Generalised Linear Modelling of Childhood Caries

ongoing work presented as part of study for PhD by

John Stephenson

PhD student
School of Dentistry
University of Cardiff
Cardiff, GB-CF14 4XY

April 2008

Objectives

- To identify risk factors and clustering effects associated with the occurrence of childhood caries in primary teeth

- To assess the future risk to caries in primary teeth from a model of primary tooth lifetimes

Cohort study design

- Primary data source is cohort study of ~2650 children undertaken by Cardiff University School of Dentistry in 1999
- Children examined on 3 occasions:
  - School Year 1 – 2 (age 5 – 7)
  - School Year 3 (age 7 – 8)
  - School Year 5 (age 9 – 10)
- Arbitrarily interval censored data
- About 9% lost to follow-up
- Both primary and permanent teeth observed
- All surfaces of all teeth examined
  - Over 400.000 recorded observations in total

CARDIFF UNIVERSITY
PRIFYSGOL CAERDYDD
coleg meddygaeth cymru
wales college of medicine

Study areas

West Midlands (fluoridated @ 1ppm)
- Industrial region: population ~2.500.000
- Dudley area (300.000)
- Walsall area (300.000)

South Wales (non-fluoridated)
- Industrial region: population ~1.500.000
- Mid Glamorgan area (500.000)
- South Glamorgan area (400.000)

~700 children sampled from each area

Cohort study: key recorded attributes

- Gender
- Date of birth
- Standardised measure of area deprivation
  - Estimated from recorded postcode
- Fluoridation status
  - Binary variable: correlated with geographical area
- Dentition type
- Tooth location/type (implicitly from tooth location)
  - Incisor, Canine, Pre-molar (permanent teeth only), Molar
- Surface type
  - Distal, Occlusal (Molars and pre-molars only), Mesial, Buccal, Lingual

Cohort study: response measures

- Responses recorded at surface level at each examination
- Outcomes dichotomised for modelling
- *Tooth*- and *child*- level responses created from recorded *surface*-level responses
- At least one positive *surface*-level outcome per tooth ➔ assumed positive response at *tooth* level
- At least one positive *tooth*-level outcome per child ➔ assumed positive response at *child* level

Analysis

- Exploratory analysis
  - Investigates data trends
- Phase 1: multilevel logistic regression analysis
  - Logistic generalised linear model
  - Identification of risk factors and hierarchical data structures
- Phase 2: multilevel survival analysis
  - Complementary log-log generalised linear model
  - Models survival curves of teeth

Exploratory analysis: extent of primary dentition

Primary tooth type	Proportion of teeth in primary state (non-appearance of corresponding permanent tooth)		
	1st examination	2nd examination	3rd examination
Incisors	68.3%	16.5%	1.5%
Canines	~100%	97.9%	75.0%
Molars	~100%	99.5%	70.0%

Exploratory analysis: caries in primary dentition - some baseline results

- Significantly higher rates of occurrence in South Wales
  - West Midlands (1 ppm fluoridation): 29.3% ± 2.5%
  - South Wales (non fluoridated): 51.5% ± 2.6%
- Small bias towards occurrence in males
  - Males 42.9% ± 2.7%; Females 38.8% ± 2.7%
- Significantly higher rates of occurrence in molar teeth
  - Incisors 2.6%; Canines 1.4%; Molars 16.3%
- Significantly higher rates of occurrence on occlusal surfaces
  - Distal/Mesial 4.5% Occlusal 12.9%
  - Buccal/Lingual 3.3%

