



Transplant Outcomes in Older Adults with MDS and AML

Celebrating a Second Chance at Life Survivorship Symposium

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Transplant Outcomes in Older Adults with MDS and AML

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Goals of this talk

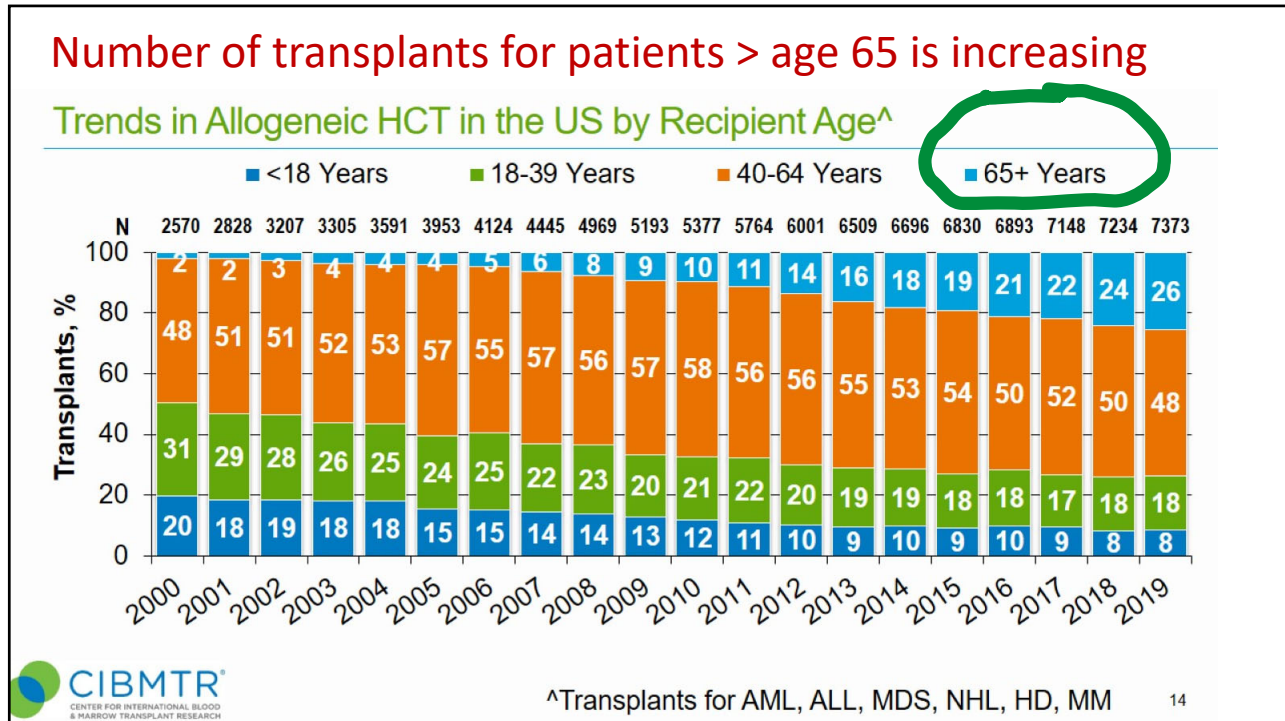
- Present information regarding transplant for AML and MDS, including:
 - Outcomes with transplant compared to outcomes *without* transplant
 - Quality of life after transplant
 - Response rates to transplant
 - Treatment before and after transplant
- Discuss strategies to improve outcomes with transplant
 - Importance of exercise and nutrition
 - Treatments to help reduce risk of relapse

