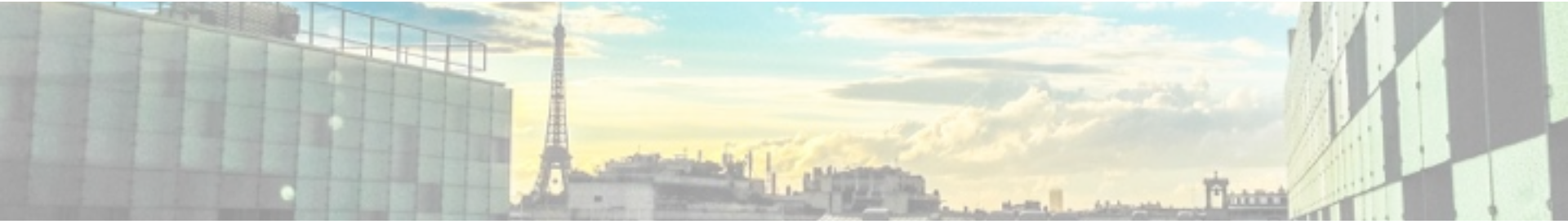

Les cardiomyopathies de l'enfant
Le syndrome de Barth

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Centre de Référence Maladies Rares
Malformations Cardiaques Congénitales Complexes-M3C

Centre de Référence Maladies Rares
Maladies Cardiaques Héréditaires- CARDIOGEN

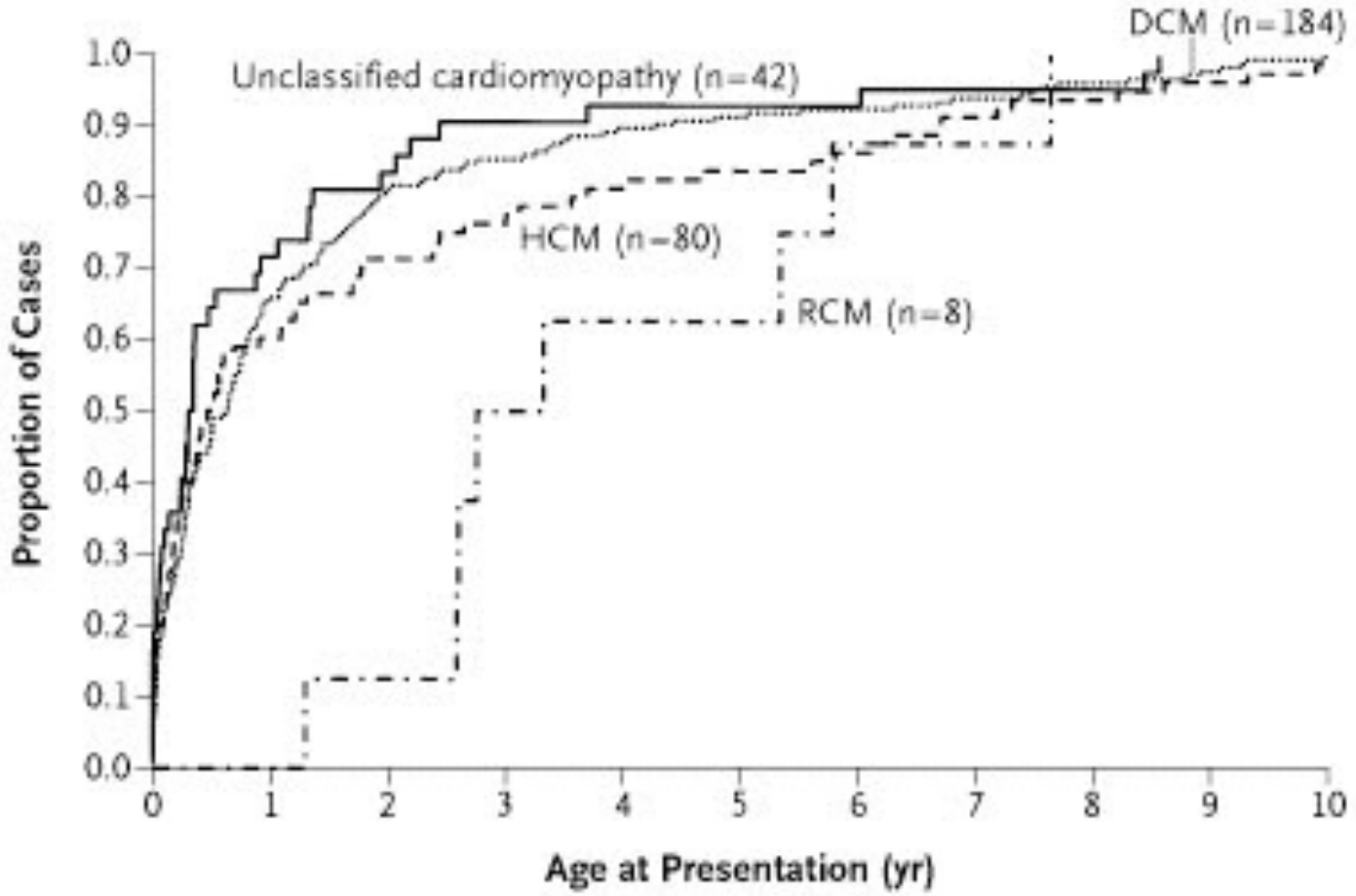
Epidemiology

- Annual incidence of childhood cardiomyopathies : 1.13 per 100,000
- Incidence higher among children <1 year :
  8.34 vs. 0.70 per 100,000
- Categorized according to type :
  - Hypertrophic 42 %
  - Dilated 51%
  - Restrictive 2.5%
  - Non compaction 9.2%
- Sudden death as presenting symptom 3.5%

