Albumin - Adult - Inpatient Clinical Practice Guideline

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Executive Summary

Guideline Overview

This guideline provides recommendations for the therapeutic use of albumin to treat several common disorders in the inpatient setting. Individual clinician experience may suggest stronger recommendations for some indications. However evidence based conclusions are derived from the currently available evidence.

Key Practice Recommendations

1. Albumin is recommended for the diagnosis and treatment of Type 1 hepatorenal syndrome with cirrhosis
2. Albumin is recommended for the treatment of spontaneous bacterial peritonitis with cirrhosis in conjunction with appropriate antimicrobial therapy
3. Repletion with albumin is recommended after large volume paracentesis in cirrhosis and after plasmapheresis
4. General use of albumin to treat all patients with sepsis is not recommended, however albumin may be considered for the treatment of septic and hemorrhagic shock following failure of isotonic crystalloid fluids
5. Albumin may be considered in patients that are edematous but intravascularly depleted and with a plasma albumin <2 g/dL. Examples populations include patients with cirrhosis that have ascites that is unresponsive to diuretics and who are not undergoing paracentesis OR patients who have undergone major surgery (e.g. > 40% hepatic resection or extensive intestinal resection)
6. Use of albumin may be considered to treat burns when appropriate administration of crystalloid fluid does not result in minimum urine output.
7. Albumin may be considered to treat volume depletion following liver transplant
8. Albumin may be considered for treatment of hypo-oncotic shock in patients with acute respiratory distress syndrome
9. Albumin may be considered to treat diuretic resistance
10. Albumin may be considered to treat symptomatic hypotension during hemodialysis
11. Albumin should not be administered to patients with traumatic brain injury and should be administered with care in the setting of other traumas

Companion Documents

1. Sepsis: Diagnosis and Management - Adult - Inpatient/Emergency Department
2. Parenteral Nutrition - Adult - Inpatient/Ambulatory

Scope

Diseases/Conditions: Cirrhosis, hepatorenal syndrome, spontaneous bacterial peritonitis, extracorporeal membrane oxygenation, septic shock, hemorrhagic shock, burns, volume depletion/ expansion, cardiac surgery, liver transplantation, nephrotic syndrome, acute lung injury/ acute respiratory distress syndrome, hemodialysis

Clinical Specialty: The following clinical specialties may use this guideline: Critical Care, Hospital Medicine, Pulmonology, Surgery, Transplantation, Hepatology, Nephrology, Cardiology, Trauma, Infectious Disease, Anesthesia, and Nutrition Support

Intended Users: Physicians, Advanced Practice Providers, Nurses, Nutrition Support, Pharmacists, Technical Support

Objective: To provide evidence-based recommendations to assist clinicians in determining the benefits of albumin use in patients with relevant disorders

Target Population: All adult inpatients cared for within UW Health who have a disorder for which albumin may be appropriate treatment

Interventions and Practices Considered: Albumin is the sole clinical intervention considered in the guideline, sometimes as a second or third line therapy

Major Outcomes Considered:

- Mortality
- Blood pressure
- Fluid balance
- Plasma albumin level

Methodology

Methods Used to Collect/Select the Evidence:
Electronic database searches (e.g., PUBMED) were conducted by the guideline author(s) and workgroup members to collect evidence for review. Expert opinion and clinical experience were also considered during discussions of the evidence.

Methods Used to Formulate the Recommendations:
The workgroup members agreed to adopt recommendations developed by external organizations and/or arrived at a consensus through discussion of the literature and expert experience. All recommendations endorsed or developed by the guideline workgroup were reviewed and approved by other stakeholders or committees (as appropriate).

Methods Used to Assess the Quality of the Evidence/Strength of the Recommendations:
Recommendations developed by external organizations maintained the evidence grade assigned within the original source document and were adopted for use at UW Health.

Internally developed recommendations, or those adopted from external sources without an assigned evidence grade, were evaluated by the guideline workgroup using an algorithm adapted from the Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodology (see **Figure 1** in Appendix A).

Rating Scheme for the Strength of the Evidence/Recommendations:
See Appendix A for the rating scheme(s) used within this document.

Cost Analysis: No formal cost analysis was done to direct the recommendations made in this guideline

Recognition of Potential Health Care Disparities: Insofar as care for the disorders described above is initiated, there are no recognized health care disparities when administering albumin.

