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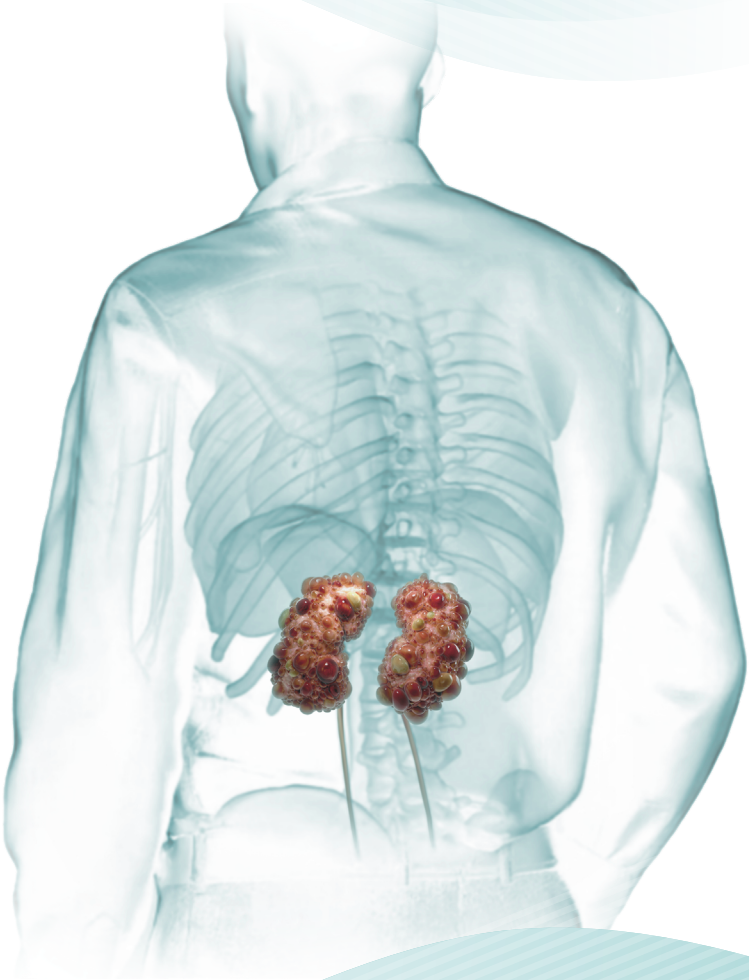
Improving Awareness & Patient Outcomes

Autosomal Dominant Polycystic Kidney Disease

ADPKD

Experience ADPKDsim, An Interactive Tool To Help Determine The Rate Of ADPKD Disease Progression



UNDERSTANDING ADPKD | DISEASE PROGRESSION SIMULATION

UNDERSTANDING Autosomal Dominant Polycystic Kidney Disease (ADPKD)

ADPKD is a progressive, systemic disease that is characterized by the propensity to develop numerous fluid-filled cysts. Overtime, cysts continue to grow and expand, which enlarges the kidneys 4-6 times their normal size and can lead to kidney failure, ultimately requiring dialysis or kidney transplantation.[1,2] Patients with rapidly progressing ADPKD reach kidney failure at a younger age. However, the rate of disease progression could vary significantly, even within the same family.[3,4] Therefore, understanding baseline clinical, genetic, and imaging data can assist the health care team in identifying patients who are risk of rapid progression.[4,8]

IN THIS GUIDE YOU WILL FIND:

- A high-level overview of the known risk factors and available assessment tools that can help health care providers determine the rate of ADPKD disease progression.
- Overview of the ADPKDSim tool, an interactive ADPKD disease progression simulation in which the user can select a hypothetical patient with specific known risk factors.
- Introduction to the patient-facing section of ADPKDsim, which can be used as a teaching tool during counseling sessions with patients and care partners.