- Barth syndrome is exceptional

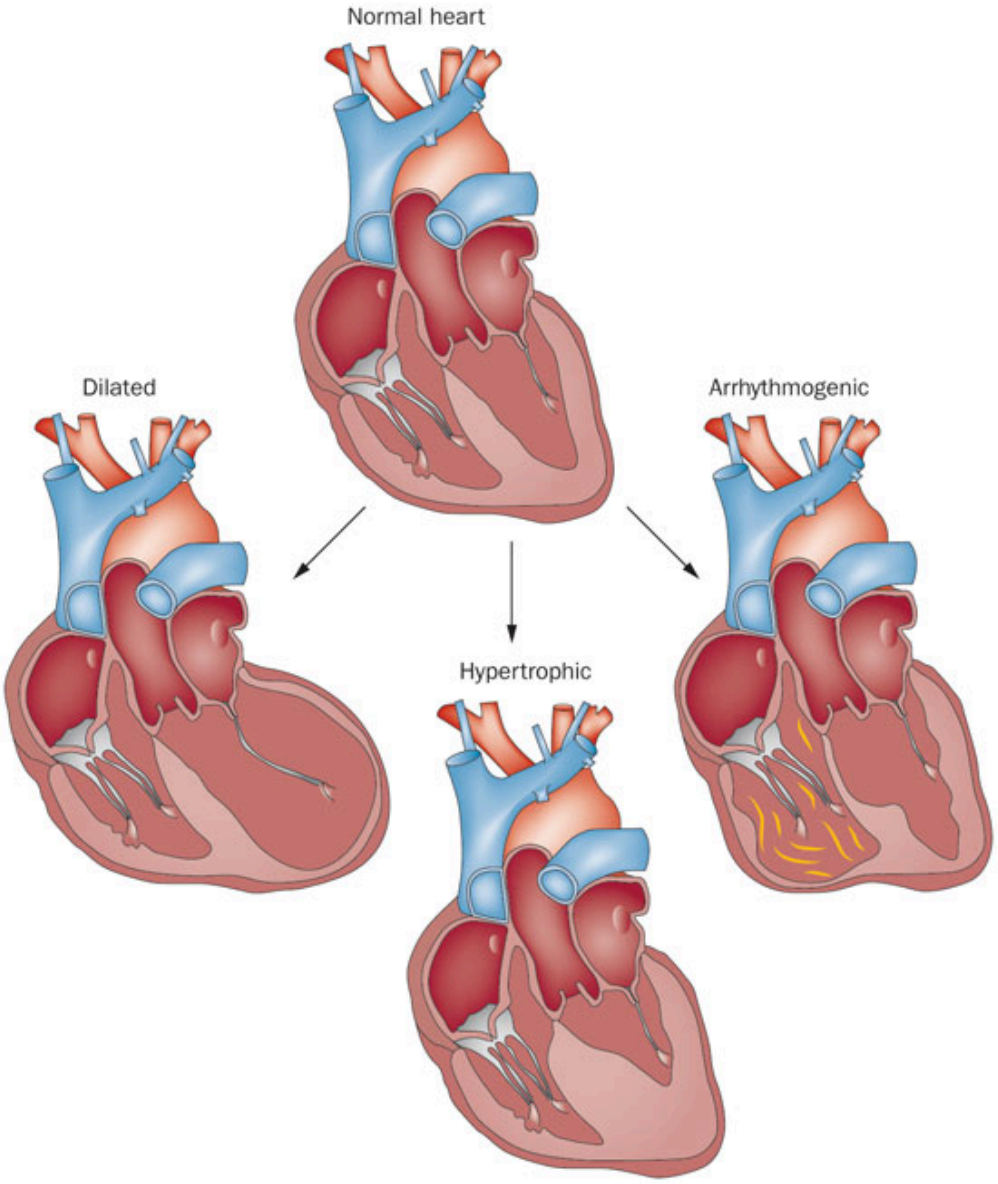
Lipshultz SE et al. NEJM 2003;348:1647-55

