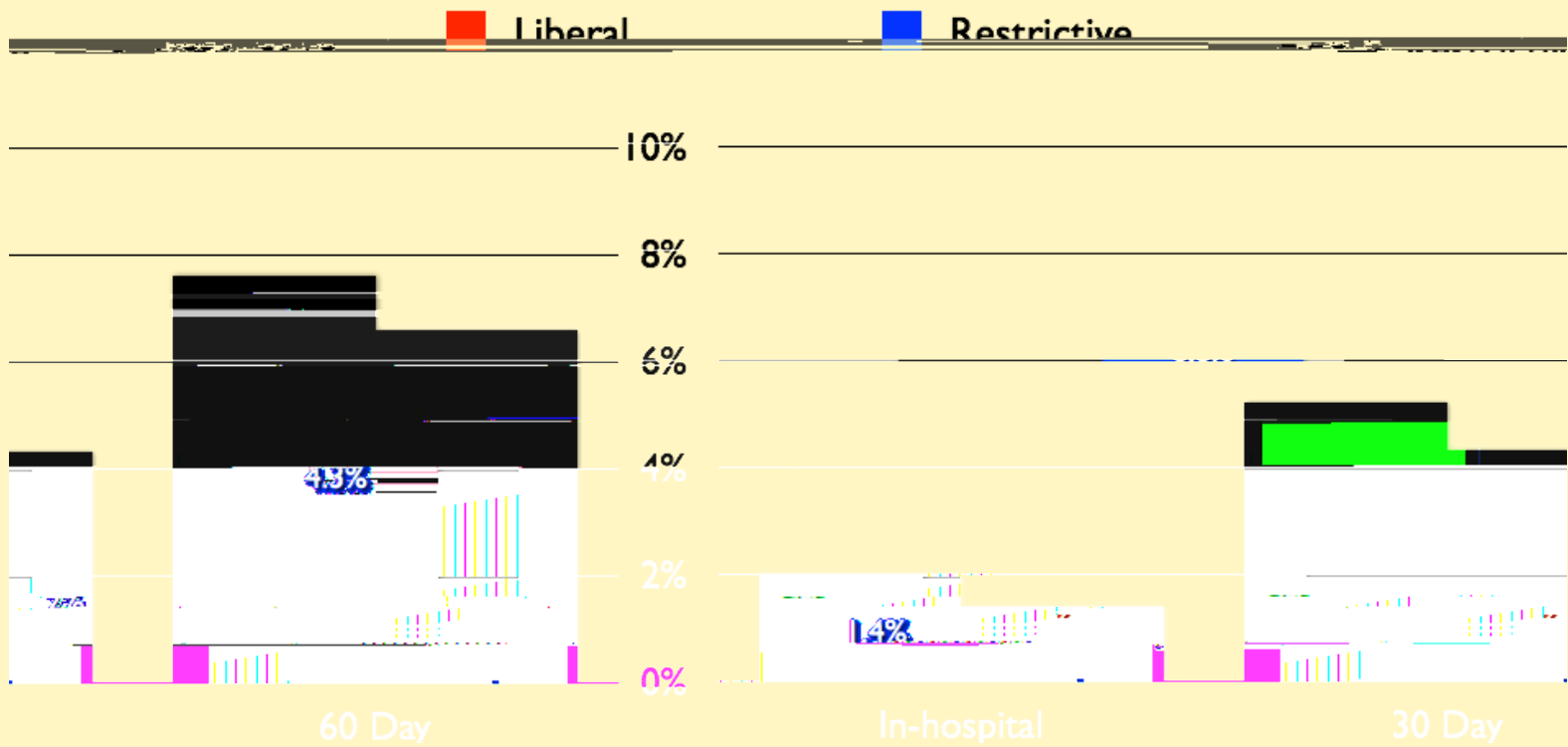


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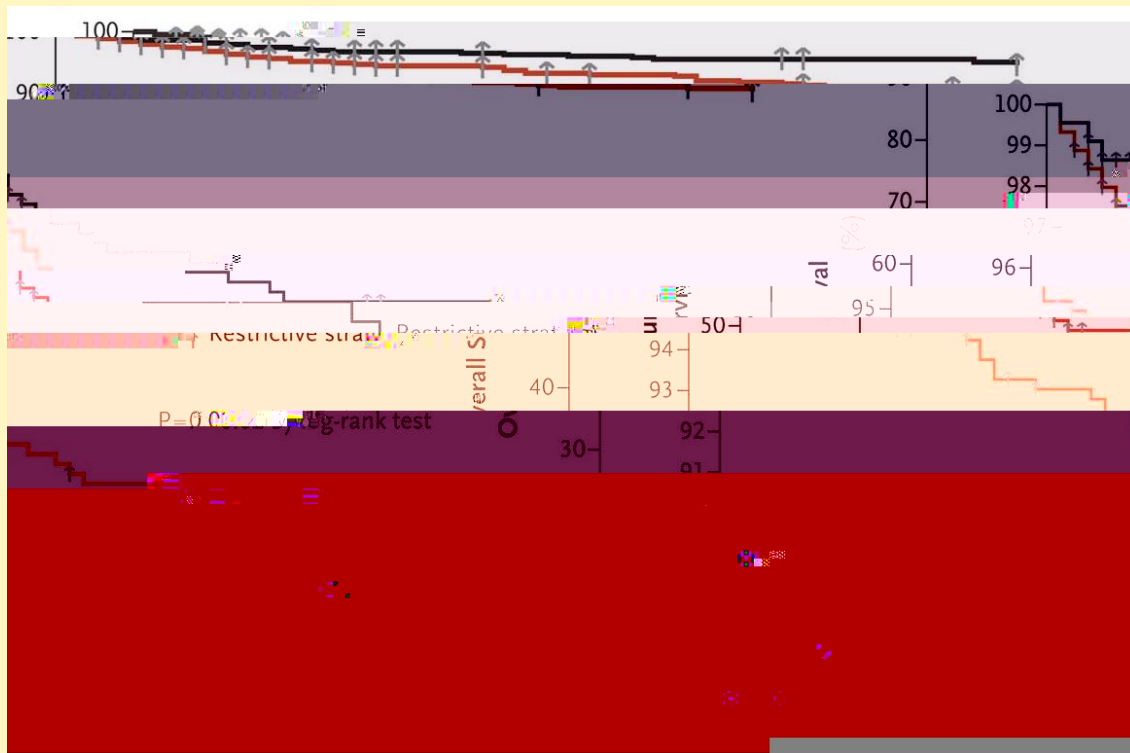
Mortality is Not Increased with Restrictive Transfusion in Hip-Fracture Patients

- Carson et al. studied liberal versus restrictive transfusion in high-risk patients after hip surgery
- N = 2016, patients with hip # and Hgb < 10 g/dL
- Compared restrictive transfusion (transfuse if Hgb < 8 g/dL or symptoms) vs. liberal transfusion (transfuse if Hgb < 10 g/dL)
- As illustrated on the next slide, restrictive transfusion strategy was not associated with increase in-hospital, 30 day, and 60 day mortality compared with liberal transfusion strategy





Overall Survival May Be Better with Restrictive Transfusion in Patients with Upper GI Bleeding



- Transfusion strategies for acute upper gastrointestinal bleeding
- Compared restrictive transfusion (transfuse if Hgb < 7 g/dL) vs. liberal transfusion (transfuse if Hgb < 9 g/dL)