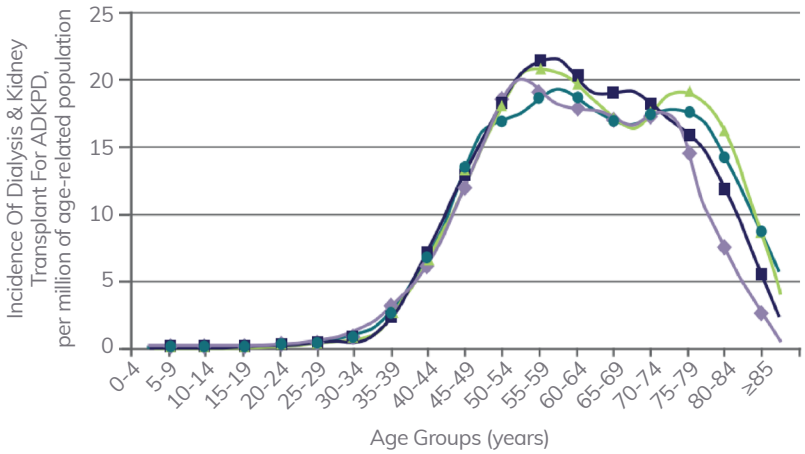
Clinical Outcomes

Historically, ADPKD treatment has been focused on slowing the progression of kidney failure and treating its symptoms such as kidney stones, abdominal and/or lower back pain, and hypertension. Ultimately, ADPKD leads to kidney failure due to continued kidney cyst growth. More than 50% of patients with ADPKD will reach kidney failure by age 60.[5]

Clinical outcomes for ADPKD have not changed in decades despite aggressive symptomatic treatment and incidence of dialysis and kidney transplant.[4,7,8] Because the rate at which ADPKD advances can be variable, monitoring progression is one way to help manage the disease.[4] Proactive monitoring and management of ADPKD may help improve outcomes for patients over time.

Outcomes For Patients With ADPKD

Despite aggressive symptomatic treatment, incidence of dialysis and kidney transplant has not changed in over 20 years.[7]



Mean age at start of dialysis:

◆ 1991-1995 **56.6** ■ 1996-2000 **57.4** ▲ 2001-2005 **58.2** ● 2006-2010 **58.0**

Quick Facts About ADPKD

01 ADPKD is a progressive kidney disease[9,10]

02 Cyst growth precedes decline in kidney function; patients with ADPKD may remain asymptomatic for years while the disease progresses[11]

03 Nearly 50% of patients with ADPKD reach kidney failure by age 60[12]

04 Rate of progression is variable from patient to patient, even within the same family*[3]

05 Predictors of rapid progression: total kidney volume (TKV), genetics, family history, clinical indicators, and laboratory biomarkers[13]

06 Prognostic tools such as the TKV-based Classification of ADPKD[8,13] may help identify those at risk for rapid disease progression before it occurs†

*A subgroup of patients have more rapidly progressive disease.
†Note: This tool has been used in research but has not been clinically validated.