Definitions

Extracorporeal membrane oxygenation: a modified form of cardiopulmonary bypass to support both cardiac and pulmonary function

Diuretic resistance: An inadequate response to typically effective doses of loop diuretics despite clear presence of hypervolemia including inadequate diuresis, worsening of renal function or development of hypotension

Cirrhosis: a late stage of progressive hepatic fibrosis characterized by distortion of the hepatic architecture and the formation of regenerative nodules

Hepatorenal syndrome: functional renal failure associated with advances cirrhosis. The diagnosis includes cirrhosis and ascites plus impaired renal function after exclusion of parenchymal renal disease

Sepsis: life-threatening organ dysfunction caused by a dysregulated host response to infection

Spontaneous bacterial peritonitis: an ascitic fluid infection without an evident intra-abdominal surgically treatable source.

Introduction

Albumin is a protein-based colloid therapy used in fluid resuscitation for hypovolemic states associated with various conditions and for correcting hypoalbuminemia in circumstances of specific symptomatology. The major indication for use of albumin therapy is volume expansion. Other classes of agents used to manage hypovolemic states include crystalloid fluids. Albumin is substantially more expensive than crystalloid fluids. A Cochrane review evaluated 74 randomized controlled trials comparing the use of colloid to crystalloid therapy for volume replacement in critically ill patients and found no evidence of decreased mortality with colloid use over crystalloids.[1] Meanwhile, a prospective cohort study in a surgical ICU demonstrated that implementing albumin use guidelines decreased albumin use by 54%.[2] The restrictive use of albumin had no negative impact on ICU mortality, but resulted in a 56% reduction in cost. This demonstrates that evidence based recommendations organized in guidelines endorsed by stakeholders can increase the probability of deriving optimal value from albumin. General guidelines for the use of albumin are available in the published literature[3-6] and were consulted in the creation of this guideline. The recommendations established in this guideline reflect current evidence and local expert opinion.

Recommendations

Albumin administration is recommended for the following indications

1. Management of hepatorenal syndrome (HRS) or acute kidney injury (AKI) in patients with cirrhosis and probable non-structural injury (i.e. pre-renal azotemia)
   a. Establish differential diagnosis[7, 8]
      i. Use of albumin as fluid challenge is recommended *(UW Health low quality evidence; strong recommendation)*
         1. When patient is clinically volume depleted
            a. Albumin type: 5%
            b. Dose until clinical volume repletion is achieved; suggested initial dose is 12.5 g to 25 g (250-500 mL)
         2. When there is no evidence of obvious volume depletion
            a. Albumin type: 25%
            b. Dose: 1 g/kg per day for 2 days, maximum daily dose: 100 g (400 mL)
      ii. Assess for resolution or progression of AKI at 48 hours after initiating albumin therapy
   b. Treatment of Type 1 HRS with albumin in patients with cirrhosis is recommended[3, 5, 6, 9-11] *(UW Health high quality evidence; strong recommendation)*
      i. Albumin type: 25%
      ii. Dose: 1 g/kg on day 1, maximum daily dose: 100 g (400 mL)
      iii. Suggested subsequent daily dose is 25 g/day (100 mL)
      iv. Must be given in combination with octreotide and midodrine with a goal to increase mean arterial pressure by at least 15 mmHg from baseline[6]
         1. Octreotide dose: Initially, 100 mcg subcutaneously 3 times daily; titrate to 200 mcg subcutaneously 3 times daily
         2. Midodrine dose: Initially 5-10 mg orally 3 times daily; titrate to 12.5 mg orally 3 times daily
      v. Alternatively a norepinephrine infusion, titrated to appropriate dose, may be used for vasoconstriction in combination with albumin if the patient resides in an intensive care unit.
      vi. The following duration of therapy for albumin is recommended[3]
         1. In patients that respond to vasoconstrictors and albumin as evidenced by a decrease in creatinine, discontinue albumin when creatinine has returned to or is close to baseline, or has not decreased further after 3 days of treatment
         2. In patients that do not respond to vasoconstrictors and albumin, discontinue albumin after a maximum of 7 days
         3. Discontinue albumin if patient is started on renal replacement therapy or the plasma albumin concentration is >3 g/dL