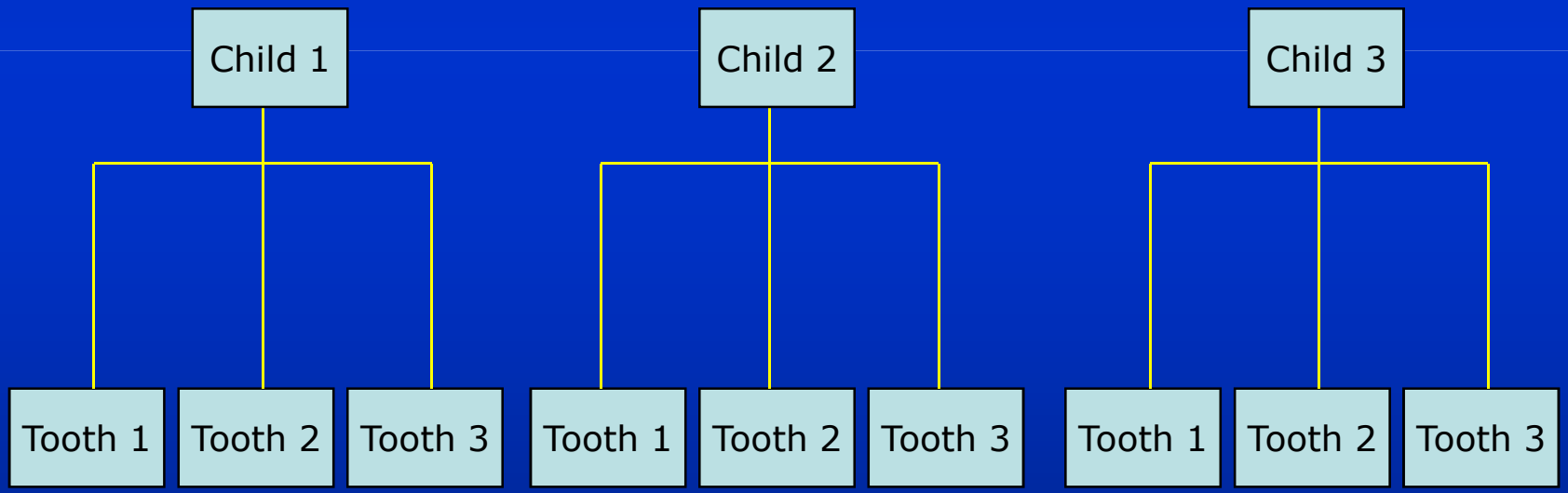
Hierarchical Data Structure

- Existence of hierarchical structure ➔ clustering of data
  - lack of independence of units (e.g. teeth within children)
- Many possible hierarchical structures, for example:
  - *surfaces* nested within *teeth* nested within *child* nested within *school*
- Other interpretations of hierarchy are possible
  - *Quadrant*, *tooth type*, *surface type*, *area* etc.
  - May be more appropriately modelled as fixed effects
- Disregarding hierarchical structure may lead to:
  - spurious indications of parameter significance
  - Loss of information concerning variability at higher model levels