WHY IT MATTERS

The Importance Of Determining The Rate Of ADPKD Disease Progression

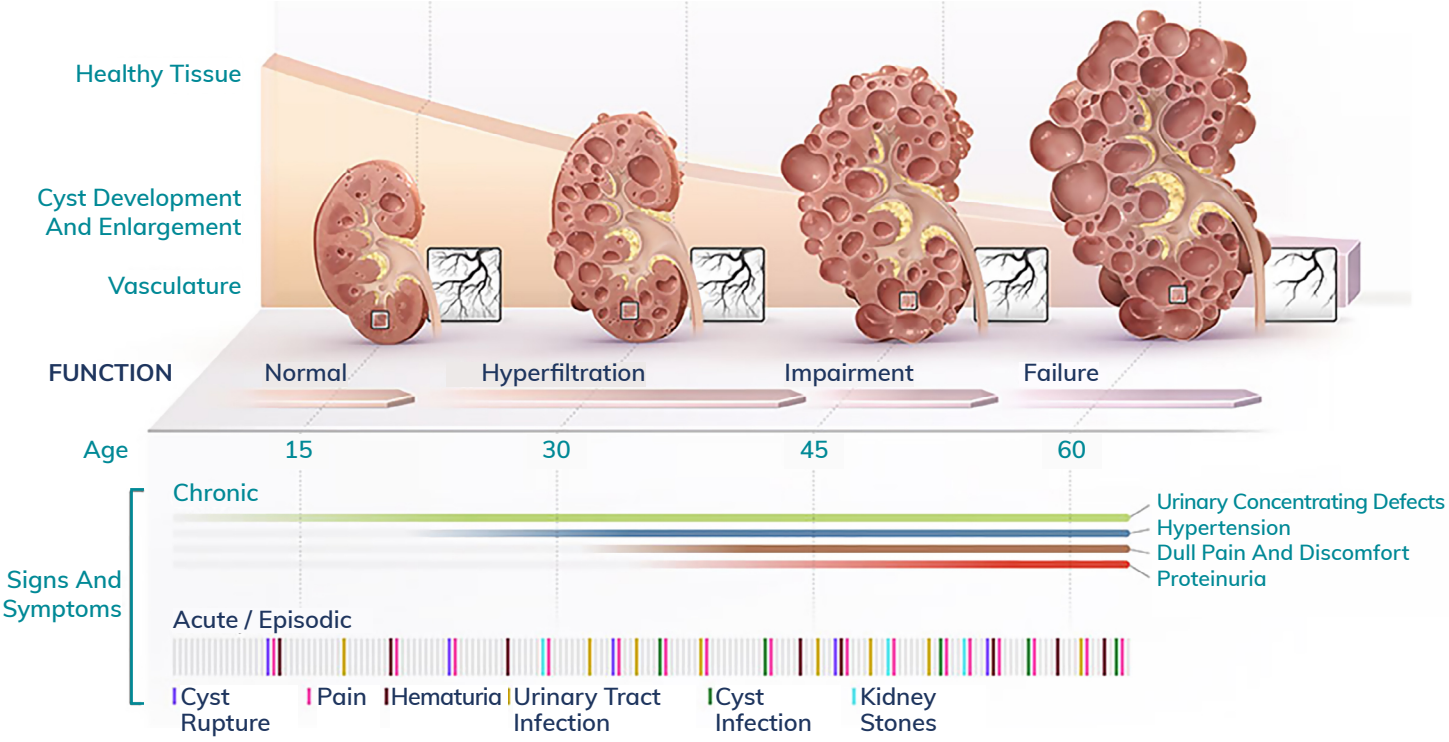
While ADPKD is an inherited condition, the age of onset and rate of progression can be unpredictable, varying from patient to patient, even in the same family.[1,3] Assessing the rate of disease progression is an important part of disease management. Predicting which patients with ADPKD will progress rapidly to kidney failure is critical to assess the risk-benefit ratio of any intervention and to consider early initiation of long-term kidney protective measures that will maximize the cumulative benefit of slowing disease progression.[8] In addition, identifying patients at risk for rapid progression early may provide an opportunity for intervention.

Predictors of Rapid Disease Progression in ADPKD[8]

1. **Environmental:** High caffeine intake, high protein intake, low water intake, and smoking[8,5]
2. **Imaging:** High total kidney volume, low renal blood flow[8]
3. **Clinical:** Early onset hypertension, gross hematuria, early decrease in glomerular filtration rate (GFR)[8]
4. **Genetic:** Truncating mutations in the *PKD1* gene[8]
5. **Laboratory:** Overt proteinuria, microalbuminuria, and elevated copeptin[8]

Indicates best-validated markers

Cyst Burden & Patient Complications in ADPKD*



*Adapted from ADPKD Burden of Disease An Overview for Healthcare Providers: US.UNB.X.21.0007

The ADPKDsim Tool

HOW IT WORKS

ADPKDSim is an interactive tool in which users can select from hypothetical patient profiles with simulated disease progression to see the utilization of prognostic tools in ADPKD.

1. Visit **ADPKDsim.org** and click on "ADPKD Simulator."
2. Select a hypothetical patient. (See image below.)
3. Click on the orange flags to walk through an assessment that confirms rapid disease progression risk and assesses how rapidly the disease may progress.