2. Treatment of spontaneous bacterial peritonitis (SBP) with albumin in patients with cirrhosis is recommended[3, 10, 12, 13] *(UW Health moderate quality evidence; strong recommendation)*
   a. Albumin type: 25%
   b. Dose: 1.5 g/kg on day 1, followed by 1 g/kg on day 3, Maximum daily dose: 100 g (400 mL)
   c. Albumin should be given with appropriate antibiotics

3. For large volume serial paracentesis (>5 L) in patients with ascites due to cirrhosis and without infection, an albumin infusion of 6 g to 8 g per liter of ascitic fluid removed is recommended to decrease the risk of post-paracentesis circulatory dysfunction and to improve survival.[3, 6, 14-17] *(UW Health moderate quality evidence; weak/conditional recommendation)*
   a. Albumin type: 25%
   b. Dose: Albumin dose is determined by the volume of ascitic fluid removed (approximately 6 to 8 g per liter of fluid removed)[6]
   c. Routine replacement of albumin is not recommended if 0-4.9 L are removed. The instructions of the ordering provider should be followed to determine the need for albumin based on patient comorbidities such as renal dysfunction, small body habitus, severe hypoalbuminemia or symptomatic hypotension following paracentesis.
   d. Maximum dose: 100 g (400 mL)

Paracentesis Volume Removed	Albumin Dose (grams)
0-4.9 L	Follow instructions of ordering provider to determine need for albumin
5-6.9 L	37.5 g
7-8.9 L	50 g
9-10.9 L	62.5 g
11-12.9 L	75 g
13-14.9 L	87.5 g
≥15 L	100 g

4. Volume repletion with albumin following therapeutic large-volume plasmapheresis is recommended when the following criteria are met[5, 18] *(UW Health low quality evidence; strong recommendation)*
   a. More than 20 mL/kg in a single session or more than 20 mL/kg/week in successive sessions
   b. Albumin type: 5%
   c. Dose: replace 70-80% of plasma volume removed with albumin

Albumin administration may be considered for the following indications

1. Treatment of shock states with albumin may be considered after failure of crystalloids to restore adequate fluid volume[19-26] *(UW Health moderate quality evidence; weak/conditional recommendation)*
   a. Septic shock
      i. Crystalloids are recommended as the initial fluid of choice in the resuscitation of septic shock[26] *(UW Health moderate quality evidence; strong recommendation)*
      ii. Albumin (5%) may be considered for resuscitation in specific patients with septic shock that require substantial fluid support in addition to crystalloids to maintain adequate mean arterial pressure. However, given the high cost of albumin compared to crystalloid fluid, routine administration of albumin is not recommended in the setting of septic shock.[26] *(UW Health low quality evidence; weak/conditional recommendation)*
         1. Albumin type: 5%
         2. Dose: 12.5 g (250 mL), repeat as needed
   b. Hemorrhagic shock[1, 27] (*UW Health moderate quality evidence; weak/conditional recommendation*)
      i. Albumin may be considered as last line therapy after crystalloids and blood products have been used at maximal doses without adequate clinical response. Albumin administration is contraindicated in patient with traumatic brain injury and should be used with care in patients with traumatic injuries.
         1. Albumin type: 5%
         2. Dose: 12.5 g (250 mL) is suggested, repeat as needed

2. Treatment with albumin may be considered in patients who are edematous but intravascularly depleted and who have a plasma albumin <2 g/dL.[3, 6, 28-34] *(UW Health moderate quality evidence; weak/conditional recommendation)*. Example populations include:
   a. Patients with cirrhosis and ascites which is unresponsive to diuretics but who are not undergoing paracentesis
   b. Patients who have undergone major surgery (e.g. >40% hepatic resection, extensive intestinal resection)
   c. Albumin type: 25%
   d. Dose: 12.5-25 g (50-100 mL), repeat as needed

3. Treatment with albumin may be considered in patients who have cirrhosis without ascites who have a plasma albumin <3 g/dL. The utility of giving albumin in patients with cirrhosis without ascites with serum albumin >3 g/dL is minimal and is not recommended.[35, 36] (*UW Health moderate quality evidence; weak/conditional recommendation*).
   a. Albumin type: 25%
   b. Dose: 12.5 g to 25 g (50-100 mL), repeat as needed