Cumulative frequency distribution of age at presentation

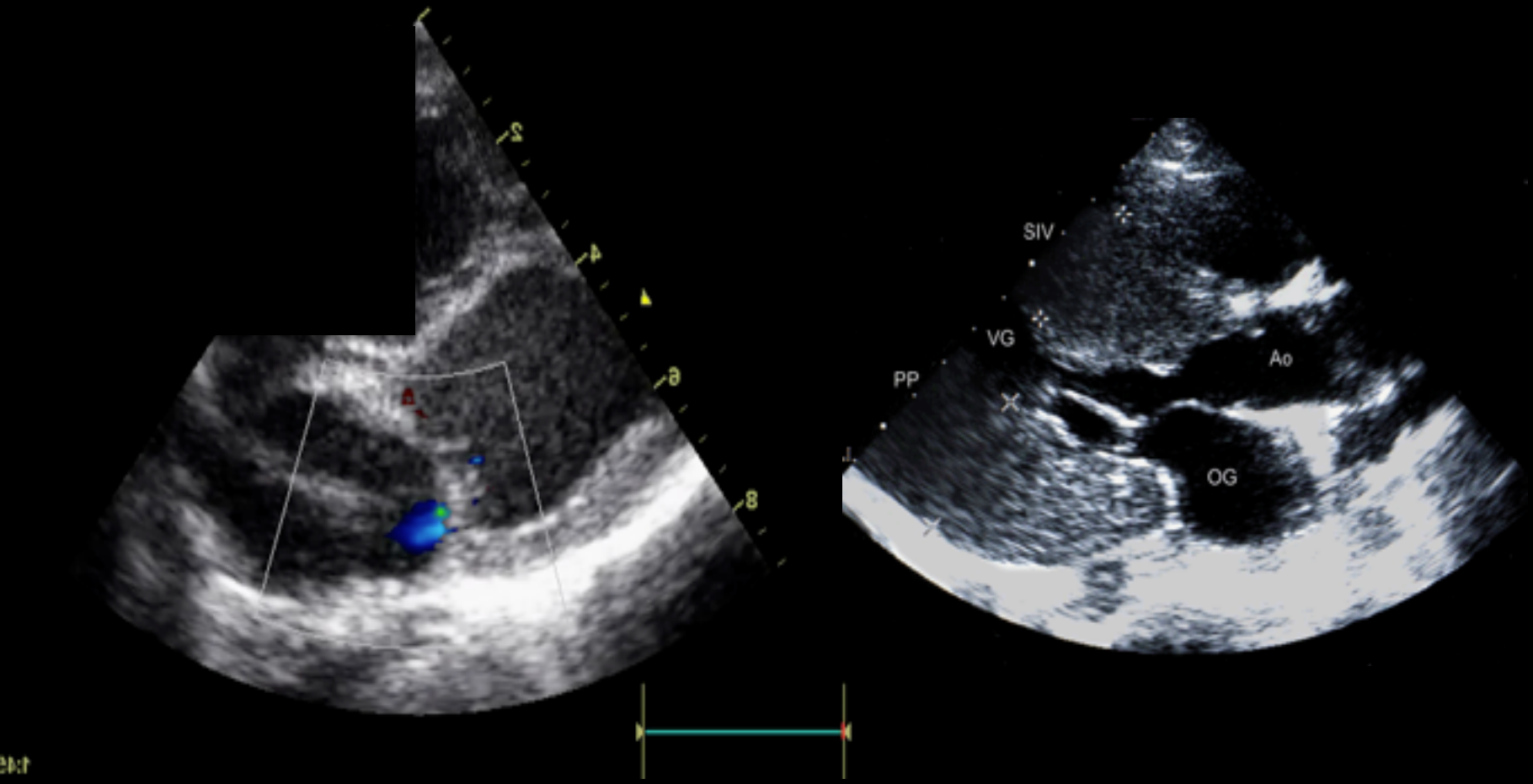


Nugent AW et al. NEJM 2003;348:1703-5

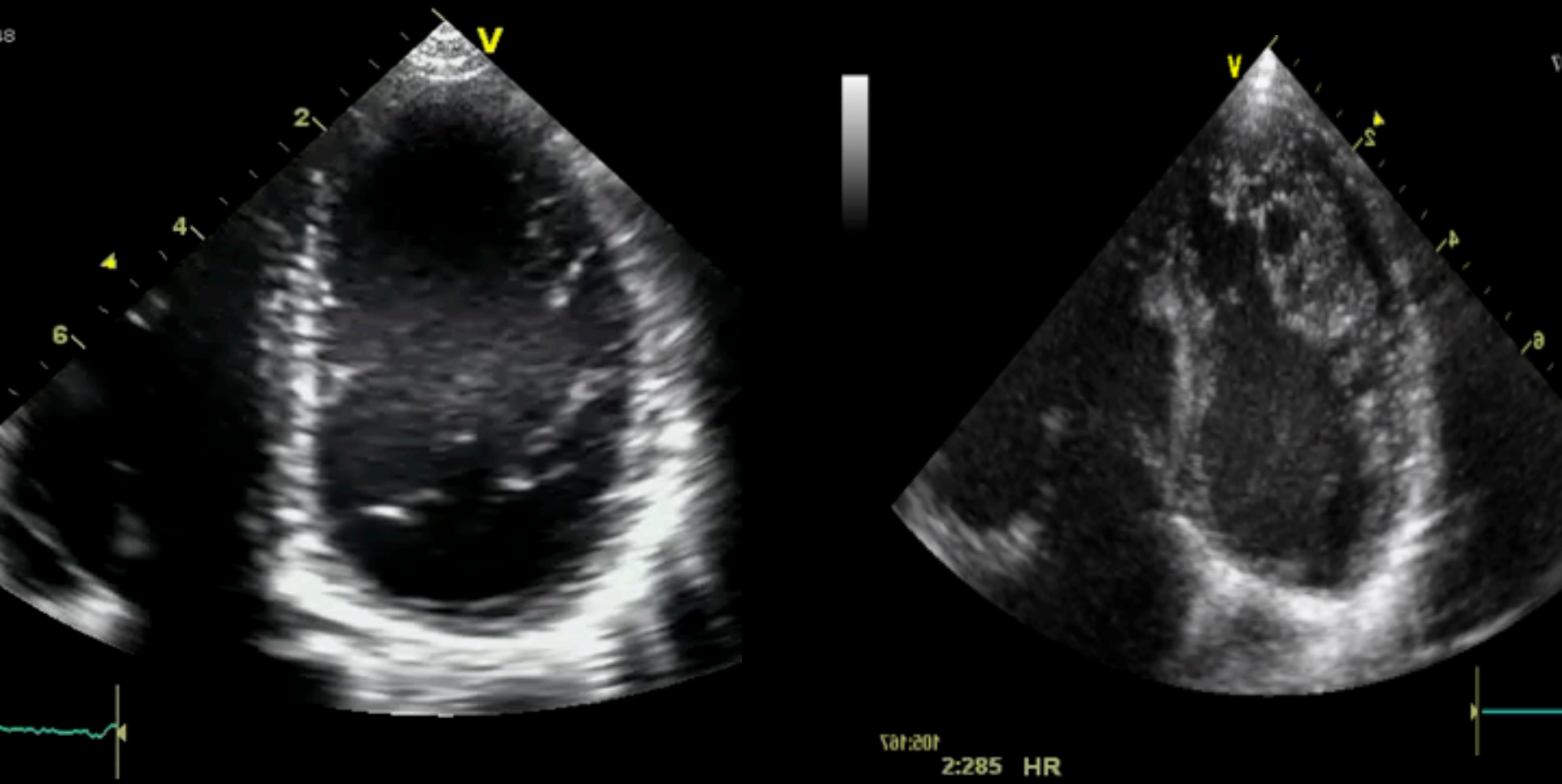
Cardiac phenotypes in cardiomyopathies



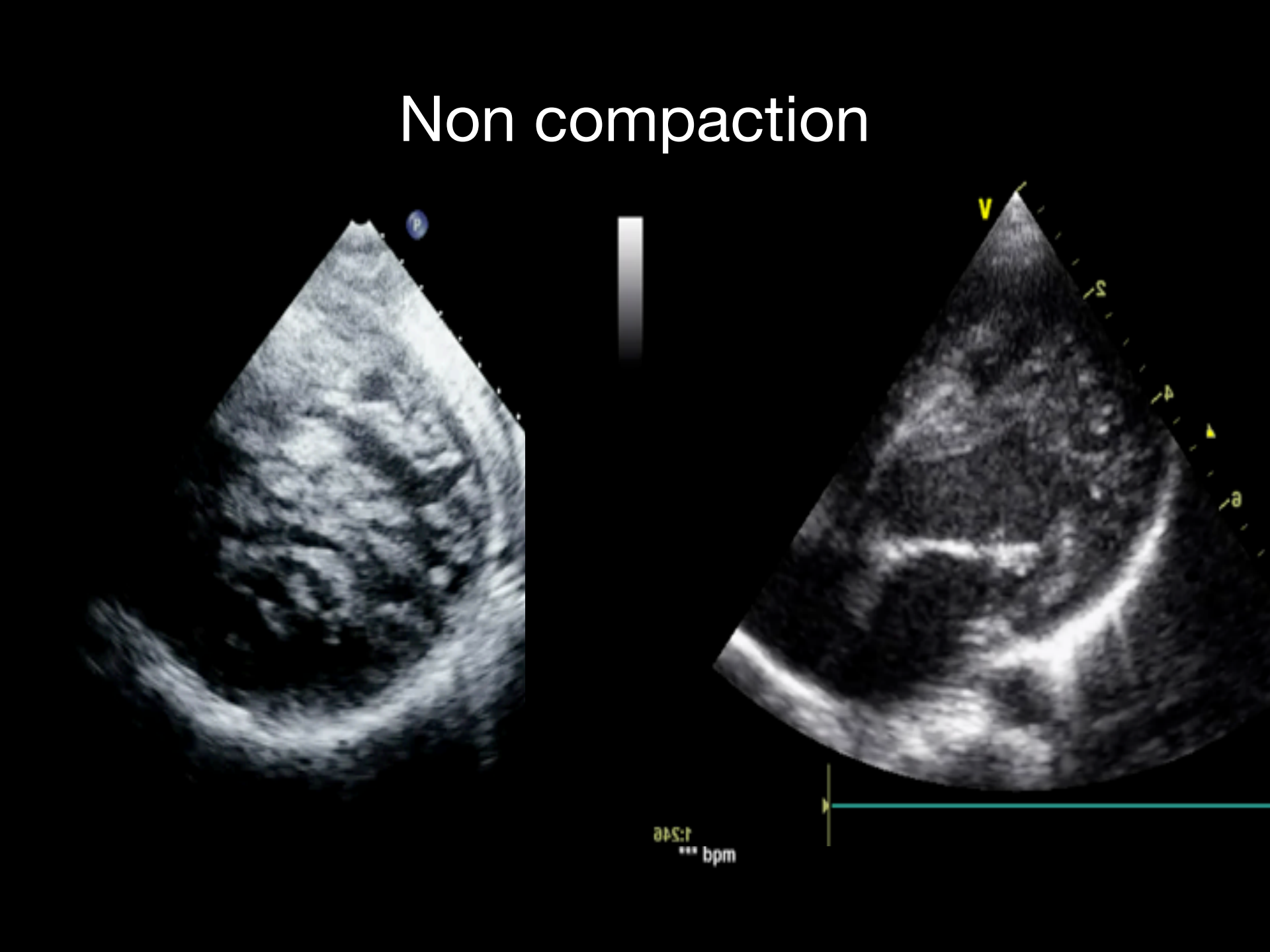
A variable phenotype



Non compaction



Non compaction



Difficulties in phenotyping

- Unusual phenotypes
  - Dilated with hypertrophic walls and non compaction
- Changing phenotype
  - From hypertrophic to dilated
- Variability in cardiac function

