

Comorbidities increase In-Hospital Mortality in Dengue Patients in Brazil

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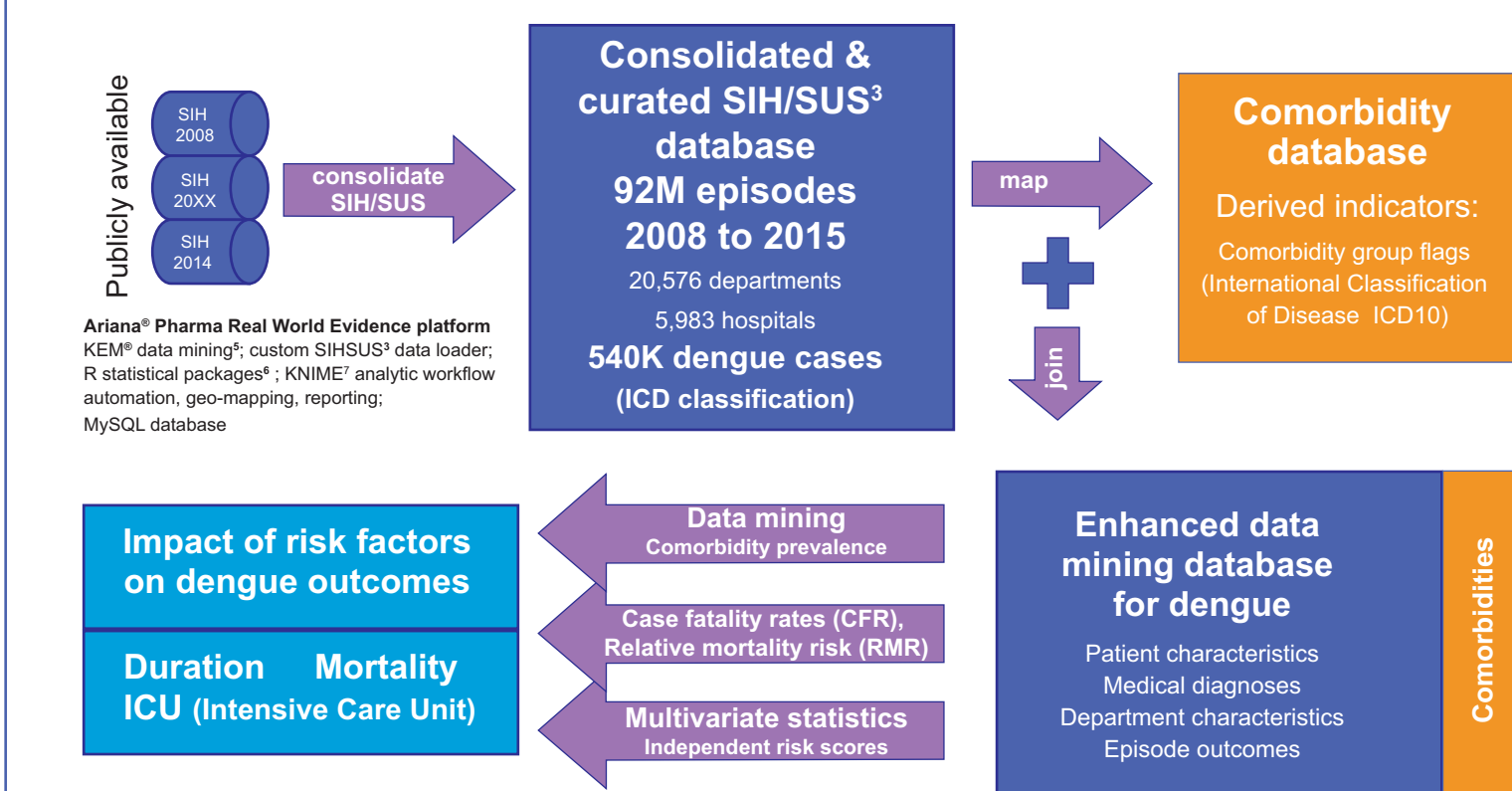
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BACKGROUND

- Dengue represents an unmet medical and public health issue with more than half of the world's population at risk¹
- Dengue patients with comorbidities may be at higher risk of death; however, there are few large-scale studies²
- Data mining of hospital databases provides insights on the impact of diseases on the healthcare infrastructure³⁻⁴ and contributes to document the disease burden on public health
- Predictive factors for dengue mortality in high risk populations could aid in determining those that would benefit most from dengue preventative measures