4. Albumin may be considered for the treatment of burns when the projected 24-hour crystalloid fluid requirement to achieve urine output of >0.5 mL/kg/hr exceeds twice the volume calculated by the Parkland formula[1, 5, 37-40] *(UW Health low quality evidence; weak/conditional recommendation)*
   a. Albumin type: 25%
   b. Dose: Initiate albumin at a rate of 10 mL/hr until crystalloid fluid requirements for adequate urine output (>0.5 mL/kg/hr) return to the volume calculated by the Parkland formula (2-4 mL/kg/% Total Burn Surface Area)

5. Treatment of volume depletion due to cardiothoracic and vascular surgery with albumin may be considered[5, 41, 42] *(UW Health low quality evidence; weak/conditional recommendation)*
   a. For volume expansion during cardiac surgery (in addition to crystalloids)
      i. Albumin type: 5%
      ii. Dose: 12.5 g to 25 g (250-500 mL)
   b. For volume expansion following cardiac surgery (in addition to crystalloids)
      i. Albumin type: 5%
      ii. Dose: 12.5 g (250 mL) is suggested, repeat as needed
   c. For priming of the extracorporeal cardiopulmonary bypass circuit[42]
      i. Albumin type: 25%
      ii. Dose: 12.5 g to 25 g (50-100mL)
   d. For volume expansion necessary when there is large blood loss as a result of abdominal aortic aneurysm (AAA) or thoracic aortic aneurysm (TAA) repair
      i. Albumin type: 5%
      ii. Dose: 12.5 g (250 mL) is suggested, repeat as needed

6. Treatment of volume depletion due to liver transplantation with albumin may be considered[43, 44] *(UW Health low quality evidence/ weak conditional recommendation)*
   a. Albumin administration is appropriate when plasma albumin is <2.5 g/dL and patient is determined to be fluid responsive
      i. For postoperative control of ascites and peripheral edema
         1. Albumin type: 25%
         2. Dose: 12.5 g to 25 g (50-100 mL) is suggested: repeat as needed
      ii. To replace large volumes of ascitic fluid through drainage tubes
         1. Albumin type: 5%
         2. Dose: 12.5 g to 25 g (250-500 mL) is suggested; repeat as needed
         3. Consider stopping albumin when drain output is <500 mL/day

7. Prevention of edema and graft reperfusion injury during and immediately following pancreas transplant with albumin may be considered for solitary pancreas and simultaneous pancreas/kidney transplants *(UW Health very low quality evidence; weak/conditional recommendation)*
   a. Albumin type: 25%
   b. Dose: 12.5 g to 25 g (50-100 mL) is suggested, repeat as needed

8. Albumin may be considered for the treatment of diuretic resistance in the setting of total body hypervolemia with intravascular depletion or low effective circulating volume and serum albumin <2.5 g/dL. Administration of albumin for diuretic resistance should be discontinued when serum albumin >3 g/dL or if negative fluid balance is not achieved within 24 hours of use if hypertension develops. Routine use of albumin for diuretic resistance in patients not meeting these criteria is not recommended.[33, 45-47] (*UW Health low quality evidence; weak/conditional recommendation*)
   a. Albumin should be used in conjunction with diuretics
   b. Albumin type: 25%
   c. Dose: 12.5 g to 25 g (50-100 mL) is suggested up to twice per day

9. Albumin may be considered for the treatment of acute lung injury or acute respiratory distress syndrome[48-50] *(UW Health moderate quality evidence; weak/conditional recommendation)*

   a. Albumin administration is appropriate when the total plasma protein, level is less than 6 g/dL (note the distinction between total plasma protein and albumin; the plasma albumin level is not used as criteria for albumin administration in these disorders)
   b. Albumin should be used in conjunction with furosemide
      i. Albumin type: 25%
      ii. Dose: 25 g (100 mL) every 8 hours as needed for 3 days
      iii. Discontinue when total plasma protein level is greater than 8 g/dL

10. Albumin may be considered for the treatment of symptomatic hypotension during hemodialysis[51, 52] *(UW Health moderate quality evidence; weak/conditional recommendation)*
    a. Albumin administration is appropriate as second line volume expansion after crystalloid administration
       i. Albumin type: 25%
       ii. Dose: 12.5 g to 25 g (50-100 mL) every 15 minutes as needed to keep systolic blood pressure (SBP) above 90 mmHg