n = 921, patients with acute upper GI bleed



Overall Survival is Not Reduced with Restrictive Transfusion

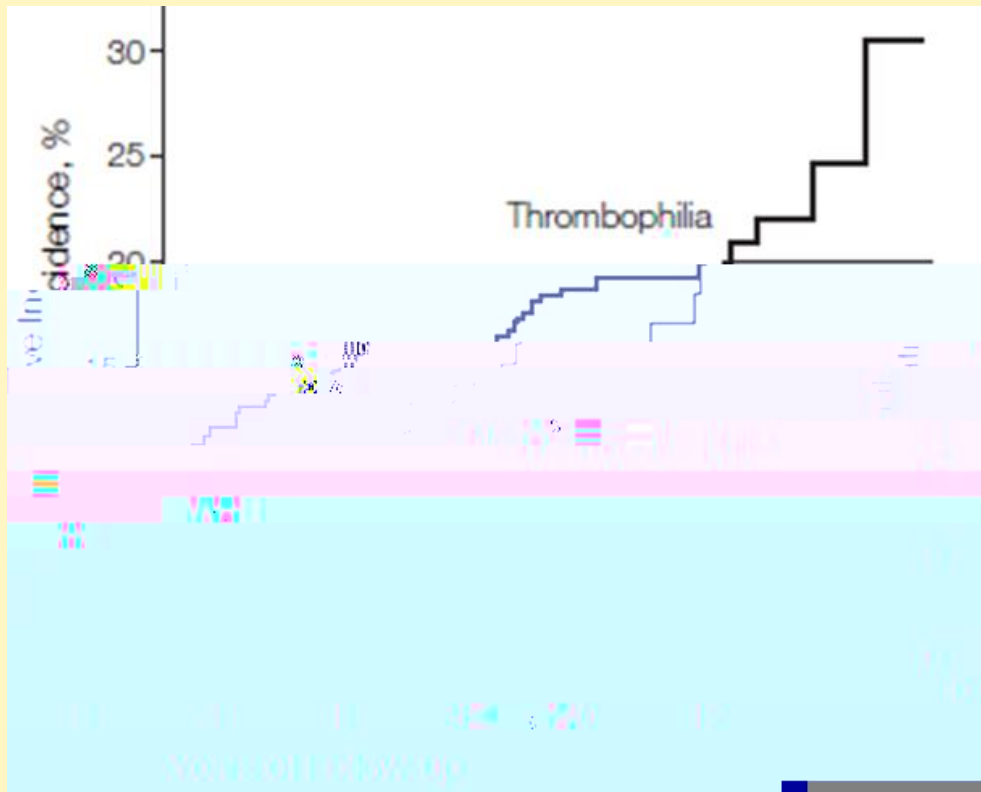
- Evidence from 14 studies in a 2012 meta-analysis showed that overall survival is not significantly reduced with restrictive versus liberal transfusion (RR 0.84, 95% CI 0.69 to 1.01)



- Thrombophilia can result in harm if the duration of anticoagulation is inappropriately prolonged, if a patient is inappropriately labeled as thrombophilic, or if negative testing is misinterpreted to suggest a patient does not have a risk of recurrent thrombosis.
- Testing is expensive (\$500 - \$1300 and up)
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Thrombophilia is not associated with Risk of VTE Recurrence



N = 474

HR = 1.3 (95% CI, 0.8 – 2.0)



Thrombophilic Defects Are Not Associated with a Higher Risk of Recurrent VTE





Reported Predictors of VTE Recurrence

- Prior history of thrombosis



IVC Filters

- Introduced in the 1960's as a physical device to impede embolization of DVTs
- No prospective trials demonstrating net benefit
- Many reports of adverse events including increased risk of DVT, vessel erosion, device embolization etc.
 - 08/09/2010 FDA Safety Alert - Inferior Vena Cava (IVC) Filters: Initial Communication: Risk of Adverse Events with Long Term Use