Possible 2 level structure

Tooth level 1; *child* level 2

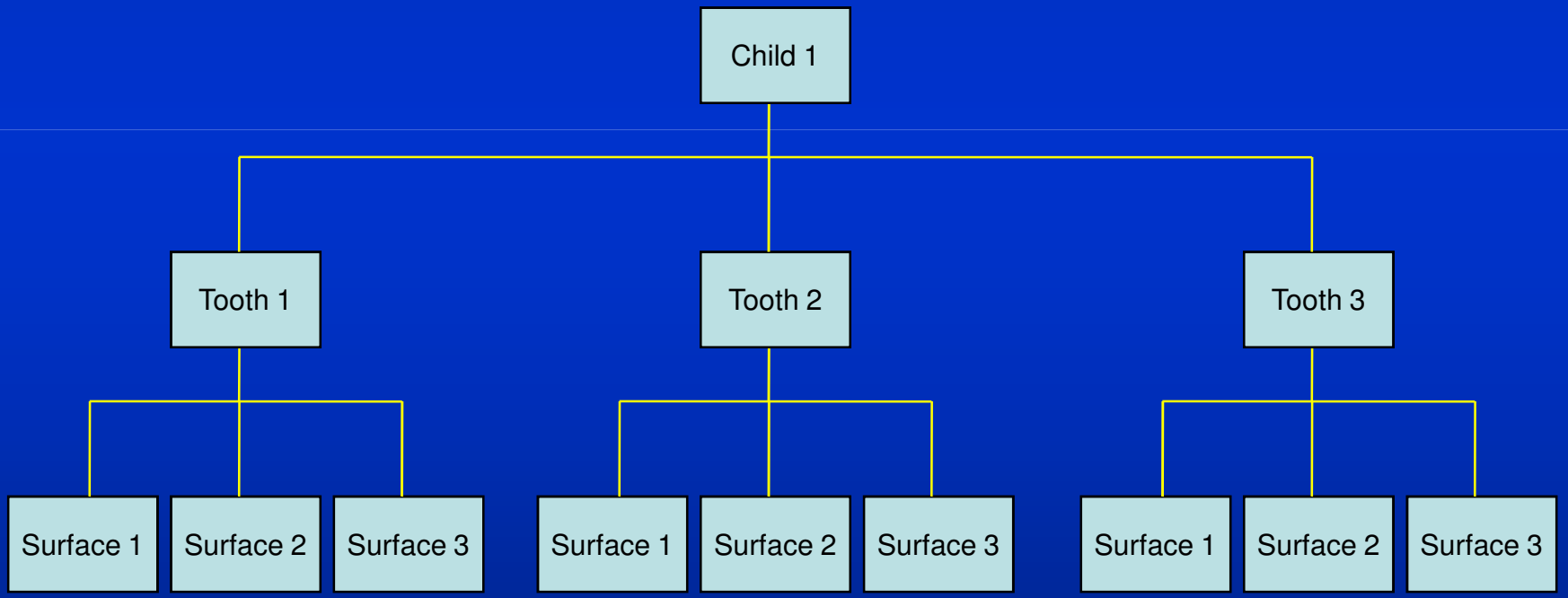
Responses at *tooth* level



Possible 3-level structure

Surface level 1; *tooth* level 2; *child* level 3

Responses at *surface* level



Phase 1 Analysis

- A series of multilevel logistic regression analyses using s*urface*, *tooth* and *child* level measures

- Analysis aims to determine:
  - appropriate model hierarchies
  - factors significantly associated with occurrence of caries
  - appropriate multilevel model type

- Current presentation considers response of occurrence of caries in primary dentition at 1st examination

Phase 1 analysis: key modelling approximations

- Assume no variation in ages of experimental units observed at any given examination
- Assume measured dentition has reached “steady state”
- Does not utilise most updated data

Phase 1 Analysis: assessment of possible model hierarchies

- Contribution of each level to model variance may be assessed by Variance Partition Coefficient (VPC)
  - VPCs calculated for variance components models
  - Simulation method developed for binary data
- Low VPC for a particular level suggests model structure should be reformulated excluding this level

Phase 1 Analysis: Partitioning of model variance – *child* level variance components models

Response	Model	Proportion of model variance	
		Level 1 (child)	Level 2 (school)
Caries at 1st exam	C1	**100.0%**	**-**
	C2	**92.5%**	**7.5%**

Phase 1 Analysis: Partitioning of model variance - *tooth* level variance components models

Response	Model	Proportion of model variance		
		Level 1 (tooth)	Level 2 (child)	Level 3 (school)
Caries at 1st exam	T1	**100.0%**	**-**	**-**
	T2	**75.3%**	**24.7%**	**-**
	T3	**78.4%**	**15.3%**	**6.3%**

Phase 1 Analysis: Partitioning of model variance - *surface* level variance components models

Response	Model	Proportion of model variance			
		Level 1 (surface)	Level 2 (tooth)	Level 3 (child)	Level 4 (school)
Caries at 1st exam	S1	**100.0%**	-	-	-
	S2	**41.4%**	**58.6%**	-	-
	S3	**42.7%**	**41.3%**	**15.9%**	-
	S4	**47.3%**	**33.2%**	**15.3%**	**4.1%**

Phase 1 analysis: covariate assessment

- Significance of risk factors assessed in logistic regression analysis by calculation of odds ratios and *p*-values
- Covariates initially tested using univariate analyses with increasing levels
  - tested for evidence of collinearity
- Significant covariates carried forward to multivariate analyses

Multivariate logistic regression – *tooth* level models

3-level hierarchy: tooth-child-school

Covariate	*p*-value	Odds ratio	Inference
Gender	**0.000**	**0.76** (0.65, 0.88)	Significant
Age at 1st examination	**0.001**	**1.30** (1.06, 1.60)	Significant
SEC	**0.000**	**1.10** (1.08, 1.13)	Significant
F - status	**0.000**	**0.25** (0.21, 0.30)	Significant
Molar tooth	**0.000**	**12.4** (11.3,13.6)	Significant