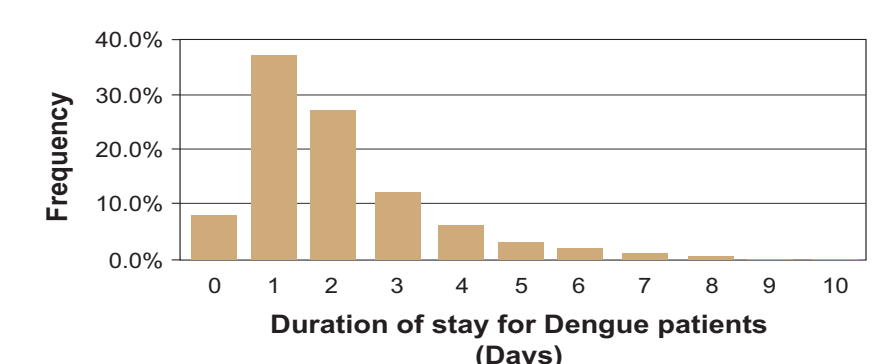
MATERIALS & METHODS

Retrospective analysis of risk factors for dengue mortality in a hospitalized patient database



Modeling the relative impact of comorbidities on dengue patient outcome using risk factors

Measure of patient outcome (cases): ICU, death and duration of stay



| | not ICU | ICU |
|-------|---------|-------|
| Alive | 526,513 | 3,707 |
| Dead | 1,875 | 854 |

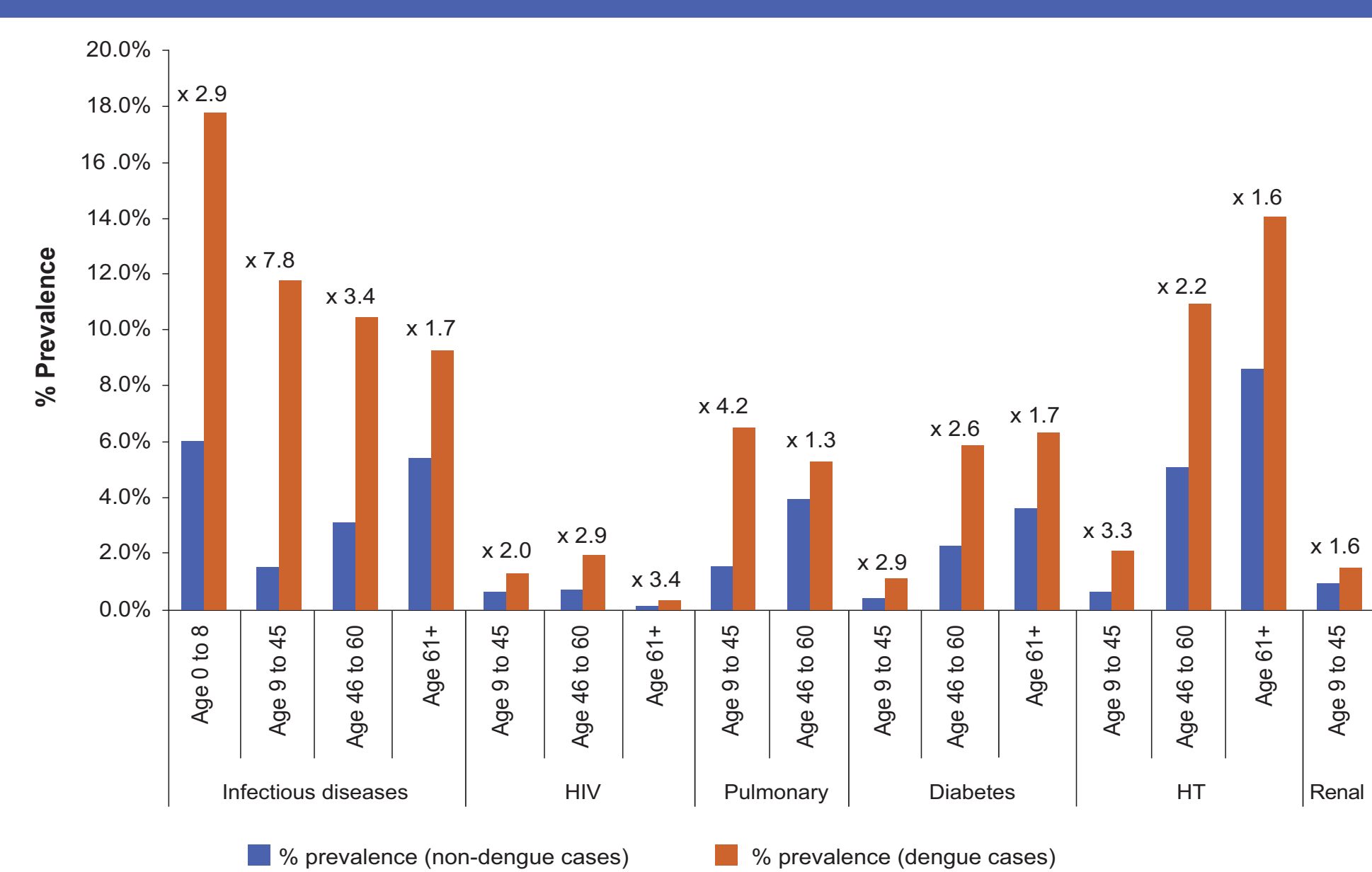
Example of Modeling⁶:

- Risk factors analysis to estimate independent effect on patient fatality
 - Empirical risk scores determined and patient outcomes compared
 - Risk scores are relative to reference cases= dengue, 9-45 year old, 2008, no comorbidities
 - Measure of risk of death: Log odds ratio
- Tools:**
- Cox survival for Duration and Logistic regressions for Death and ICU admission after controlling by potential confounders (as age, year of inclusion).

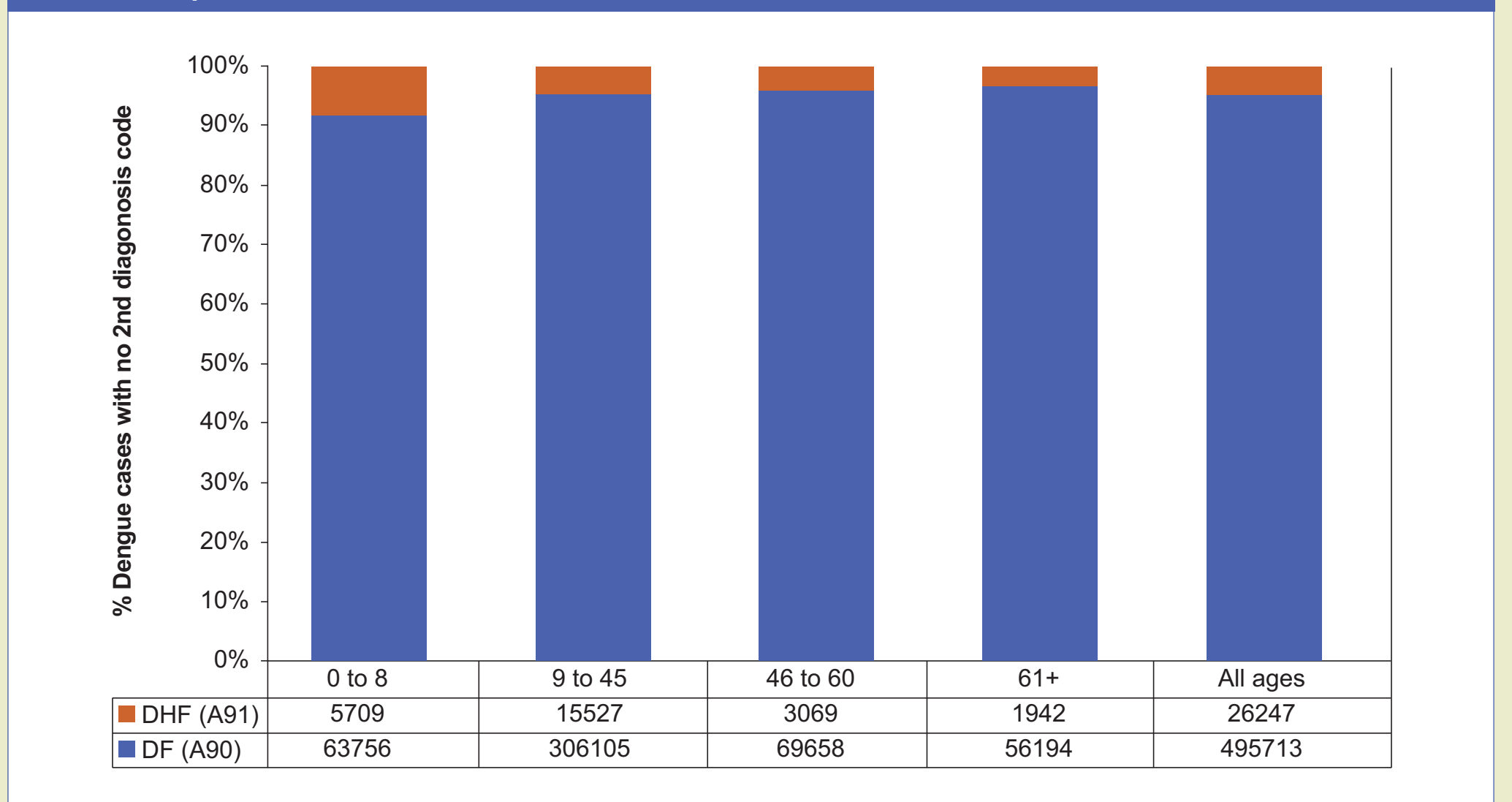
RESULTS

Prevalence of Risk factors

Comorbidities with increased prevalence in hospitalized dengue patients by age



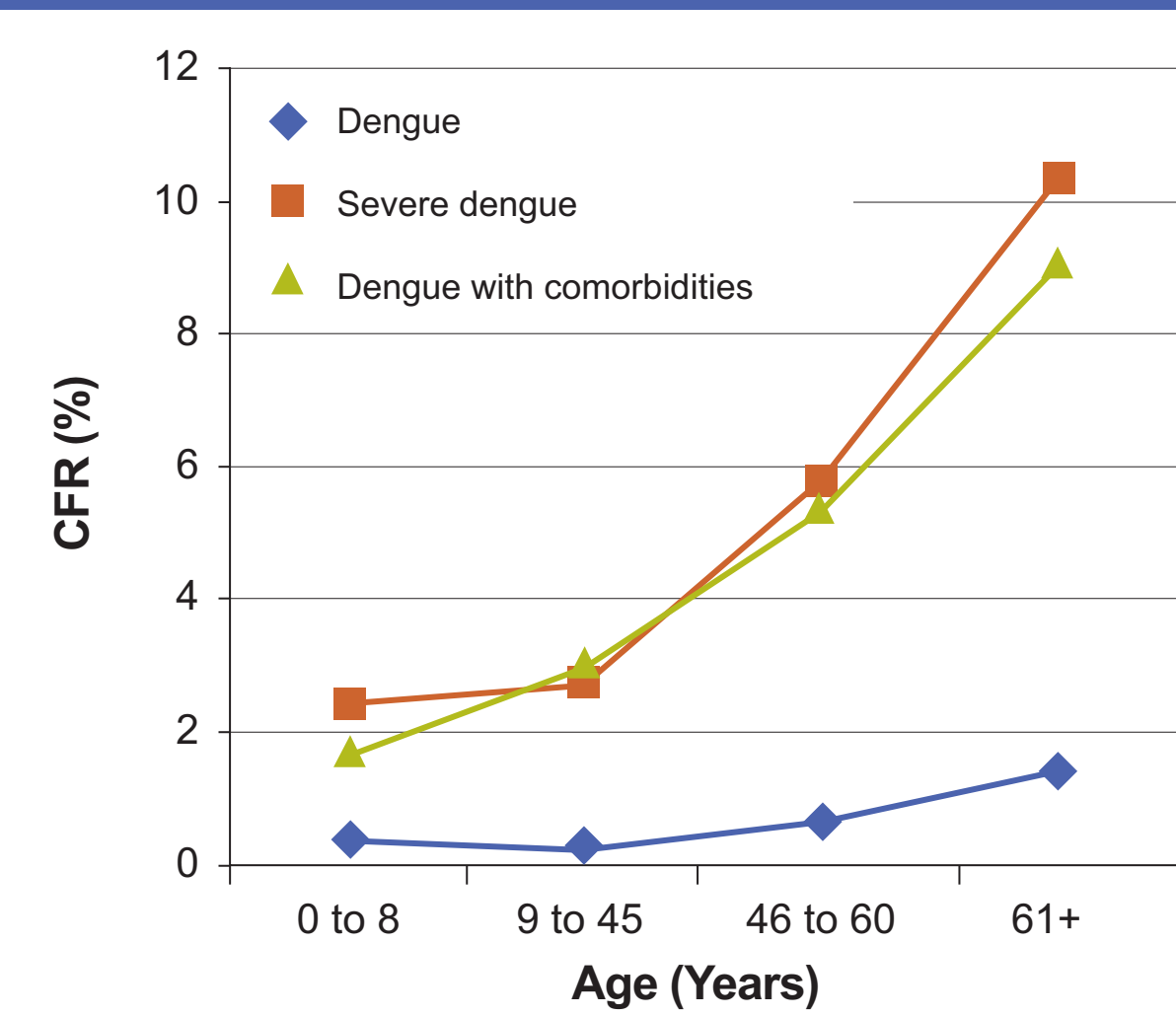
Severe hospitalized dengue affects all ages but majority of cases occur in preadolescents and adults (9 + yo)