11. Albumin may be considered to increase the extracorporeal membrane oxygenation (ECMO) flow rate when the rate is less than 10% of ordered flow for at least 5 minutes *(UW Health very low quality evidence; weak recommendation).*
    a. Albumin type: 25%
    b. Dose: 12.5 g to 25 g (50-100 mL) for each administration

12. Albumin administration may be considered in non-traumatic neurosurgery patients when use of crystalloid solutions may result in adverse effects. This includes albumin administration in the operating room and the endovascular/hybrid suite to manage volume depletion resulting from diuretic use or to prevent or treat vasospasm *(UW Health very low quality evidence; weak/conditional recommendation)*
    a. Albumin type: 5%
    b. Dose: 12.5 g to 25 g (250-500 mL), repeat as necessary

13. Albumin may be considered for sustaining organ function in brain dead patients while awaiting organ procurement when crystalloid fluid or pressor administration fails to maintain mean arterial pressure above 70 mmHg and the plasma albumin is less than 2 g/dL[53] *(UW Health low quality evidence; weak/conditional recommendation)*
    a. Albumin type: 25%
    b. Dose: 12.5 g to 25 g (50-100 mL)

Albumin is harmful and is contraindicated for the following indications

1. Fluid resuscitation in patients with traumatic brain injury.[54] A post-hoc, subgroup analysis of fluid resuscitation among critically ill patients with traumatic brain injury revealed a higher mortality rate when albumin was administered as compared to saline. The subgroup was identified from all critically ill subjects studied in the Saline versus Albumin Fluid Evaluation Study.[21] *(UW Health low quality evidence; strong recommendation)*

Albumin administration is not recommended for the following indications as available evidence is insufficient to support use

1. To correct plasma albumin in patients not described above with plasma albumin >2.5 g/dL[55-57] *(UW Health low quality evidence; weak/conditional recommendation)*
2. To treat sepsis without shock[19, 24] *(UW Health moderate quality evidence; weak/conditional recommendation)*
3. To treat malnutrition, protein losing enteropathies, or malabsorption[58, 59] *(UW Health very low quality evidence; weak/conditional recommendation)*
4. As fluid resuscitation in patients with acute trauma[21, 57] (*UW Health moderate quality evidence; weak/conditional recommendation*)
5. Treatment of hepatic encephalopathy in patients with cirrhosis[60] *(UW Health low quality evidence; weak/conditional recommendation)*

6. Treatment of hypoalbuminemia without signs of edema or hypotension[55-57] *(UW Health low quality evidence; weak/conditional recommendation)*
7. Preoperative hemodilution[61] *(UW Health low quality evidence; weak/conditional recommendation)*
8. Fluid expansion in the immediate postoperative period following minor surgery *(UW Health very low quality evidence; weak/conditional recommendation)*
9. Treatment of aneurysmal subarachnoid hemorrhage[62] *(UW Health low quality evidence; weak/conditional recommendation)*
10. To treat diuretic resistance in patients who do not meet criteria as defined above (*UW Health low quality evidence; weak/conditional recommendation*)

Monitoring of albumin administration

Continued need for albumin administration should be assessed daily. Albumin should be discontinued as soon as therapy is no longer required according to monitored parameters. *(UW Health low quality evidence; strong recommendation)*

1. Laboratory
   a. Albumin therapy may not be necessary in patients with plasma albumin ≥2.5 g/dL
2. Physical assessment: consider discontinuing albumin when goal is reached
   a. Blood pressure: SBP >100 mmHg or MAP >60 mmHg
   b. Urine output: >0.5 mL/kg/hour
   c. Improvement in condition(s) for which albumin was initiated
   d. Edema improvement (total body fluid overload and intravascular volume depletion)
   e. Other measures of fluid responsiveness

UW Health Implementation

Potential Benefits:

Implementation of and adherence to the guideline recommendations should result in use of albumin that is consistent, evidence-based, and cost effective

Potential Harms:

Patients may experience adverse effects to albumin, even when receiving it for an approved indication and at a recommended dose