Multivariate logistic regression – *surface* level models

4-level hierarchy: surface-tooth-child-school

Covariate	*p*-value	Odds ratio	Inference
Gender	**0.000**	**0.63** (0.52, 0.77)	Significant
Age at 1st exam	**0.065**	**1.30** (0.98, 1.71)	Not significant
SEC	**0.000**	**1.13** (1.09, 1.17)	Significant
F - status	**0.000**	**0.23** (0.18, 0.29)	Significant
Molar tooth	**0.000**	**9.08** (8.33, 9.90)	Significant
Occlusal surface	**0.000**	**2.00** (1.91, 2.10)	Significant

Phase 1 analysis: conclusions

- Most appropriate model hierarchies:
  - *Surface – tooth – child*
  - *Surface – tooth – child – school*
  - *Tooth – child - school*
- *Tooth* level largest contributor to model variance in most cases
- Significant risk factors associated with caries in primary dentition at baseline
  - all covariates generally significant
- Model type:
  - Random intercepts model adequate in most cases
- Inferences to be carried forward to Phase 2

Phase 2 analysis

- Survival analysis of primary dentition
- Makes use of inferences from Phase 1 analysis regarding model hierarchies and parameter significance
  - Requires assumption of survival function and proportional hazards model
- Modelling approximations
  - Caries and exfoliation failure modes assumed to be independent
  - Remineralisations disregarded
  - Interval censored data equivalent to left censored

Phase 2 analysis: method

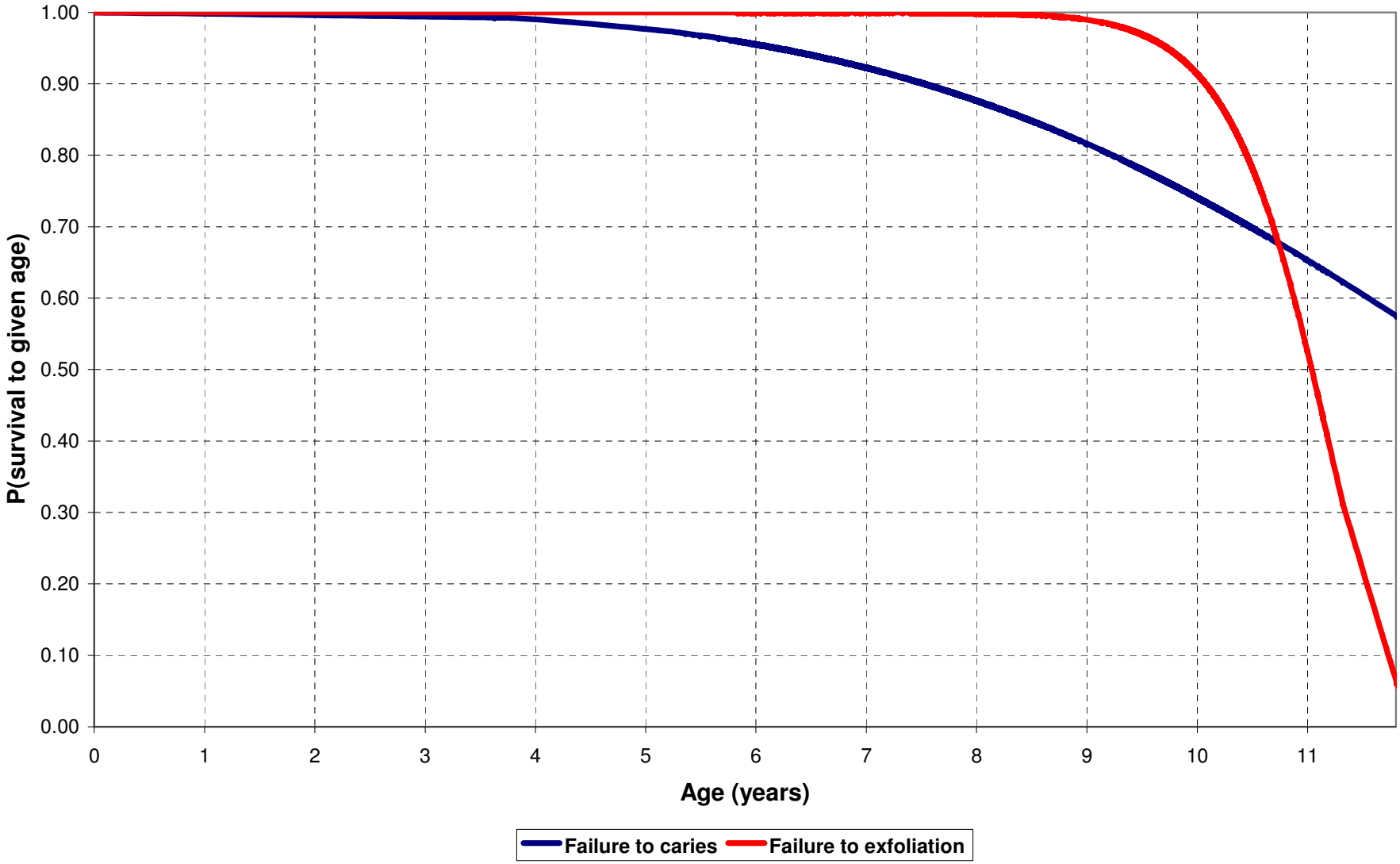
- Survival data transformed using complementary log-log GLM
  - Leads to 2-parameter Weibull survival curve