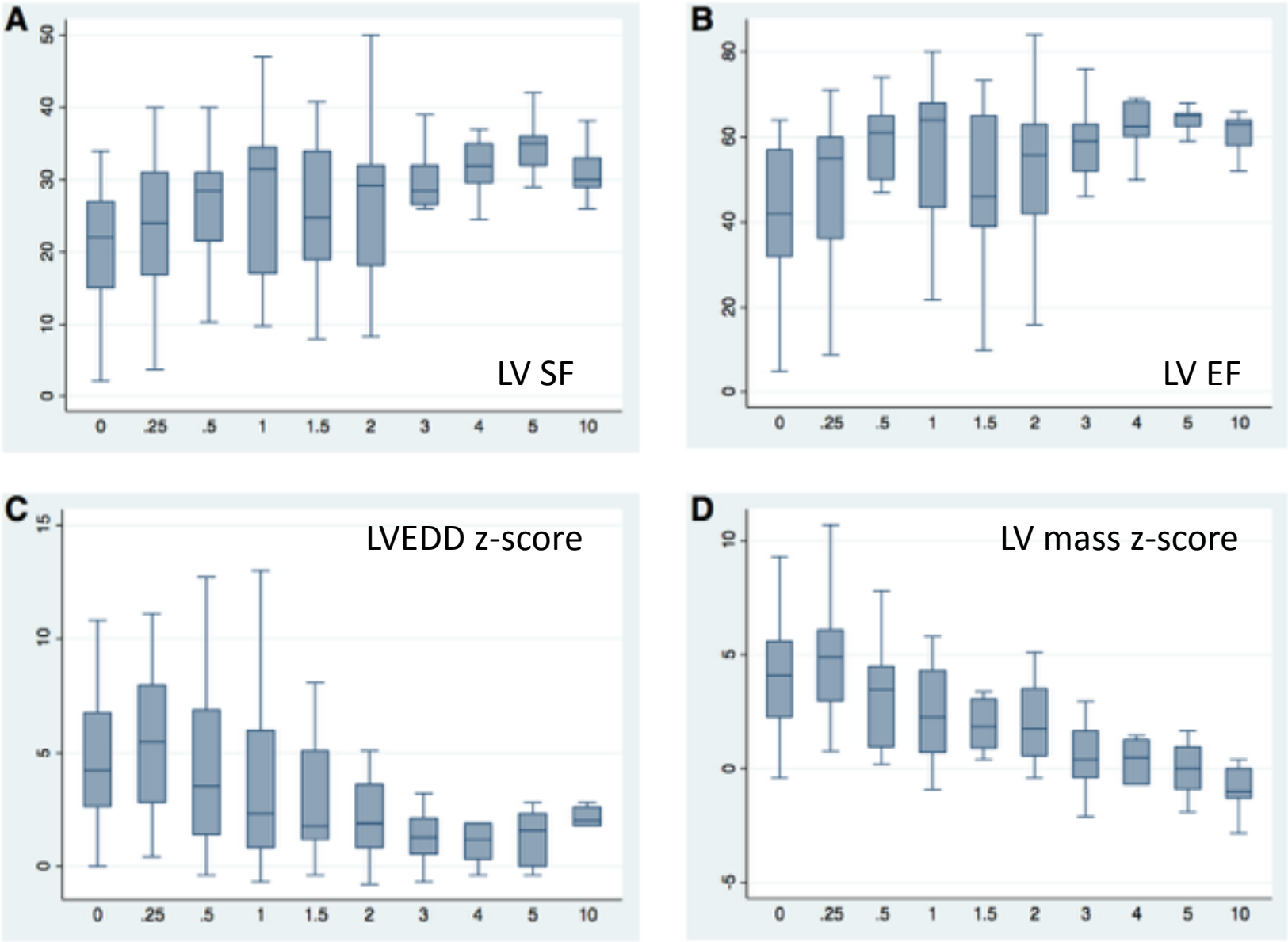
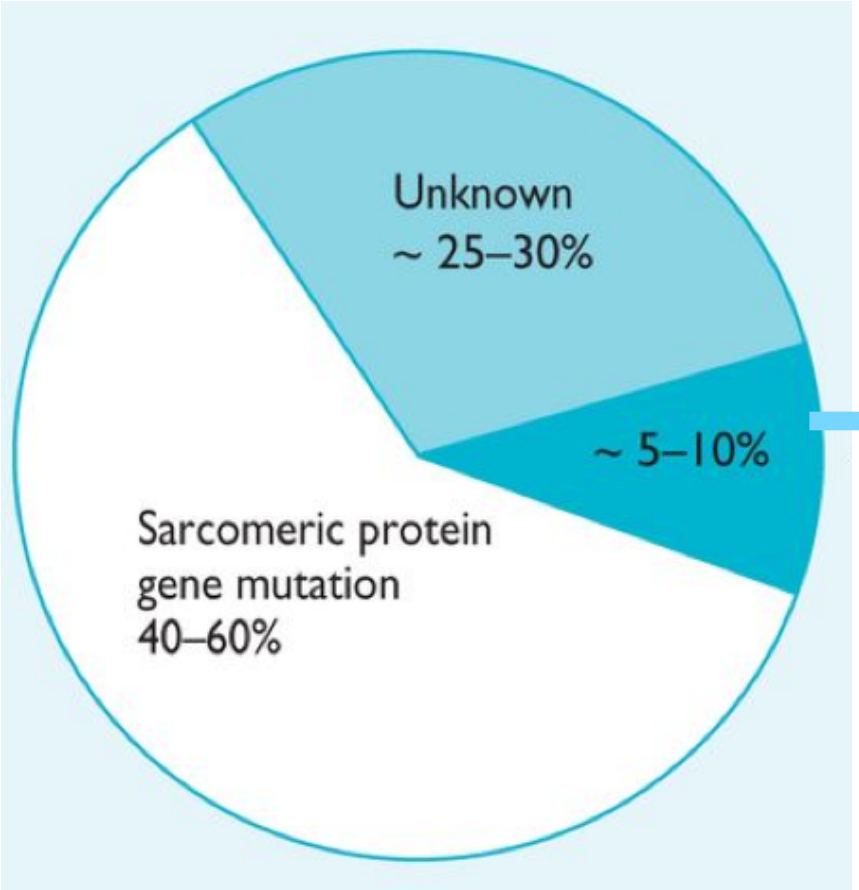