IVC filter that has perforated the inferior vena cava



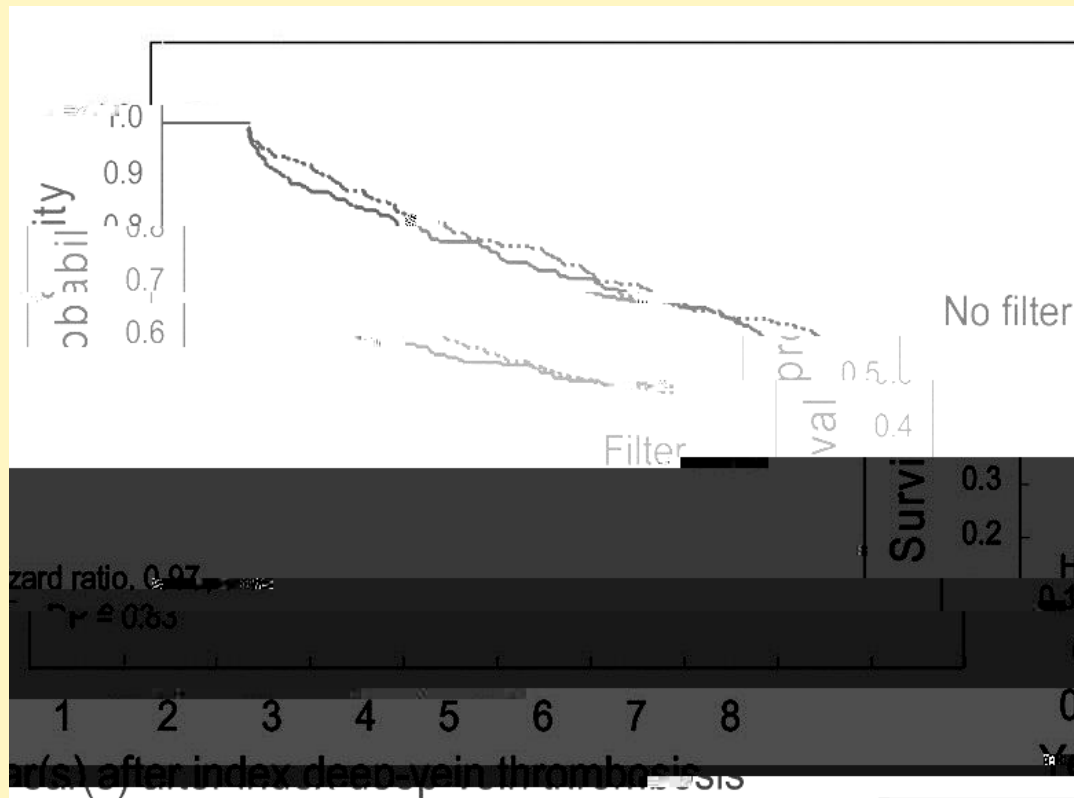
- Single RCT of IVC filters compared permanent IVC filter + anticoagulation to anticoagulation alone in patients with proximal DVT

Conclusion:

- "...vena cava filters reduced the risk of pulmonary embolism but increased that of deep-vein thrombosis and had no effect on survival"
 - PREPIC Study Group. *Circulation* 2005;112:416-22



IVC Filters Have No Impact on Survival





IVC Filters are Rarely Removed

- Expert consensus guidelines recommend *temporary* IVC filters be considered in patients with acute DVT and a contraindication to anticoagulation *and* that they be removed when anticoagulation can be safely resumed
 - ACCP, AHA, NICE, ICSI, BCSH, SIGN Guidelines

But...

- Of the approx. 250,000 IVC filters placed in the US each year, estimated that only 5,000 are placed for this indication
 - Sarosiek S et al. JAMA Intern Med 2013;173(7):513-7

And...

- A retrospective cohort study at a large US teaching institution reported: "Of 679 retrievable IVC filters that were placed 58 (8.5%) were successfully removed"
 - Sarosiek S et al. JAMA Intern Med 2013;173(7):513-7, Angel LF et al. J Vas Interv Radiol 2011;22(11):1522-30.e3



4

Don't administer plasma or prothrombin complex concentrates for non-emergent reversal of vitamin K antagonists (i.e. outside of the setting of major bleeding, intracranial hemorrhage or anticipated emergent surgery).