$$S(t)=\exp(-\lambda t^{\gamma})$$

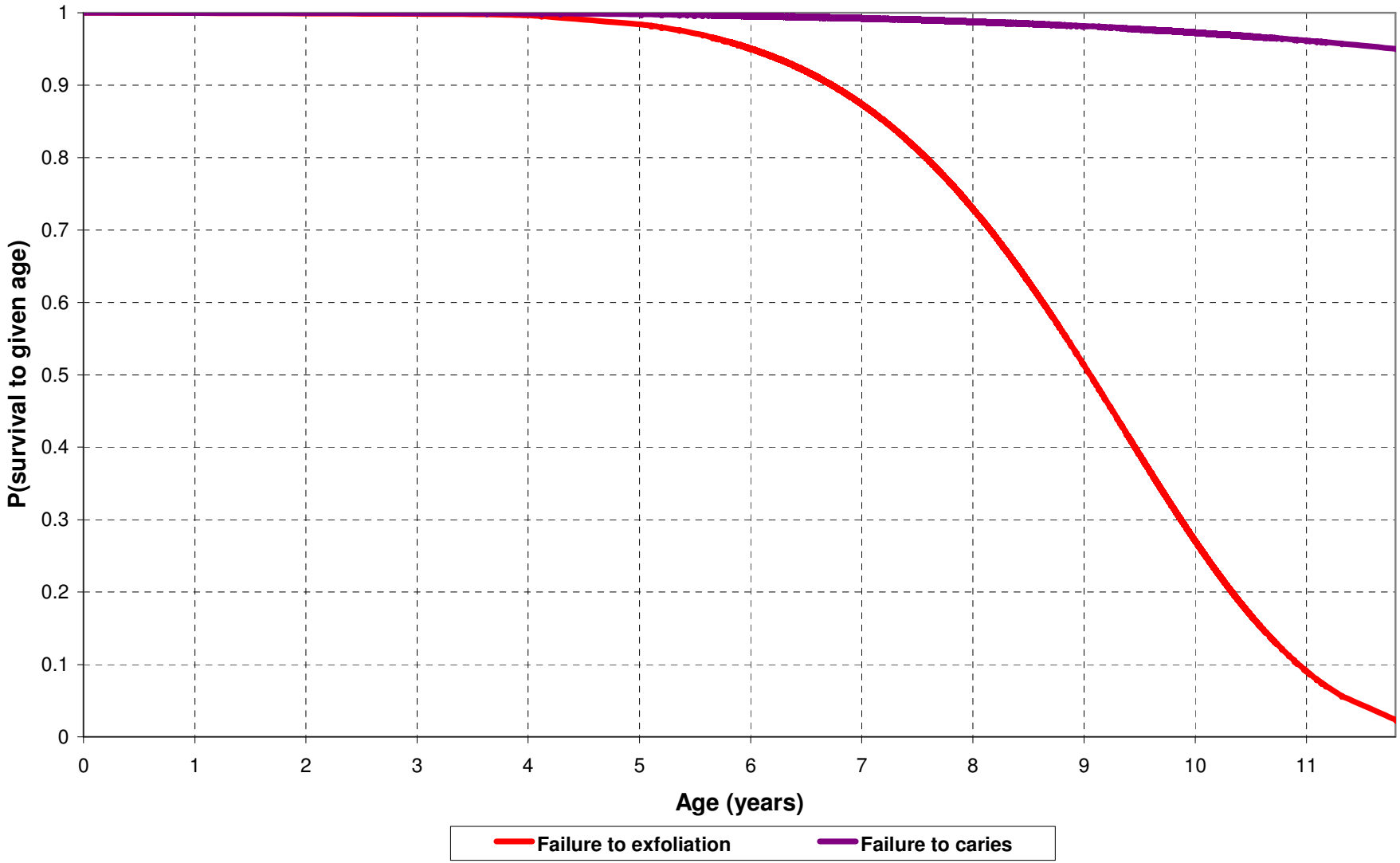
- Baseline function extended to incorporate covariates