Figure 2 Box plots showing the distribution of cardiology parameters as determined by ultrasound according to age. Age is shown for the following categories: 0, birth to age 3 months; 0.25, between 3 months and 6 months; 0.5, between 6 months and 1 year; 1, between 1 and 1.5 years; 1.5, between 1.5 and 2 years; 2, between 2 and 3 years; 3, between 3 and 4 years; 4, between 4 and 5 years; 5, between 5 and 10 years; 10, >10 years old. The heart indicators are as follows: **A**) shortening fraction (SF), reported as %; **B**) ejection fraction (EF), reported as %; **C**) z-score of the left ventricular end diastolic diameter (LVEDD); **D**) z-score of the left ventricular mass (LV mass).



- **Inborn errors of metabolism**
  Glycogen storage diseases:
  - Pompe
  - Danon
- AMP-Kinase (PRKAG2)
- Carnitine disorders
- Lysosomal storage diseases
  - Anderson-Fabry

- **Neuromuscular diseases**
  - Friedreich's ataxia
  - FHL1

- **Mitochondrial diseases**
  - MELAS
  - MERFF

- **Malformation Syndromes**
  - Noonan
  - LEOPARD
  - Costello
  - CFC

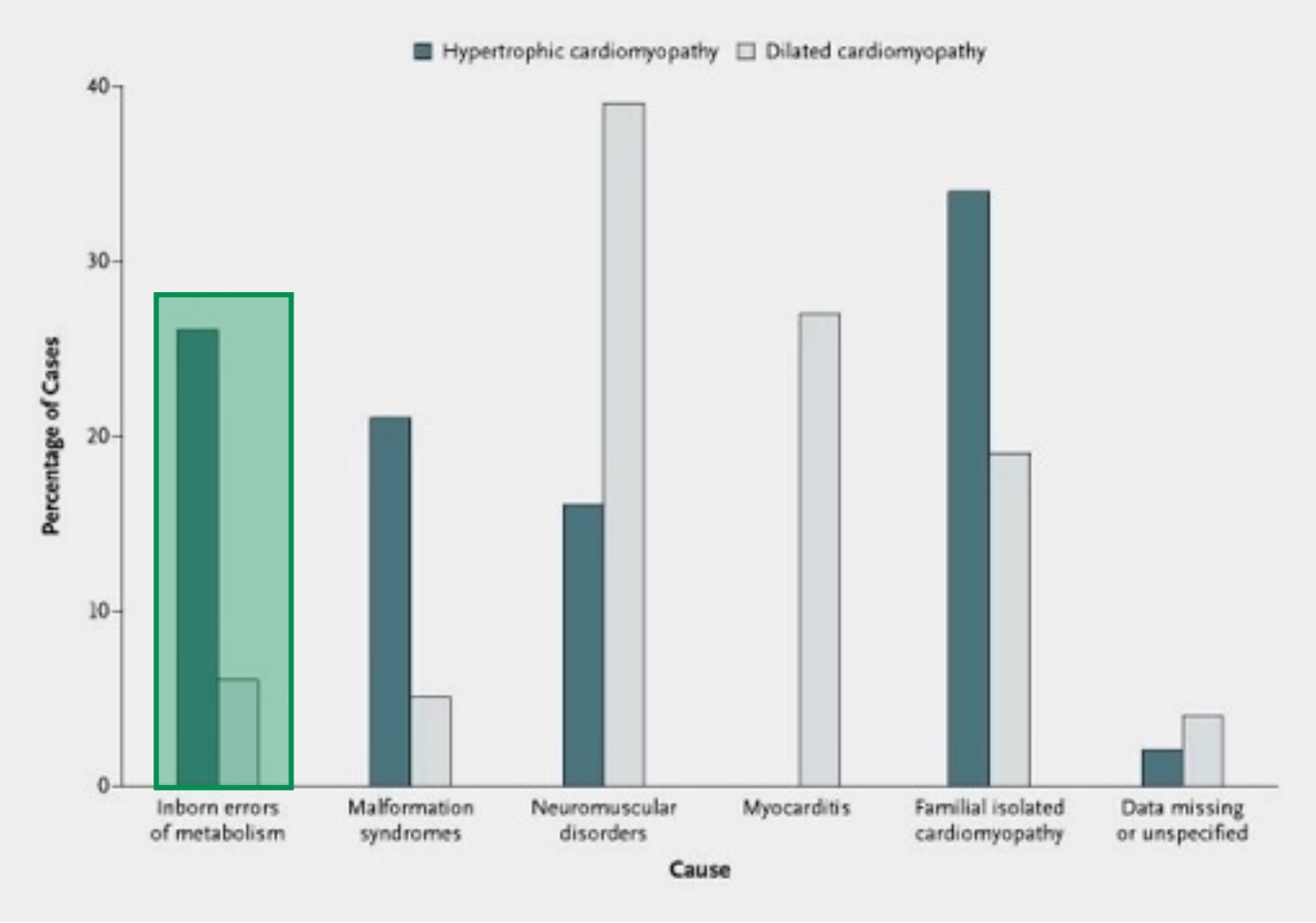
- **Amyloidosis**
  - Familial ATTR
  - Wild type TTR (senile)
  - AL amyloidosis