- Blood products can cause serious harm to patients, are costly and are rarely indicated in the reversal of vitamin K antagonists (VKAs)
- In non-emergent situations, elevation in the INR is best addressed by withholding the VKA and/or by administering vitamin K



FFP Is Potentially More Dangerous Than Other Blood Products

Transfusion-Related Fatalities Reported to FDA 2008-2012

TRALI	HTR	Infection	TACO	Anaphylaxis	Other
37%	27%	11%	18%	6%	1%



FFP Is Often Unnecessary

Non-Bleeding Medical ICU Patients with INR > 1.5

Outcome	FFP (n=44)	No FFP (n=71)	p Value
Median INR	2.7	2.5	0.532
New bleeding episode	3 (6.8%)	2 (2.8%)	0.369
Hospital mortality	11 (25.6%)	20 (28.2%)	0.763
Median ICU Length of Stay	2.4 d	2.0 d	0.184
New onset acute lung injury	8 (18.2%)	3 (4.2%)	0.021



Plasma is Often Used Inappropriately

- 47.6% of FFP orders were for non-bleeding ICU patients with modest elevation of INR, or in preparation for surgery
 - Lauzier et al. Crit Care Med 2007;35(7):1655-9
- 43% of FFP transfused to non-bleeding patients to correct INR, reverse warfarin, prepare for surgery
 - Stanworth SJ et al. Transfusion 2011;51(1):62-70
- 28.6% of FFP transfused to non-bleeding patients with INR \leq 1.5 and normal PTT, for reversal of warfarin, or in preparation for surgery
 - Tinmouth A et al. Transfusion 2013;53(10):2222-9



An Opportunity to Avoid Harm and to Save \$

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5

Limit surveillance computed tomography (CT) scans in asymptomatic patients following curative-intent treatment for aggressive lymphoma.

- CT surveillance in asymptomatic patients in remission from aggressive lymphoma may be harmful, is costly (approximately \$1000 per scan), and has not been demonstrated to improve survival
- In particular, surveillance CT scans more than 2 years beyond the completion of curative treatment for lymphoma are rarely advisable



A Minority of Relapses of Non-Hodgkin Lymphoma are Detected by CT

- Retrospective study of 341 patients with Diffuse Large B Cell Lymphoma or Grade 3 Follicular lymphoma, 113 relapses
 - 60% of relapses detected due to patient symptoms
 - 13% of relapses detected due to physical exam findings
 - 4% of relapses detected due to abnormal lab work
 - 22% of relapses detected due to findings on routine CT
 - Survival not different between patients whose lymphoma was detected by CT vs. those detected by other means



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Potential Harms of CT Scans

- Has been reported that 30% CT scans report incidental findings (Lumbreras et al. Br J Radiol 2010; 83(988):276-89)
 - With the passage of time the probability of a true positive decreases, but the false positive rate is constant
- Thus over time, the cumulative risk of a false positive becomes substantially higher than the probability of a true positive



6

Don't treat with an anticoagulant for more than three months in a patient with a first venous thromboembolism (VTE) occurring in the setting of a major transient risk factor.

- Patients with secondary VTE have a particularly low risk of recurrent thrombosis and have the same risk of bleeding as other patients
- After three months, the consequences of anticoagulation probably outweigh the risks, suggesting discontinuation is preferred strategy
- Patient values and preferences should also be considered



Foundational Basis for Recommendation

- A decision to terminate anticoagulants should always weigh the relative risks and benefits of discontinuation
- Risks - recurrent thrombosis (DVT, PE, fatal PE, CTPH, PTS)
- Benefits - return to baseline risk of bleeding, elimination of cost, complexity and inconvenience of anticoagulants
- Since risks are so consequential this decision should be carefully considered



Practice Guidelines

- ACCP: "In



Summary

- Based on our current understanding of risks and benefits, extending anticoagulation beyond three months in patients with clear secondary episodes of VTE probably causes net harm due to otherwise avoidable bleeding that outweighs the risk of thrombosis



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Is Blood Transfusion Indicated?