Pertinent UW Health Policies & Procedures

1. Nursing Policy #11.10: Percutaneous Paracentesis
2. Nursing Policy #1.01AP: Therapeutic Plasma Exchange

Patient Resources

1. Health Facts For You #5790: Transplant desensitization with plasma exchange and IVIG

Guideline Metrics

1. Periodic medication use evaluation of albumin to assess outcomes, including mortality, adverse effects, and cost.

Order Sets

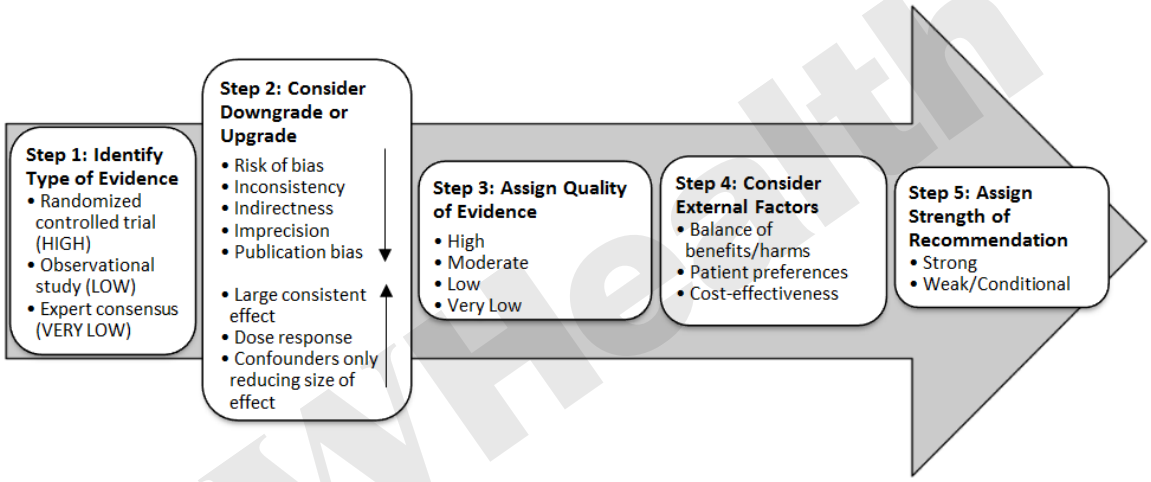
- IP - General Care - Adult [692]
- Anesthesiology - Adult - Recovery/PACU [1396]
- IP - Anesthesiology - ICU - Adult - Postoperative [2952]
- IP - Cirrhosis - Adult - Admission [1673]
- IP - ECMO - Adult - Post-Cannulation [2459]
- IP - Hemodialysis - Adult - Procedure [5138]
- DHC - Body - Paracentesis - Adult - Postprocedure [5398]
- IP - Body - Paracentesis - Adult - Postprocedure [1607]
- IP - Paracentesis - Bedside - Adult - Pre/Postprocedure [2469]
- IP - Donor Hepatic Lobectomy - Adult - Postoperative [2884]
- IP - Pancreas Transplant - Adult - Postoperative [2889]

- IP - Renal/Pancreas Transplant - Adult - Postoperative [2927]
- IP - Comprehensive Brain Dead Donor (BDD) Delegation Protocol - Adult - Intensive Care - Supplemental [4078]
- IP - Comprehensive Donation After Cardiac Death (DCD) - Adult - Intensive Care - Supplemental [3627]

Disclaimer
Clinical practice guidelines assist clinicians by providing a framework for the evaluation and treatment of patients. This guideline outlines the preferred approach for most patients. It is not intended to replace a clinician's judgment or to establish a protocol for all patients. It is understood that some patients will not fit the clinical condition contemplated by a guideline and that a guideline will rarely establish the only appropriate approach to a problem.

Appendix A. Evidence Grading Scheme(s)

Figure 1. GRADE Methodology adapted by UW Health



GRADE Ranking of Evidence

High	We are confident that the effect in the study reflects the actual effect.
Moderate	We are quite confident that the effect in the study is close to the true effect, but it is also possible it is substantially different.
Low	The true effect may differ significantly from the estimate.
Very Low	The true effect is likely to be substantially different from the estimated effect.

GRADE Ratings for Recommendations For or Against Practice

Strong	The net benefit of the treatment is clear, patient values and circumstances are unlikely to affect the decision.
Weak/conditional	Recommendation may be conditional upon patient values and preferences, the resources available, or the setting in which the intervention will be implemented.

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