Question
In children with type 1 diabetes mellitus, what factors are associated with increased risk for microalbuminuria and macroalbuminuria?

Methods
Design: Inception cohort followed for a mean of 9.8 years.
Setting: St. Bartholomew's Oxford Diabetes Register, Oxford, England, UK.
Patients: 527 children < 16 years of age (mean age 9 years) who were diagnosed with type 1 diabetes mellitus and included in the Diabetes Register from 1986 to 1997 (90% follow-up).
Prognostic factors: Mean glycated hemoglobin concentration (HbA_{1c}), female sex, mean blood pressure, history of smoking, and age at diagnosis.
Outcomes: Microalbuminuria (albumin-to-creatinine ratio 3.5 to 35 mg/mmol in boys and 4.0 to 47 mg/mmol in girls, in 2 annual, consecutive, early morning urine samples), and macroalbuminuria (albumin-to-creatinine ratio > 35 mg/mmol in boys and > 47 mg/mmol in girls).

Main results
135 patients (26%) developed microalbuminuria, with a cumulative prevalence of 25.7% (95% CI 21 to 30) after 10 years and 51% (CI 41 to 61) after 19 years. Of the 135 patients with microalbuminuria, there was a cumulative prevalence of regression to the normoalbuminuric range of 52% (CI 42 to 62) after 4.9 years from the onset of microalbuminuria. 18 patients (3%) developed macroalbuminuria, with a cumulative prevalence of 14% (CI 13 to 15) after 3.2 years from onset of microalbuminuria. HbA_{1c} and female sex were associated with increased risk for microalbuminuria (Table). HbA_{1c} and persistent and intermittent microalbuminuria were associated with increased risk for macroalbuminuria (Table).

Conclusions
In children with type 1 diabetes mellitus, poor glycemic control and female sex were associated with development of microalbuminuria. About half of patients with microalbuminuria regressed to normoalbuminuria. Poor glycemic control and persistent or intermittent microalbuminuria were associated with development of macroalbuminuria.

Sources of funding: Diabetes UK; Juvenile Diabetes Research Foundation; Wellcome Trust; NIHR Cambridge Biomedical Research Centre.

Structured abstract based on: Amin R, Widmer B, Prevost AT, et al. **Risk of microalbuminuria and progression to macroalbuminuria in a cohort with childhood onset type 1 diabetes: prospective observational study.** BMJ. 2008;336:697-701. 18349042

Factors associated with renal outcomes in children with type 1 diabetes mellitus*

Outcomes	Prognostic factors	At a mean 9.8 years of follow-up
		Hazard ratio (95% CI)
Microalbuminuria	HbA_{1c} (per % increase)	1.4 (1.3 to 1.5)
	Female sex	1.4 (1.02 to 2.1)
	Diastolic blood pressure	1.0 (1.0 to 1.0)
	Systolic blood pressure	1.0 (1.0 to 1.0)
	History of smoking	1.3 (0.9 to 2.0)
	Younger age at diagnosis	1.0 (1.0 to 1.1)
Macroalbuminuria	HbA_{1c} (per % increase)	1.4 (1.2 to 1.8)
	Persistent microalbuminuria†	28 (8.0 to 96)
	Intermittent microalbuminuria‡	8.8 (2.4 to 31)
	Female sex	1.3 (0.5 to 3.3)
	Diastolic blood pressure	1.1 (0.9 to 1.1)
	Systolic blood pressure	1.1 (0.9 to 1.1)
	History of smoking	1.3 (0.4 to 4.1)
	Younger age at diagnosis	1.0 (1.0 to 1.1)

*HbA_{1c} = glycated haemoglobin.
†Presence of microalbuminuria at every annual visit after first detection.
‡Positive microalbuminuria followed by regression to normoalbuminuria, then recurrence to microalbuminuria at a later date.

A 12-year-old girl is brought to the office for a follow-up examination 6 months after being diagnosed with type 1 diabetes mellitus. The patient feels well. She says she smokes cigarettes occasionally when with friends. She is not sexually active. She is at the 60th percentile for BMI. Her temperature is 37.0°C (98.6°F), pulse is 80/min, respirations are 16/min, and blood pressure is 108/72 mm Hg. Physical examination shows no other abnormalities. Results of urinalysis are within the reference ranges. Her father, who has type 1 diabetes mellitus and chronic renal disease, asks what markers will be followed to determine his daughter's risk for developing chronic renal disease. Which of the following patient characteristics most increases her risk for developing microalbuminuria over the next 10 years?

(A) Age at diagnosis
(B) BMI
(C) Diastolic blood pressure
(D) Gender
(E) Smoking history

Answer: D

Which of the following current or potential future findings is most likely to increase the patient's risk for developing macroalbuminuria?

(A) Age at diagnosis
(B) Cigarette use
(C) Elevated systolic blood pressure
(D) Gender
(E) Poor glycemic control

Answer: E

One year later, the patient's urinalysis shows microalbuminuria for the first time. In a population of children of a similar age who have type 1 diabetes mellitus and had microalbuminuria detected for the first time, which of the following outcomes is most likely?

(A) Hemoglobin A_{1c} will normalize within 10 years
(B) Hypertension will be diagnosed within 2 years
(C) Macroalbuminuria will be detected within 1 year
(D) Microalbuminuria will resolve within 5 years

Answer: D