- Know or Determine the Sickle Cell Patient's Specific Circumstances
 1. SCD genotype
 - SS/S⁺ Thal vs. SC/S⁺ Thal
 - Baseline Hb and risk of complications varies (less severe in the latter group)
 2. Baseline "steady state" hemoglobin concentration
 - Varies greatly from patient to patient
 3. Current or recent clinical event which might affect hemoglobin concentration
 - Acute illness
 - Hospitalization
 - Recent transfusion
 - Hemoglobin above steady state level
 - Hemoglobin below steady state level (e.g., following hemolytic transfusion reaction)



Indications for Transfusion

Acutely

-



Transfusion Carries Risks for Complications

Acute Sequelae



8 Don't perform baseline or routine surveillance computed tomography (CT) scans in patients with asymptomatic, early-stage chronic lymphocytic leukemia (CLL).

- CT scans introduce risks, including acute toxicity from IV contrast and small increased risk of secondary malignancy
- CT scans can lead to increased patient anxiety related to the presence of lymph nodes or other incidental findings that likely have no clinical significance but often prompt additional CT scans or testing at increased cost and risk to the patient
- CT scans are costly (approximately \$1000 per scan)
- There is no evidence of a survival or other clinical benefit with the use of baseline or routine surveillance scans in patients with early stage CLL



Chronic Lymphocytic Leukemia

- Most prevalent adult leukemia seen in hematology practice
- Majority of patients have absent symptoms at time of diagnosis
- CLL diagnosis and initial staging requires
 - Flow cytometry with immunophenotype showing CD3, CD5, CD10, CD20, and CD23. If atypical phenotype, cyclin D1 negative stain to rule out MCL
 - Absolute monoclonal B lymphocyte count ($> 5 \times 10^9/L$)
 - CBC to assess for cytopenias
 - Physical exam for palpable lymph nodes, spleen, and liver
- CLL diagnosis and initial staging does not require CT scans



Limitations of Clinical Staging

- Majority of patients at diagnosis have early stage disease (Rai 0-



So What is the Wise Choice in CLL Patients at Early Diagnosis?

- Do routine history focusing closely on new symptoms, physical, lab



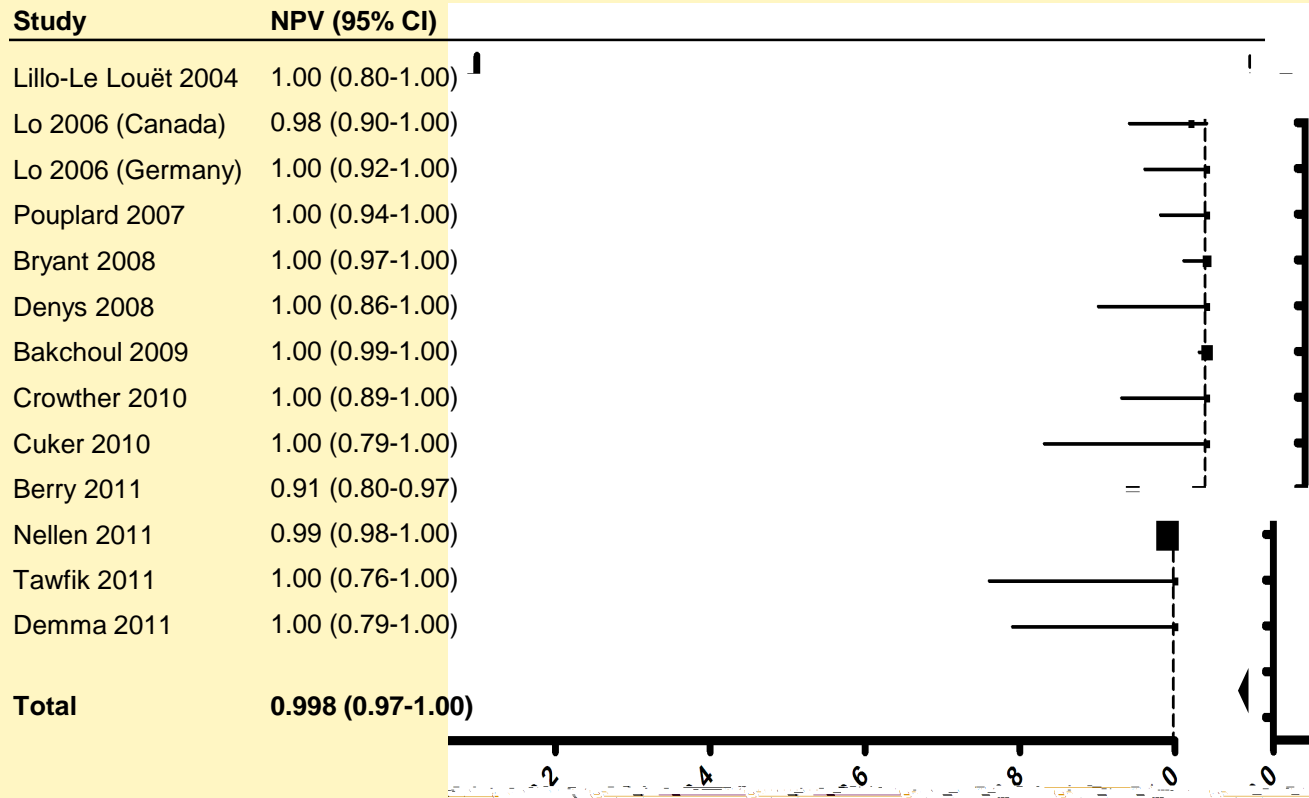
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Don't test or treat for suspected heparin-induced thrombocytopenia (HIT) in patients with a low pre-test probability of HIT.