SCAN TO TRY ADPKDsim

Disease Progression Simulation*

Select a **hypothetical** patient

KNOWN RISK FACTORS:	Bill (35)	Angela (45)	Denise (35)	Frank (52)	Jeremy (29)
Being male	•			•	•
Rapid historical eGFR decline*				•	
US-KL >16.5 cm in patients less than 45 years old†			•		
Hypertension before age 35	•		•	•	
Urologic events before age 35	•	•	•	•	•
Family history of ESKD by age 58			•	•	•
Truncating *PKD1* mutation	•				
TKV greater than expected for age	•			•	
Other Risk Factors			•	•	

To view variations in ADPKD progression for Bill, Angela, Denise, Frank, and Jeremy, visit ADPKDsim.org/expert/adpkd-simulator

You can see from the chart that Frank, Age 52, has the greatest number of known risk factors associated with an ADPKD diagnosis, whereas Angela, age 45, has only one risk factor.

Let's take a closer look at the risk factors for Frank.

*Adapted from ADPKDsim.org/expert/adpkd-simulator

The ADPKDsim website is intended for healthcare professionals and for educational purposes only. The tool and content on this site are not meant to be a substitute for medical judgment and should not be used for diagnosis and/or treatment decisions. Healthcare professionals should use independent judgment when considering these educational resources.

ADPKDsim Tool For Health Care Professionals

Selected **hypothetical** patient

Frank (52)

KNOWN RISK FACTORS:	Frank (52)
Being male	●
Rapid historical eGFR decline*	●
US-KL >16.5 cm in patients less than 45 years old†	
Hypertension before age 35	●
Urologic events before age 35	●
Family history of ESKD by age 58	●
Truncating *PKD1* mutation	
TKV greater than expected for age	●
Other Risk Factors	●

Frank's Risk Factor Details

1. **eGFR:** Baseline eGFR of 52.8 (mL/min/1.73 m2) places Frank at CKD Stage 3.
2. **Historical eGFR:** Frank's historical eGFR values show rapid decline of more than 5 mL/min/1.73m^2 over 1 year. An inflection point had occurred even earlier at about age 45, while he was at CKD Stage 2. At this point, Frank's rate of eGFR decline increased.
3. **htTKV:** Baseline htTKV is 1,669 mL/m, which is greater than expected for age (normal adult htTKV range at this age is ~150-250). We can plot Frank's htTKV and age on the ADPKD Imaging Classification graph. This confirms that Frank is at high risk for rapid progression and helps assess how rapidly his disease may progress.
4. **ADPKD Imaging Classification:** With ADPKD Imaging Classification based on MRI/CT-calculated htTKV, we can assess Frank's risk for eGFR decline.
5. **MRI/CT-Calculated TKV:** With MRI-calculated htTKV, we can estimate historical values for htTKV growth. In early disease progression, htTKV steadily increased even when eGFR levels remained within a normal range. We can also estimate projected values for htTKV growth and future eGFR decline.

Frank

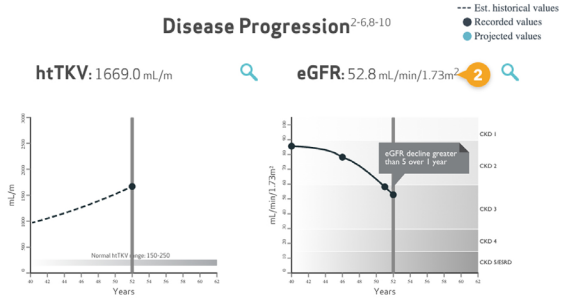
Frank is 52 years old and has been diagnosed with ADPKD by a kidney ultrasound. Frank is at risk for rapid disease progression, as indicated by the following risk factors: being male, rapid historical eGFR decline*, hypertension before age 35, urologic events before age 35, proteinuria/albuminuria, family history of ESKD by age 58, and TKV greater than expected for age. Let's take a closer look with some prognostic tools to confirm the risk of rapid disease progression and assess how rapidly his disease may progress.[1,2]

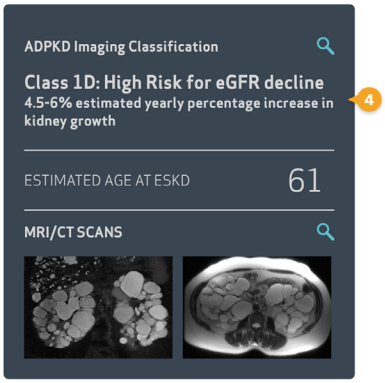
AGE	HEIGHT	WEIGHT	SEX	RACE (AA/O)
52	5'9"	181 lbs	M	O