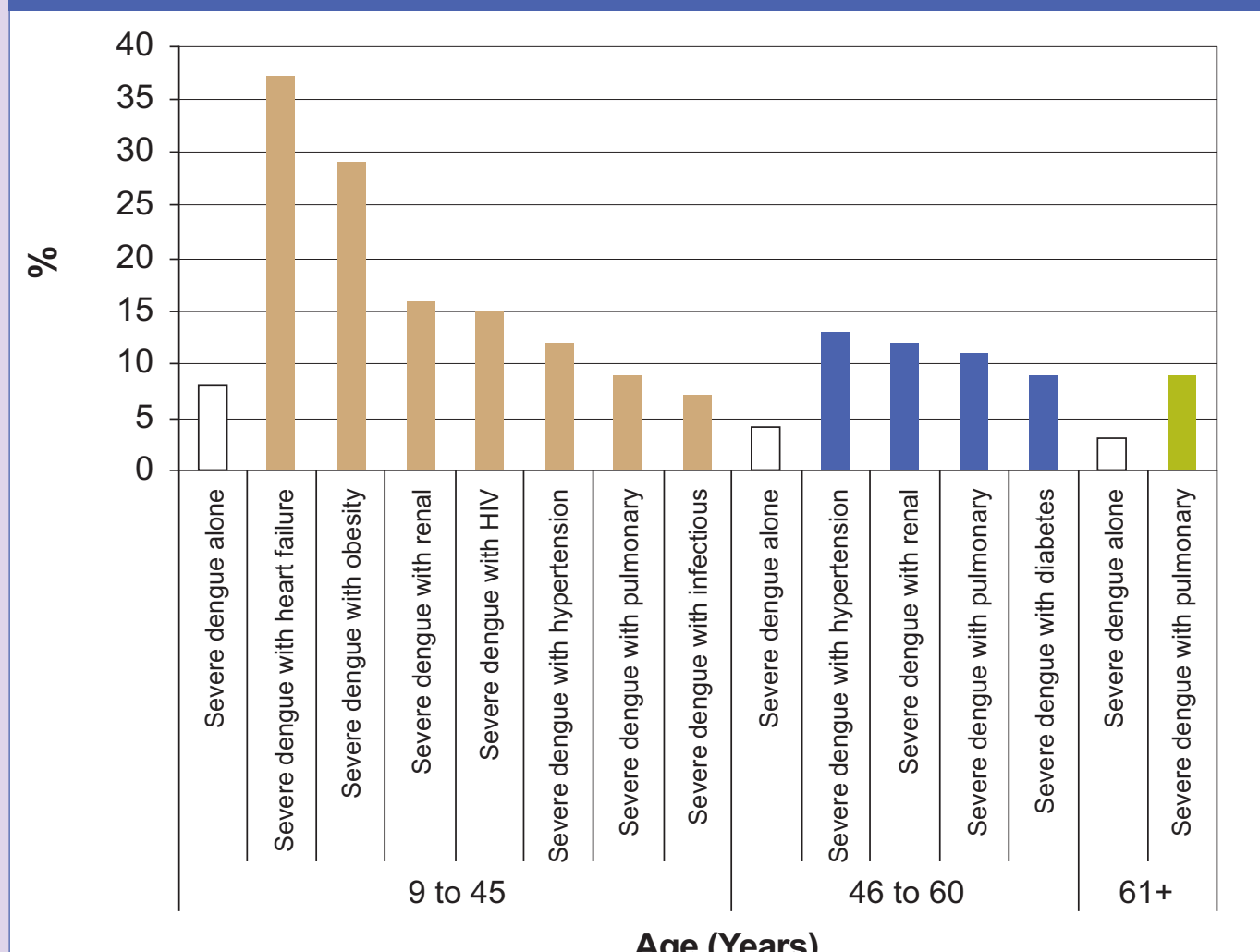
- Of 26,247 severe dengue cases with no comorbidities, 15,527 (59%) were 9-45 years old