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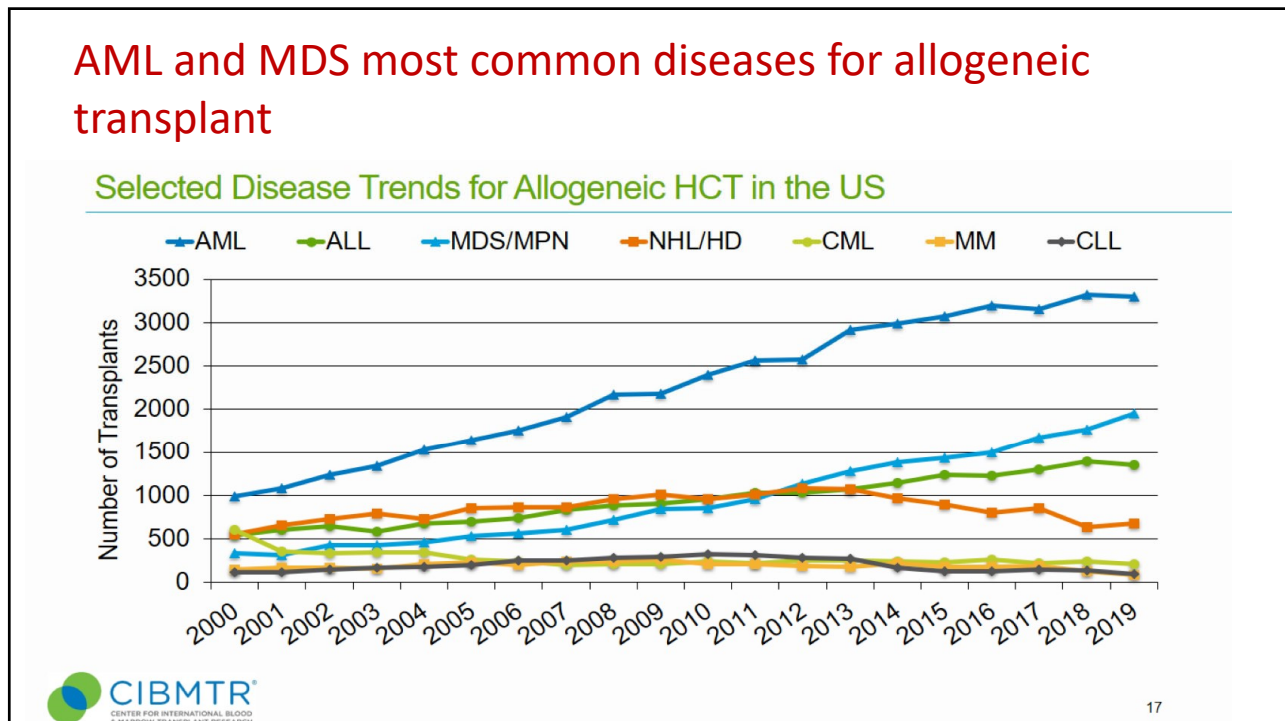
Key Points

- Most AML and MDS can only be cured with a stem cell transplant
- Allogeneic transplant in older adults is becoming much more common
- Studies show that age alone is not a barrier to a successful transplant
- Studies show a survival advantage for transplant in higher risk MDS and AML in older adults compared to not getting a transplant.
- How strong and fit you are prior to transplant effects how well you do
- Overall, transplant outcomes continue to improve, including in those over the age of 60.

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Let's start by talking about MDS, and transplant for MDS

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Myelodysplastic Syndrome (MDS)

- MDS is primarily a disease of older adults
 - Average age at diagnosis around **71 years old**
- MDS is a bone marrow stem cell problem
- The bone marrow stem cells in MDS are “damaged” and dysfunctional, so that they don’t make blood cells like they are supposed to (“lazy”)
- MDS is associated with low blood cell counts
 - Patients frequently require blood transfusions
 - Patients are at increased risk of infections and bleeding
- MDS has a risk of developing into acute leukemia (AML in particular)
- While there are treatments to help make the MDS cells function better, the only way to potentially cure MDS is with a stem cell transplant from a donor