- Use the 4T score to estimate the clinical probability of HIT
- A low probability 4T score excludes HIT
- Do not test or treat patients with a low probability 4T score:
 - Testing may lead to false-positive results and misdiagnosis
 - Alternative anticoagulants are costly and increase bleeding risk
 - Unnecessary suspension of heparin may increase thrombotic risk



High probability: 6-

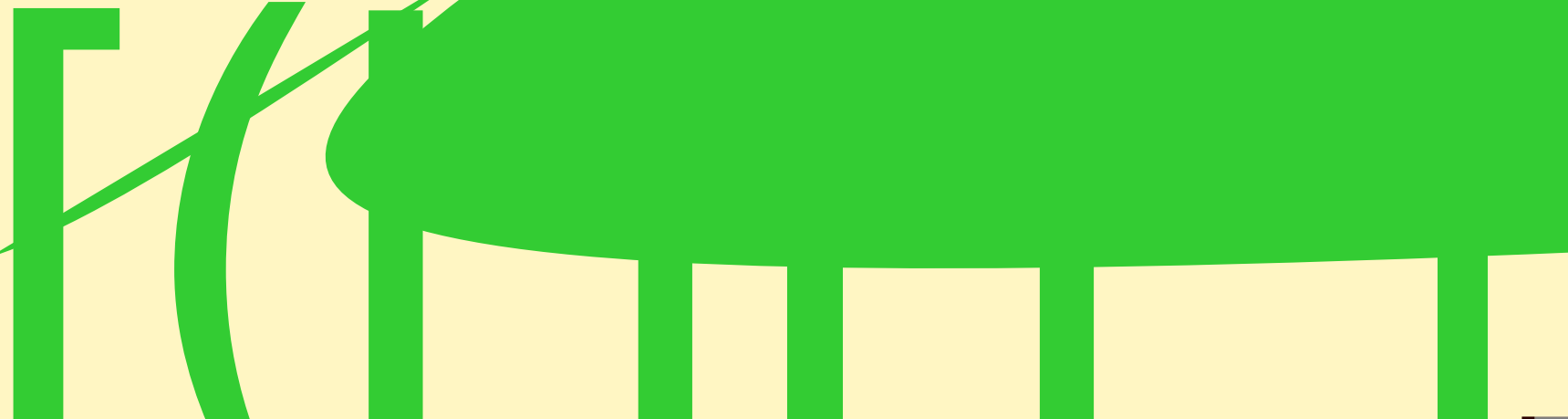




Evidence-Based Approach to the Patient with a Low Probability HIT Score

HIT suspected

Low probability



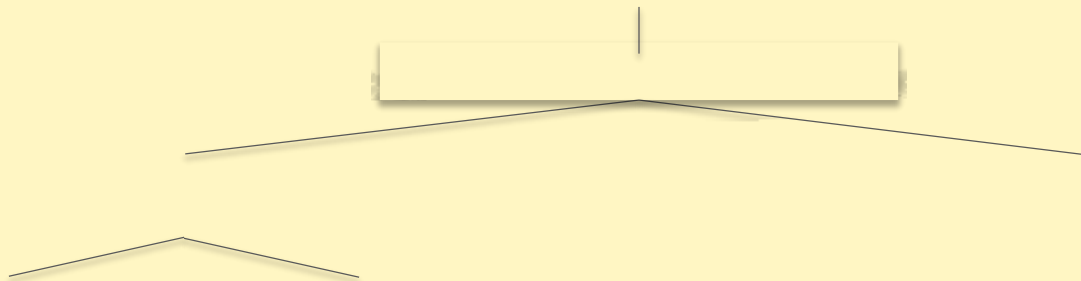


Do Not Label a Low Probability Patient with HIT

- Once heparin is entered as an allergy in the chart, it is almost never removed
- Patients are denied heparin and treated with alternative anticoagulants during subsequent encounters



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- In adults treatment should be reserved for a platelet count $< 30 \times 10^9/L$ and/or bleeding (Grade 2C)
 - Neunert, Lim, et al., Blood 2011;117:4190-4207
- Most adults with ITP have a good outcome
- Platelet count $< 30 \times 10^9/L$



- In patients with platelet counts persistently $< 30 \times 10^9/L$, modeling data suggests a predicted 5-year fatal bleeding risk of 48% in patients > 60 years old and of 2.2% in patients < 40 years old

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- Treatment is associated with adverse events

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Side Effects and Cost

Treatment	Side Effects
Corticosteroids	Mood changes, hypertension, hyperglycemia, gastritis, adrenal suppression, increased risk of infection
IVIg	Infusion reaction, headache, aseptic meningitis, thrombosis