Mortality Rates

High in-hospital Case Fatality Rate with severe dengue, comorbidities and increasing age



Severe hospitalized Dengue is significantly higher in the presence of common comorbidities at any age



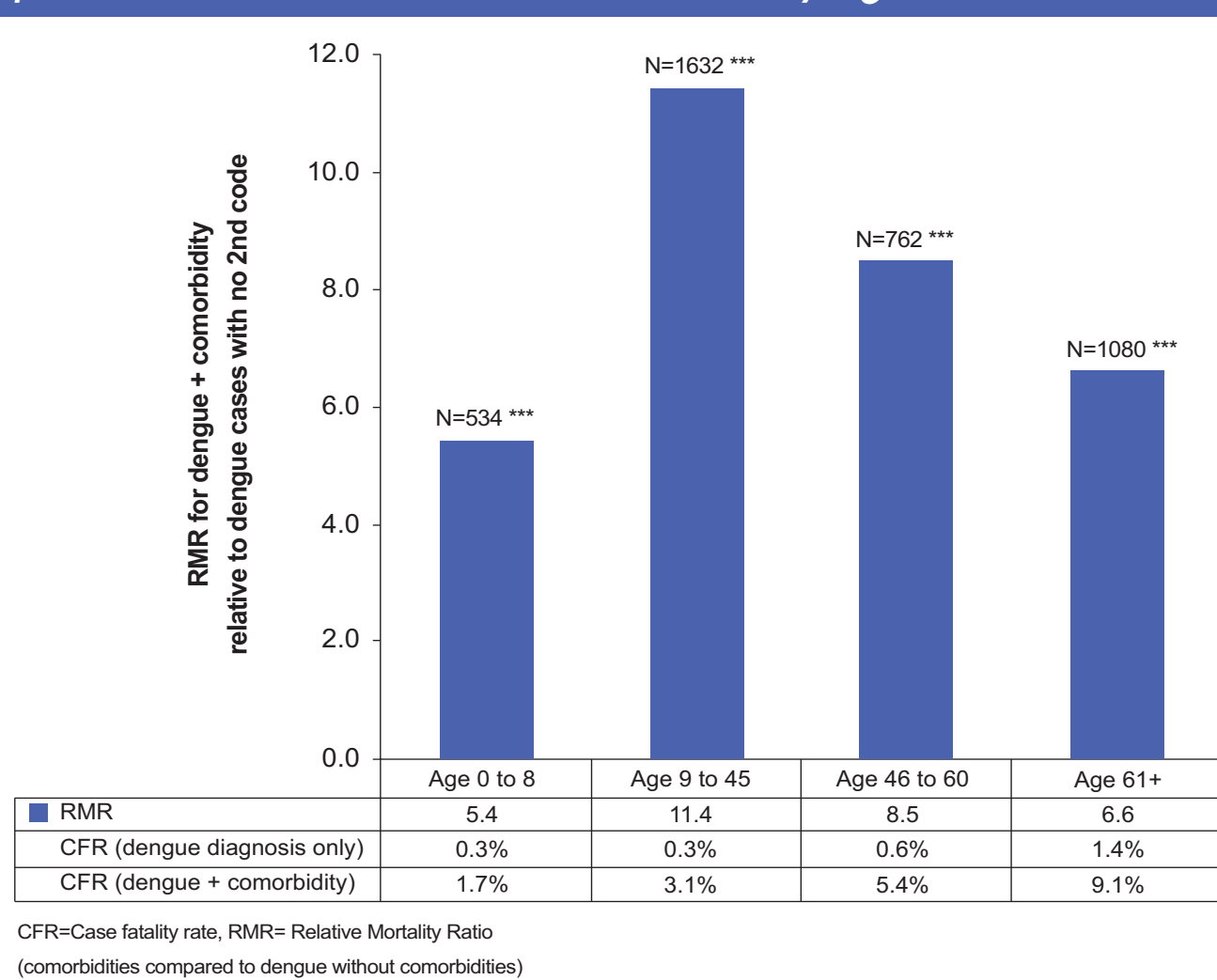
Modeling

- Risk of death from severe dengue was similar to IHD and pulmonary disease
- Duration of hospital stay, ICU admission and death were strongly correlated

Age, dengue severity, comorbidities are independent and cumulative risk factors for longer hospital duration, ICU admission and death

| RISK SCORES ⁵ | Duration | ICU | Death |