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Not all MDS is the Same

- We think of MDS as being in 2 categories
 - LOWER RISK
 - HIGHER RISK
- The short term and long term treatment options vary between lower risk and higher risk MDS
- While all MDS can only be cured by transplant, lower risk MDS may not benefit from a transplant if it is done “too early”
- Let’s talk more about risk of MDS and how that helps us decide about transplant

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Risk Assessment in MDS

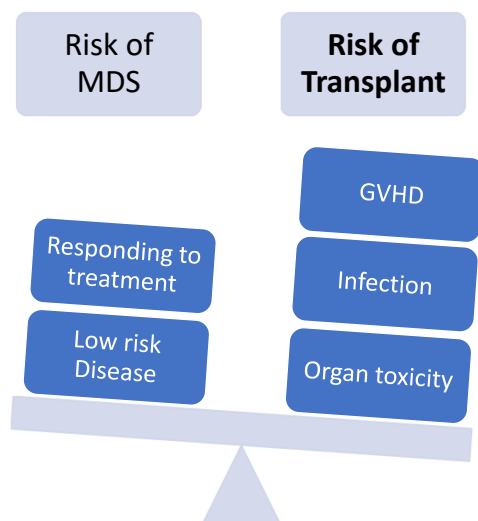
- MDS scoring systems take into account features of the disease:
 - Need for blood transfusions
 - How low is the neutrophil count and platelet count?
 - What is the blast count in the bone marrow?
 - What, if any, chromosome changes are present?
 - What, if any, mutations in genes are present?
 - Is the MDS responding to treatment?
- For many patients with truly lower risk MDS, their expected life span is many years
- On the other side are patients with high-risk MDS - these patients have a high risk of transforming into leukemia or having another life-threatening complication of their disease
- Before deciding to pursue transplant, you have to balance the risks of the procedure with the risks of the disease

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Considerations for Transplant in Lower Risk MDS

In this case, the risk of the transplant is HIGHER than the risk of the MDS.

We wouldn't want to transplant right now.

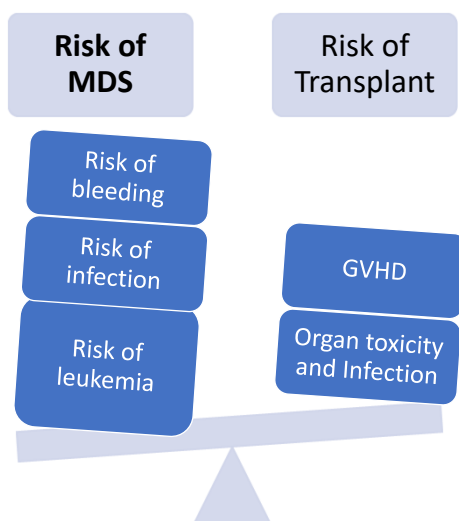


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Considerations for Transplant in Higher Risk MDS

In this situation, the risk of the MDS is much higher than the risk of the transplant. This would be a situation where we would want to proceed to transplant

Studies show that in this situation, **transplant leads to improved survival**



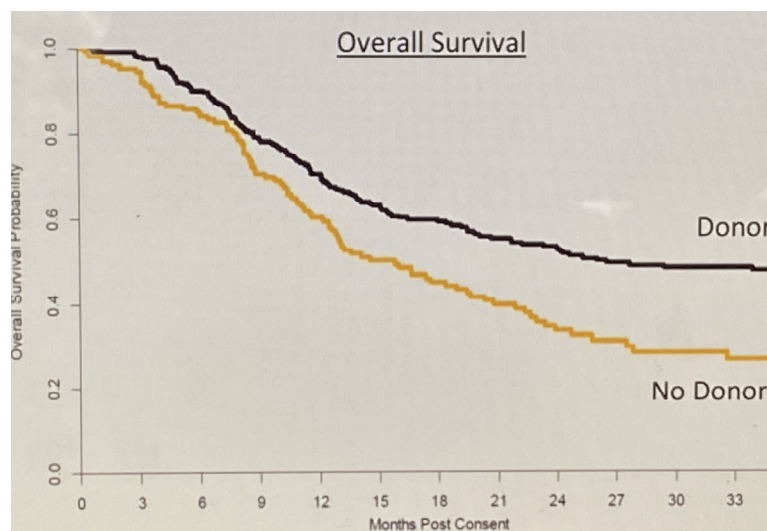
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Studies Comparing Transplant to NO Transplant in MDS