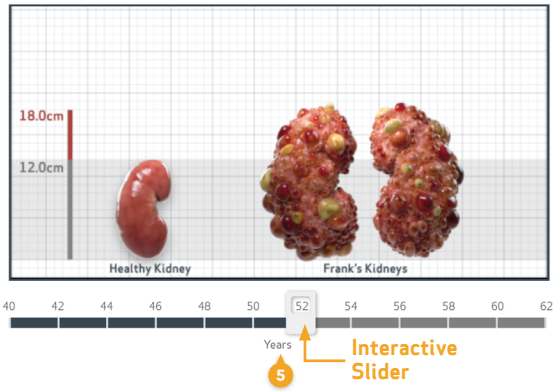
Baseline Assessment[2-7]

Serum creatinine (mg/dL)	1.5
eGFR (mL/min/1.73m^2)	52.8 (1)
Ultrasound kidney length (cm)	Not obtained
Hypertension before 35?	Yes
Urological event before 35?	Yes
Family members with ESKD?	Yes (58 yrs)
Mutations	Not available
PROPKD Score	Not available
htTKV (mL/m)	1,669 (3)
Other risk factors	Proteinuria / albuminuria

Disease Progression[2-6,8-10]







*Confirmed eGFR decline → 5 mL/min/1.73 m^2 within a year and/or → 2.5 mL/min/1.73 m^2 per year over a period of five years.[2]

ADPKD=autosomal dominant polycystic kidney disease; eGFR=estimated glomerular filtration rate; ESKD=end stage kidney disease; TKV=total kidney volume; AA=African American; O=other; PKD=polycystic kidney disease; htTKV=height-adjusted total kidney volume; MRI=magnetic resonance imaging; CT=computed tomography; CKD=chronic kidney disease

References:

1. Schrier RW, et al. Predictors of autosomal dominant polycystic kidney disease progression. *J Am Soc Nephrol.* 2014;25:2399-2418.
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SCAN TO TRY ADPKDsim

To view variations in ADPKD progression for Bill, Angela, Denise, and Jeremy, visit ADPKDsim.org/expert/adpkd-simulator

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*Adapted from ADPKDsim.org/expert/adpkd-simulator

 August 2023 US.CORP.X.23.00064

ADPKDsim Tool For Patients

On the ADPKDsim site, choose "INFORMATION FOR PATIENTS."

The patient-facing section of ADPKDsim features lay terminology, and can be used as a teaching tool during counseling sessions with patients and their care partners.

Select a **hypothetical** patient

Jennifer (41)

KNOWN RISK FACTORS [1]:	Jennifer (41)
Being male	
Rapid kidney function decline*	
Large kidney length measured by ultrasound*	●
High Blood Pressure at an early age	●
Events affecting the urinary tract (e.g. blood in the urine or lower back pain)	●
Family history of kidney failure by age 58	●
Large kidney volume compared to healthy kidneys	●
Other Risk Factors (e.g., Obesity)	●

Jennifer's Risk Factor Details

1. **eGFR:** Baseline eGFR of 88 (mL/min/1.73 m2) places Jennifer at CKD Stage 2.
2. **Blood in Urine:** Occurred at 38 years of age
3. **Lower Back Pain:** Noted at age 34, 38, and 40 years of age

Jennifer

Jennifer is 41 years old and has been diagnosed with Autosomal Dominant Polycystic Kidney Disease (ADPKD). Jennifer is considered obese and has uncontrolled high blood pressure. She suffers from repeated bouts of lower back pain and had one episode of blood in her urine. She has a family history of ADPKD and her father reached kidney failure and needed to begin dialysis at the age of 55.