Causes non génétiques

- Steroids

*** Cœur d'athlète**

Primary causes of CMP in children

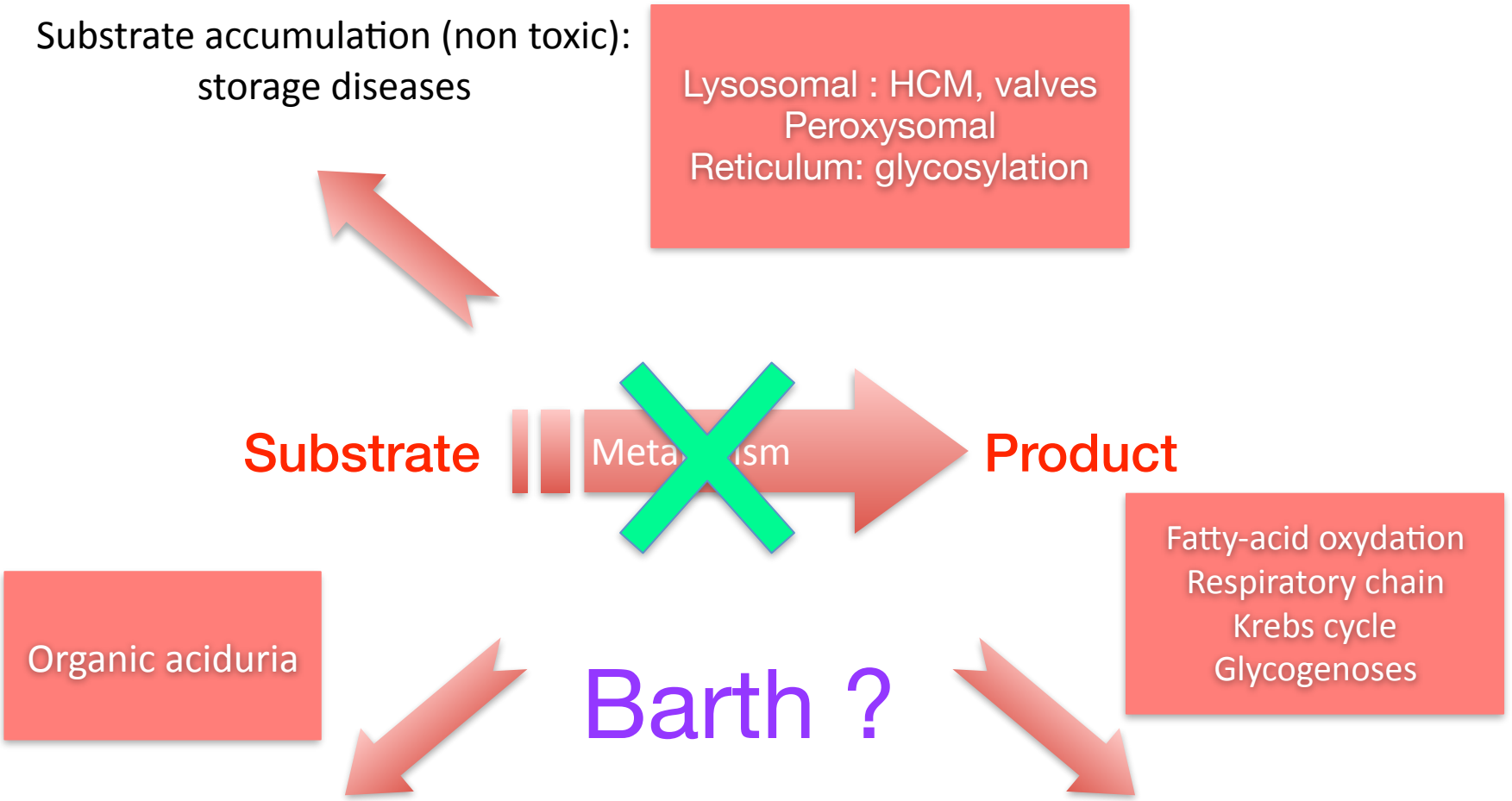


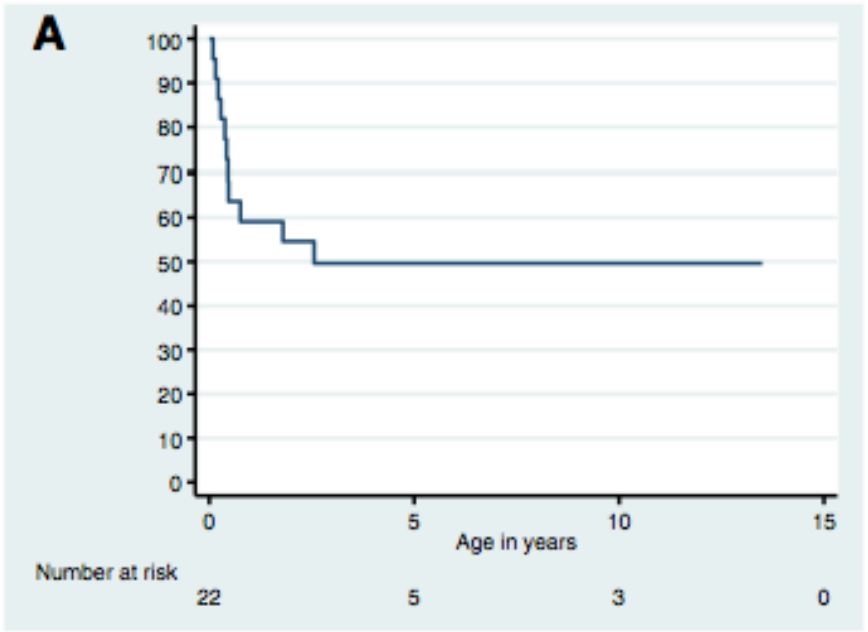
Lipshultz SE et al. NEJM 2003;348:1647-55

Quand suspecter une cardiomyopathie d'origine métabolique?

- Histoire familiale de mort subite ou inexpliquée
- Pathologie multisystémique ou associations illégitimes
- Passage d'une forme de MCP à une autre: hypertrophique à dilatée ou restrictive
- Situation clinique catastrophique hors de proportion avec la dysfonction du VG
- Anomalies atypiques de l'ECG, BAV progressif, arythmies ventriculaires

Cardiac metabolism for pediatric cardiologists





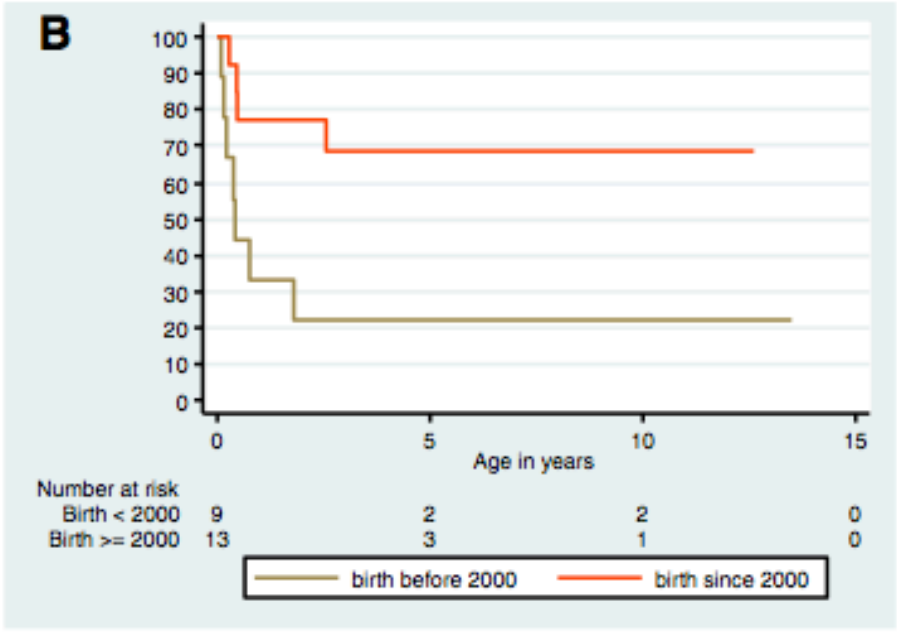


Figure 4 Overall survival and survival according to birth year of the French Barth syndrome cohort. A) Kaplan-Meier plot and 95% confidence intervals showing the overall survival of the French Barth syndrome cohort. Time is expressed in years since birth. **B**) Kaplan-Meier plot showing the survival of the French Barth syndrome cohort according to birth year (before and in or after 2000). Even though the total number of patients is quite limited, the difference in survival is both important (survival at 5 years: 22% for patients born before 2000 and 70% for patients born in or after 2000) and statistically significant ($p = 0.009$). This suggests that recent progress in the management of heart dysfunction may improve the survival of patients with BTHS.

Take-home messages Heart/Barth

- Unusual cardiac phenotype
  - morphology
  - outcome
- Prediction of risk
- Unknown pathophysiology


M3C