- Biggest and best trial was reported in December 2020.
- Randomized higher risk MDS patients to transplant or no transplant
 - Randomized based on whether they had a fully matched donor or not
- Average age both arms = 66, with ~60% of patients over age of 65. Highest age was 75
- The 3 year survival rate was **48% in transplant arm** and **27% in no transplant arm** - this difference was statistically significant
- No significant difference in quality of life
- Conclusion: all patients with higher risk MDS up to age 75 should be considered for transplant

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Transplant vs. NO Transplant in MDS



A Multi-Center Biologic Assignment Trial Comparing Reduced Intensity Allogeneic Hematopoietic Cell Transplantation to Hypomethylating Therapy or Best Supportive Care in Patients Aged 50-75 with Advanced Myelodysplastic Syndrome: Blood and Marrow Transplant Clinical Trials Network Study 1102 ASH 2020 Abstract, Nakamura R et al.

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Transplant for MDS - Key Points

- In higher risk MDS, transplant increases survival compared to non-transplant therapy
- Quality of life does not appear to be worse in those undergoing transplant, and may actually improve significantly for many patients
- Relapse can be a problem after transplant
- We will talk more about this after talking about transplant for AML

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Transplant for Acute Myelogenous Leukemia (AML) - Key Points

- Transplant for AML is best performed when patients are in an excellent remission
 - Best if there is no evidence of minimal residual disease
- AML can be very difficult to get into a second remission
- Transplant for AML leads to longer survival rates compared to no transplant, and for many patients, the only chance for cure

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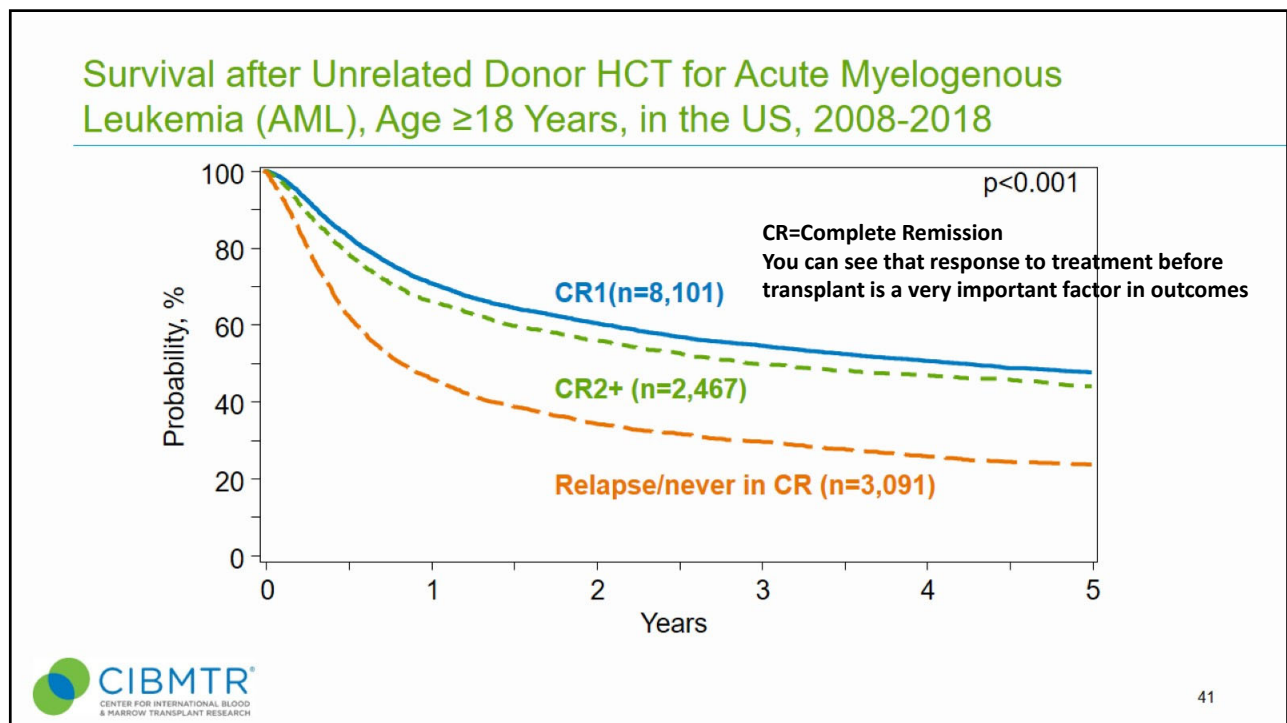
AML in Older Adults