Let's take a closer look at some tests Jennifer's kidney doctor has ordered to better understand how quickly Jennifer might progress to kidney failure. [1,2,3]

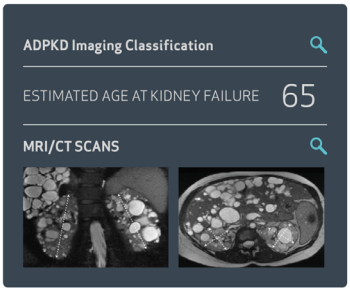
AGE	HEIGHT	WEIGHT	SEX	RACE (AA/O)
41	5'4"	210 lbs	F	0

Lab Tests

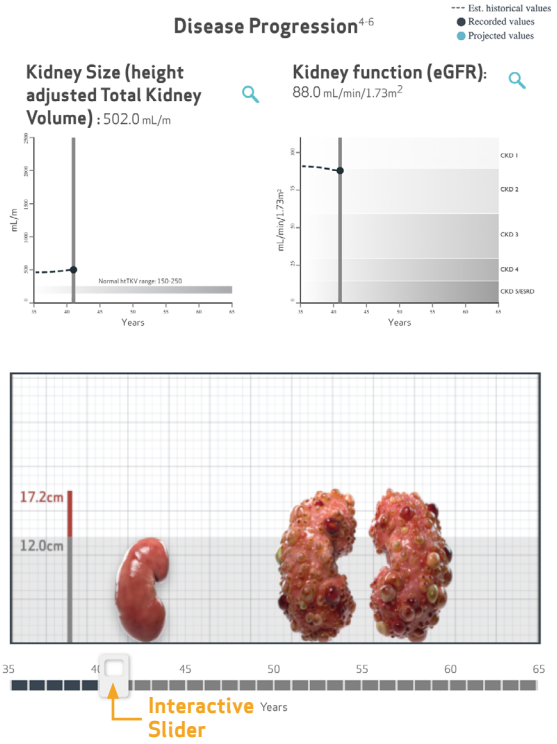
		STANDARD RANGE
Serum Creatinine (mg/dL)	0.96	0.50 - 1.20
eGFR (1) (mL/min/1.73m²)	88	≥ 60
Blood Pressure (mmHg)	140/90 (High, Uncontrolled)	< 120/80
Blood in Urine (2)	Yes	
Pain (3)	Yes	
Family History	Yes (Father reached kidney failure at 55)	
Other Risk Factors	Obesity	

Imaging Tests

		STANDARD RANGE
Ultrasound Ordered?	Yes	
Kidney Length (cm)	17.2	10-13
MRI Ordered?	Yes	
Kidney Size (mL/m)	502	150-250



Disease Progression [4-6]



*Confirmed eGFR decline → 5 mL/min/1.73 m2 within a year and/or → 2.5 mL/min/1.73 m2 per year over a period of five years.[2]

*When MRI-/CT-calculated TKV is not available, US-KL may be a useful surrogate when rapid progression is defined as CKD stage 3 development within 8 years.[2,3]

ADPKD=autosomal dominant polycystic kidney disease; PKD=polycystic kidney disease; TKV=total kidney volume; US-KL=ultrasound kidney length; ESKD=end-stage kidney disease; eGFR=estimated glomerular filtration rate; MRI=magnetic resonance imaging; CT=computed tomography.

References:

1. Schrier RW, et al. Predictors of autosomal dominant polycystic kidney disease progression. J Am Soc Nephrol. 2014;25:2399-2418.
2. Gansevoort RT, et al. Recommendations for the use of tolvaptan in autosomal dominant polycystic kidney disease: a position statement on behalf of the ERA-EDTA Working Groups on Inherited Kidney Disorders and European Renal Best Practice. Nephrol Dial Transplant. 2016;31(3):337-48.
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SCAN TO TRY ADPKDsim FOR PATIENTS

To view patient-facing ADPKD resources and hypothetical patient profiles, visit ADPKDsim.org/patient

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Conclusion

Talking With Your Patients About ADPKD

Understanding the rate of disease progression is important for the patient and his/her care team to set realistic expectations and develop a treatment plan based on shared decision making. As patients become better informed and knowledgeable about ADPKD, they can benefit from increased understanding of the disease process and their treatment plan respectively.

ADPKDsim offers effective communication strategies, providing a platform to manage the patient's expectations, which often leads to better patient engagement. This, in turn, can help engaged patients deal better with the many challenges they face living with a rare kidney disease like ADPKD.[8]

Visit ADPKDsim.org
To Learn More

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References

1. Patel V, Chowdhury R, Igarashi P. *CurrOpinNephrol Hypertens.* 2009;18(2):99-106.
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ADPKDsim

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