|-------------------------------|----------|------|-------|
| COMORBIDITIES | | | |
| Pulmonary disease | 41 | 36 | 43 |
| Ischaemic heart disease (IHD) | 28 | 49 | 36 |
| Renal disease/failure | 18 | 47 | 33 |
| Diabetes | -1 | 20 | 6 |
| Hypertension | 2 | 15 | 8 |
| Dyslipidaemia | -188 | -111 | -94 |
| DENGUE SEVERITY | | | |
| dengue | 0 | 0 | 0 |
| Severe dengue (DHF) | 47 | 52 | 41 |
| AGE | | | |
| 0 to 8 | -6 | 8 | -2 |
| 9 to 45 | 0 | 0 | 0 |
| 46 to 60 | 20 | 4 | 14 |
| 61+ | 36 | 9 | 27 |

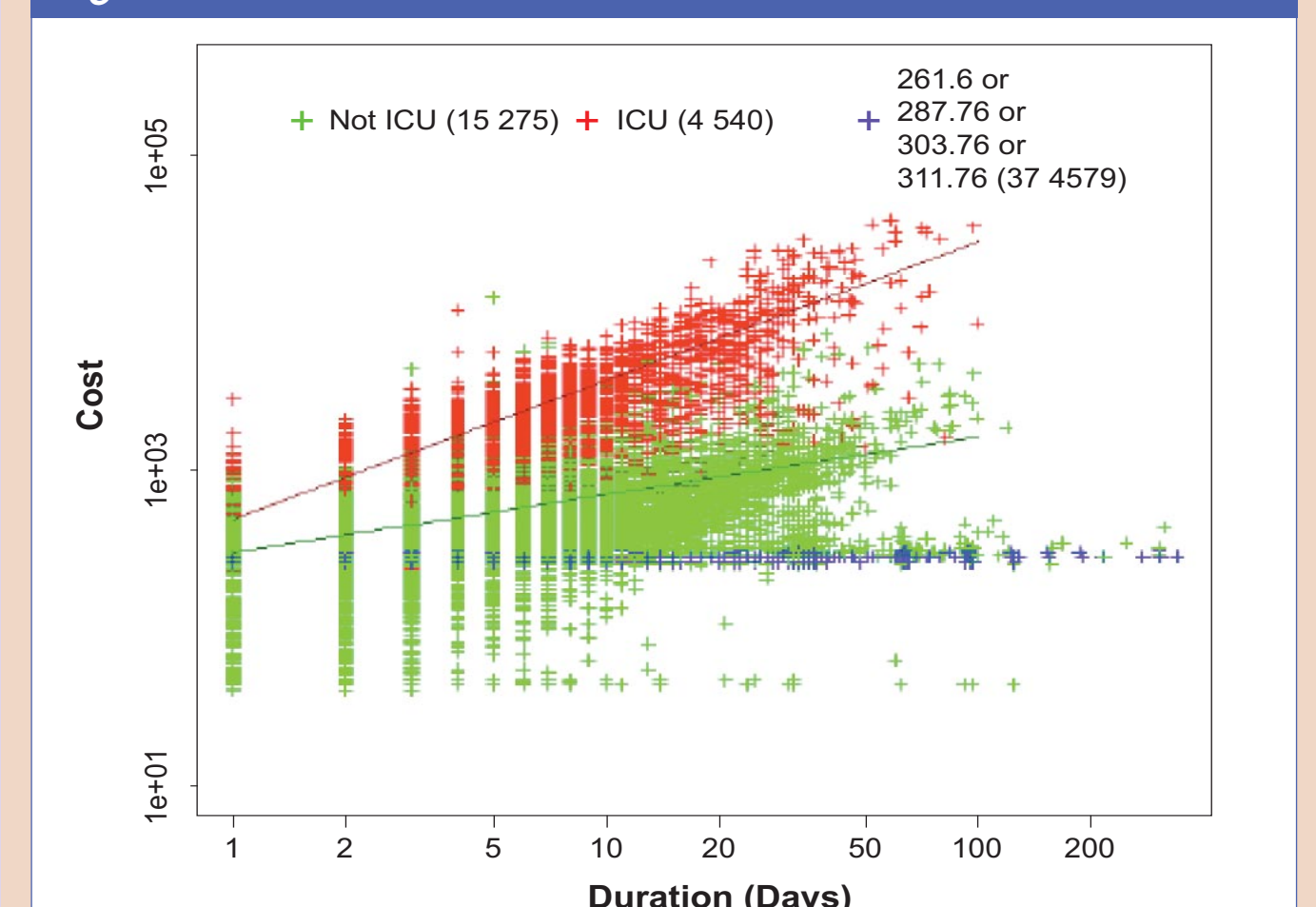
The risk of death from hospitalized Dengue is higher in the presence of common comorbidities at any age