$$S(t)=\exp(-\lambda t^{\gamma})^{\exp(B_1 x_1+B_2 x_2+\ldots)}$$

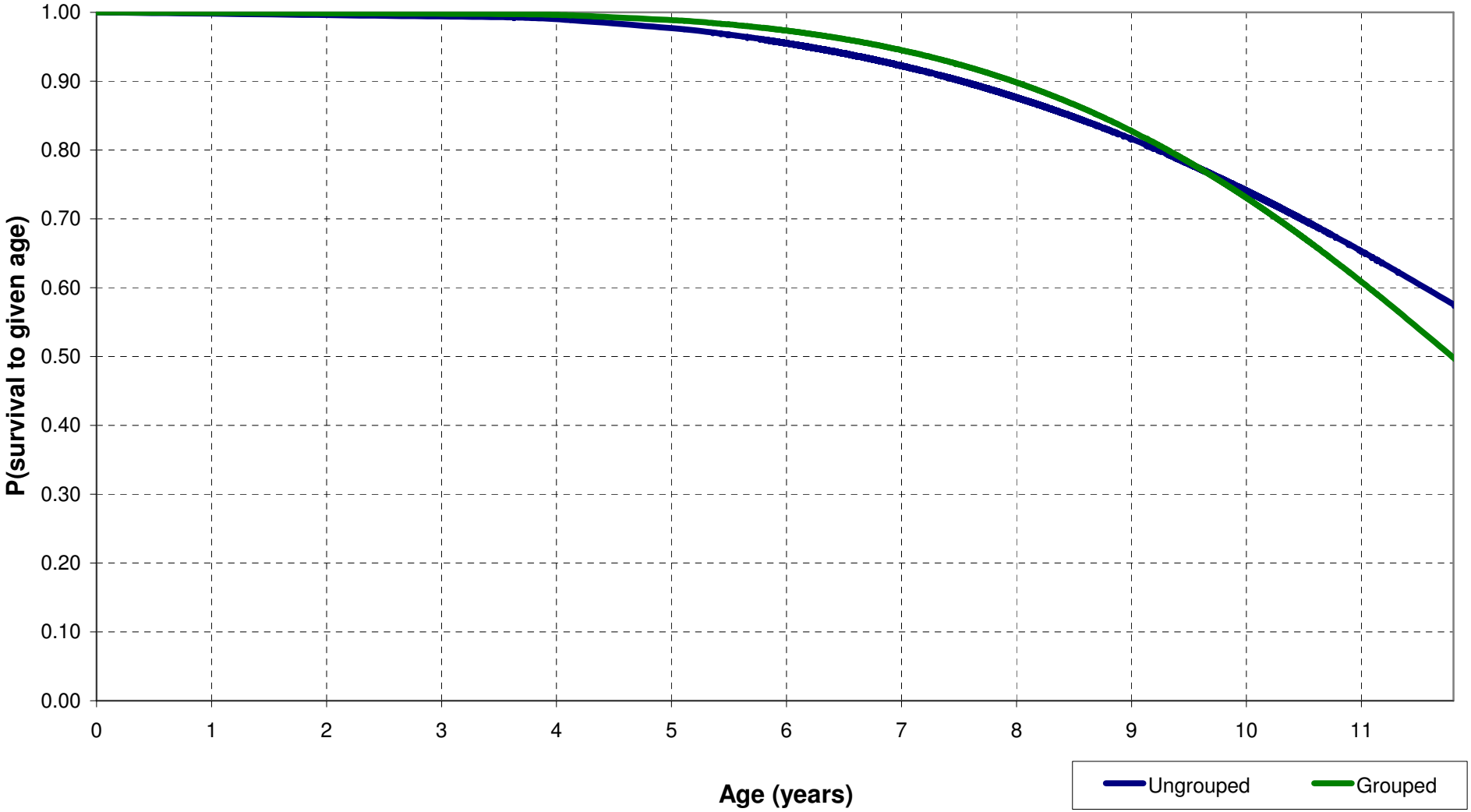
Phase 2 analysis: resistance to caries and exfoliation - molar teeth