- AML is a disease of older adults; average age of diagnosis is 68
- Like MDS, there are features of the disease that impact the risk of the disease
- Unlike MDS, over 70% of older AML patients have higher risk disease
- Therefore, almost every patient over the age of 60 with AML could be considered for transplant if we just focused on their disease
- But, there are many factors beyond disease that impact that decision to consider transplant

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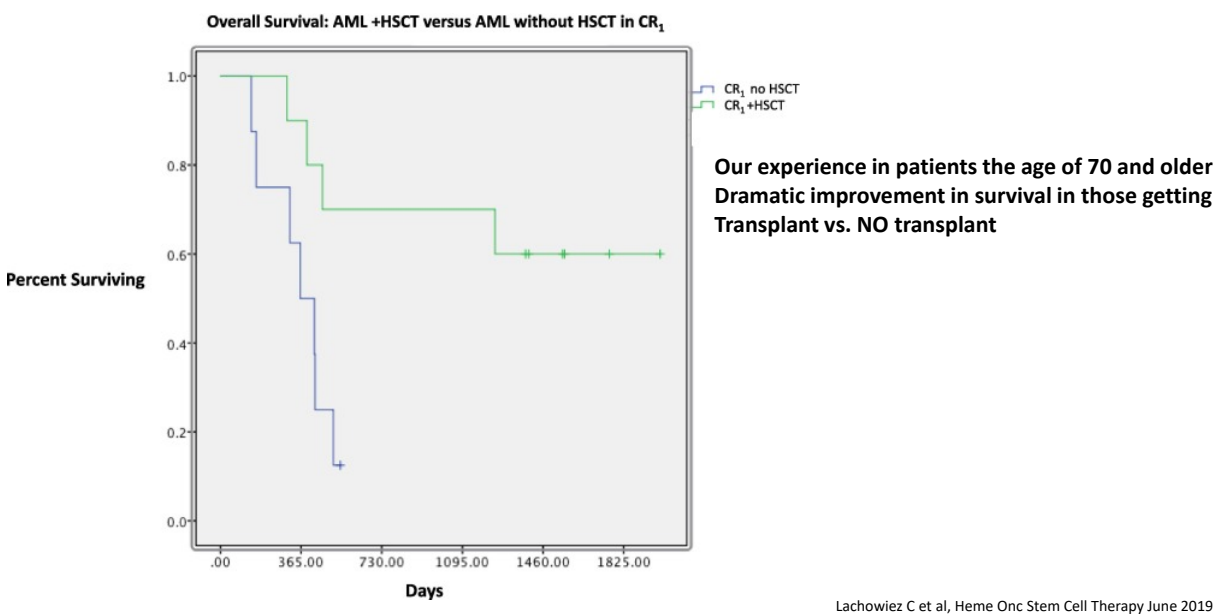
What are the outcomes for patients with AML who are undergoing a transplant?