Comorbidities increase hospitalized Dengue mortality at any age

| Age (yo) | Comorbidity | CFR (%) | RMR | 95% CI | P value |
|----------|-------------------------|---------|-----|--------|---------|
| 0-8 | Renal disease/failure | 8 | 27 | 4-175 | <0.05 |
| | Infectious disease | 3 | 8 | 4-18 | <0.001 |
| | Renal disease/failure | 7 | 27 | 13-59 | <0.001 |
| 9-45 | Infectious disease | 4 | 14 | 10-21 | <0.001 |
| | Pulmonary disease | 4 | 13 | 8-23 | <0.001 |
| | Diabetes | 3 | 12 | 3-48 | <0.05 |
| | Ischaemic heart disease | 17 | 26 | 4-158 | |
| 46-60 | Pulmonary disease | 13 | 21 | 12-35 | <0.001 |
| | Infectious disease | 10 | 16 | 10-25 | <0.001 |
| | Renal disease/failure | 9 | 15 | 6-38 | <0.001 |
| | Diabetes | 3 | 5 | 2-14 | <0.05 |
| 61+ | Pulmonary disease | 22 | 16 | 12-21 | <0.001 |
| | Infectious disease | 13 | 10 | 7-14 | <0.001 |
| | Renal disease/failure | 11 | 8 | 4-17 | <0.001 |
| | Ischaemic heart disease | 9 | 7 | 2-25 | <0.05 |
| | Hypertension | 3 | 2 | 1-4 | <0.05 |

Cost is linearly correlated with increasing hospital duration and higher with ICU admission



- Elderly patients with comorbidities stayed in hospital longer (5.5 vs 3.5 days), had higher ICU rates (6% vs 0.9%) and hospital costs (706 vs 336 BRL) compared to patients with dengue alone.

CONCLUSIONS

- In a large retrospective in-hospital database of 1/2 million dengue cases in Brazil, severe hospitalized dengue occurred at any age; however, the majority of cases were in pre-adolescents and adults.
- At any age, the risk of dying from hospitalized dengue was even higher with common comorbidities such as pulmonary disease, renal disease, diabetes, ischaemic heart disease, obesity and HIV.
- Comorbidities, older age, severe dengue were independent and cumulative risk factors for longer hospital duration, increased intensive care admission and in-hospital death.
- Ensuring access to dengue preventative measures in individuals 9 years and above including those with comorbidities could help these countries achieve the WHO objective of 50% reduction in mortality and 25% reduction in morbidity due to dengue by 2020

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Disclosures

- This study was sponsored by Sanofi Pasteur including service provision of database consolidation, data mining and analysis by Ariana Pharmaceuticals