Anti-	

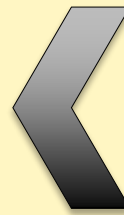


Treating ITP: Balancing Risk Versus Benefit

- Majority of patients with ITP have a favorable outcome with observation alone

Potential Benefits of Treatment

- Rise in platelet count
- Possible reduction in bleeding
- Improved HRQoL



Potential Risks of Treatment

- Adverse events (including death from infections)
- Costs
- Inconvenience
- Serious bleeding



ASH Choosing Wisely Recommendations



Don't transfuse more than the minimum necessary units of red blood cells



Don't test for thrombophilia in patients with major transient risk factors for VTE and acute VTE



Don't use IVC filters routinely in the management of VTE



Don't use plasma or prothrombin concentrate concentrates for non-emergent reversal of vitamin K antagonists



Limit CT surveillance scans in asymptomatic people following curative intent chemotherapy for aggressive lymphoma



ASH Choosing Wisely Recommendations

6

Don't treat with an anticoagulant for more than three months in a patient with a first venous thromboembolism (VTE) occurring in the setting of a major transient risk factor

7

Don't routinely transfuse patients with sickle cell disease (SCD) for chronic anemia or uncomplicated pain crisis without an appropriate clinical indication

8

Don't perform baseline or routine surveillance computed tomography (CT) scans in patients with asymptomatic, early-stage chronic lymphocytic leukemia (CLL)

9

Don't test or treat for suspected heparin-induced thrombocytopenia (HIT) in patients with a low pre-test probability of HIT

10

Don't treat patients with immune thrombocytopenic (ITP) in the absence of bleeding or a very low platelet count