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What about transplant outcomes in those over 70?



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What influences outcomes of transplant in patients with AML or MDS?

- Age alone is not a factor that influences outcome
 - Multiple studies show similar outcomes in those > or <60 years old
- Functional status and comorbidities are important factors in outcomes
- Disease relapse is a real issue after transplant
 - Use of post-transplant therapies is being studied to reduce risk of relapse
- Studies to optimize conditioning regimens, GVHD prevention and alternative donor options are showing great promise

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But what about Quality of Life?

- Quality of life (QOL) after transplant, in general, is reported as good
 - Dip initially after transplant that then heads back to pre-transplant levels in 6-12 months.
- There are factors that are known to impact quality of life
- GVHD can lead to poorer QOL
- Functional status - how strong you are - impacts QOL
- Impact on ability to work and financial security can decrease QOL
- These factors are present in younger and older adults

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How can we improve functional status?

- Exercise
 - In the cancer world there is a lot of research on “prehabilitation”
 - The idea is to build up the strength in your body before treatment
 - Higher strength/performance status leads to better QOL
 - Combination of activity as well as strengthening to counteract muscle loss
- Nutrition
 - Making sure adequate calories and adequate protein intake (goal protein intake 1.5-2 grams/kg of body weight to help gain muscle back)
- Optimizing your mood
 - Research has shown that mood and functional status are very connected; a structured prehab program was most beneficial for those with depression
 - Talk with your treatment team about how you are feeling

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Disease Control Before and After Transplant

- Before transplant we want MDS with blasts <5% and AML in complete remission
 - Best to have NO minimal residual disease in AML
 - However, if we can't get this level of disease control we can still do a transplant successfully
- Best treatments for AML include intensive chemotherapy
- Those over the age of 60 can tolerate intensive AML therapy; it's important to treat patients with the best treatment
- With transplant we can give full dose chemotherapy vs. reduced intensity chemotherapy conditioning
 - Reduced intensity conditioning has lower complications from transplant
 - But with reduced dosing we see higher risk of relapse
- The choice of the regimen is optimized for each patient taking into account health problems and disease status

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Disease Control After Transplant

- After transplant we have treatment options to help control disease without harming the graft vs. leukemia (or graft vs. MDS) activity
- Use of these agents (azacytidine, decitabine or targeted agents) after transplant in both MDS and AML has shown to be well-tolerated
- These treatments have also shown to reduce relapse risk

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	Current recommendations	Alternative options	Promising options
FLT3 positive	Sorafenib 400-800 mg/day for 24 months	-Midostaurin* - Gilteritinib*	- IDH inhibitors (IDH-mutated) - AZA+venetoclax - Hedgehog inhibitors -AZA+DLI (MRD-guided)
High risk	Azacitidine 32 mg/m ² /day for 5 days for at least 12 months	Decitabine 5 mg/m ² /day for 5 days**	
MRD positive	Azacitidine 75 mg/m ² /day for 7 days for at least 12 months		

* Phase III trials are ongoing
** Based on phase I trial

From Antar AI et al, Frontiers in Oncology November 2020

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GVHD Prevention and Management

- GVHD is the biggest fear for many patients have when considering a transplant
- Lots of focus on trying to prevent GVHD and manage GVHD if it comes
- GVHD does reduce the risk of relapsed disease
- Worth asking about clinical trial options at your institution
 - Vedolizumab is an antibody being studied to prevent gut GVHD
 - Multiple trials looking at modification of the transplanted cells to reduced the chance of GVHD

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Summary

- We can successfully transplant patients with MDS and AML over age 60
- The number of patients getting transplant in their 70's continues to rise
- The best outcomes are seen when you have:
 - Good control of your disease
 - Good performance status prior to transplant
- It is important to continue to exercise and stay strong throughout the treatment - both before and after transplant
- Treatments are available after transplant to help prevent relapse
- Age alone is not a factor, but the health status and functional status are key markers of success

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Questions?

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