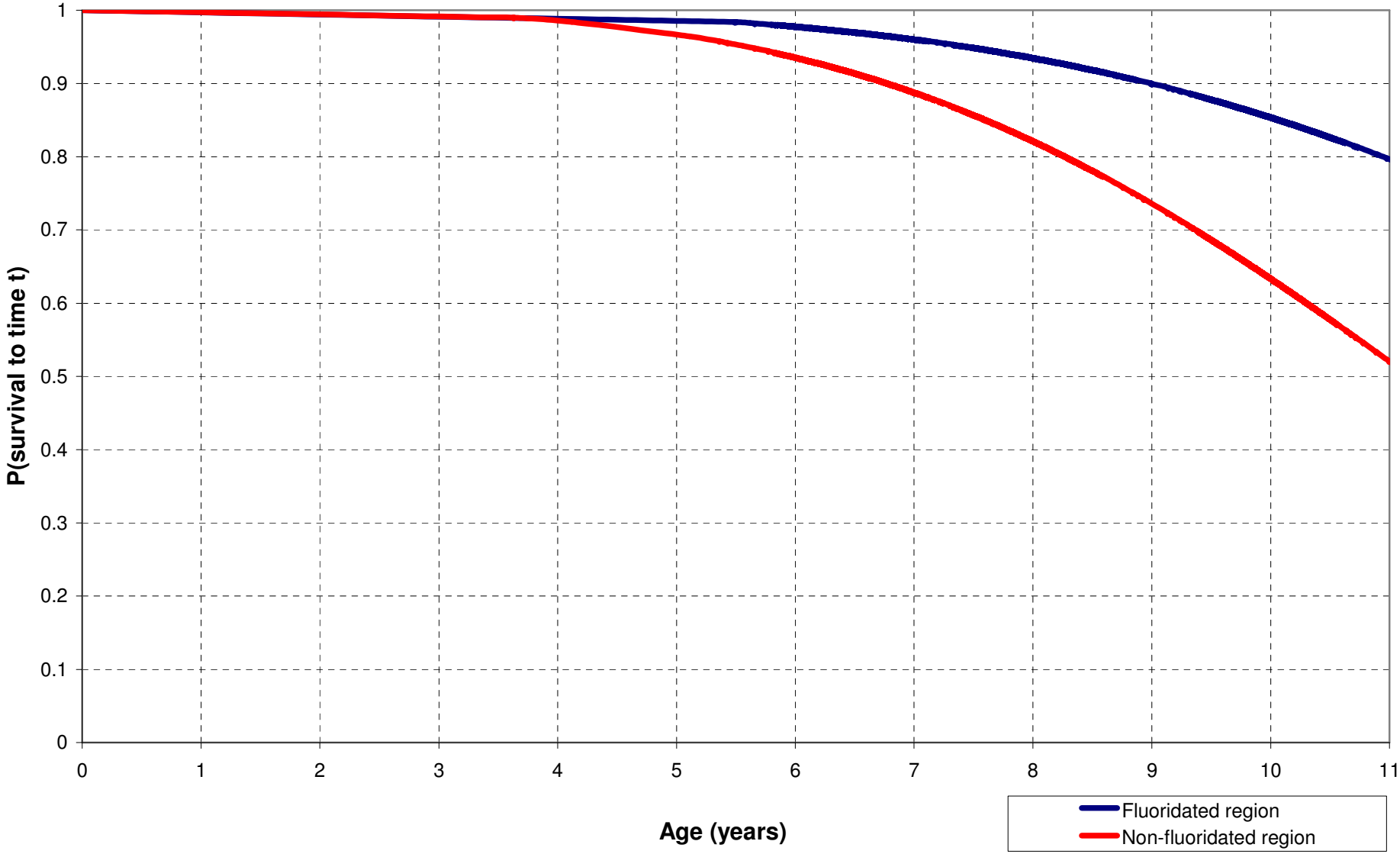
Phase 2 analysis: resistance to caries and exfoliation -non-molar teeth



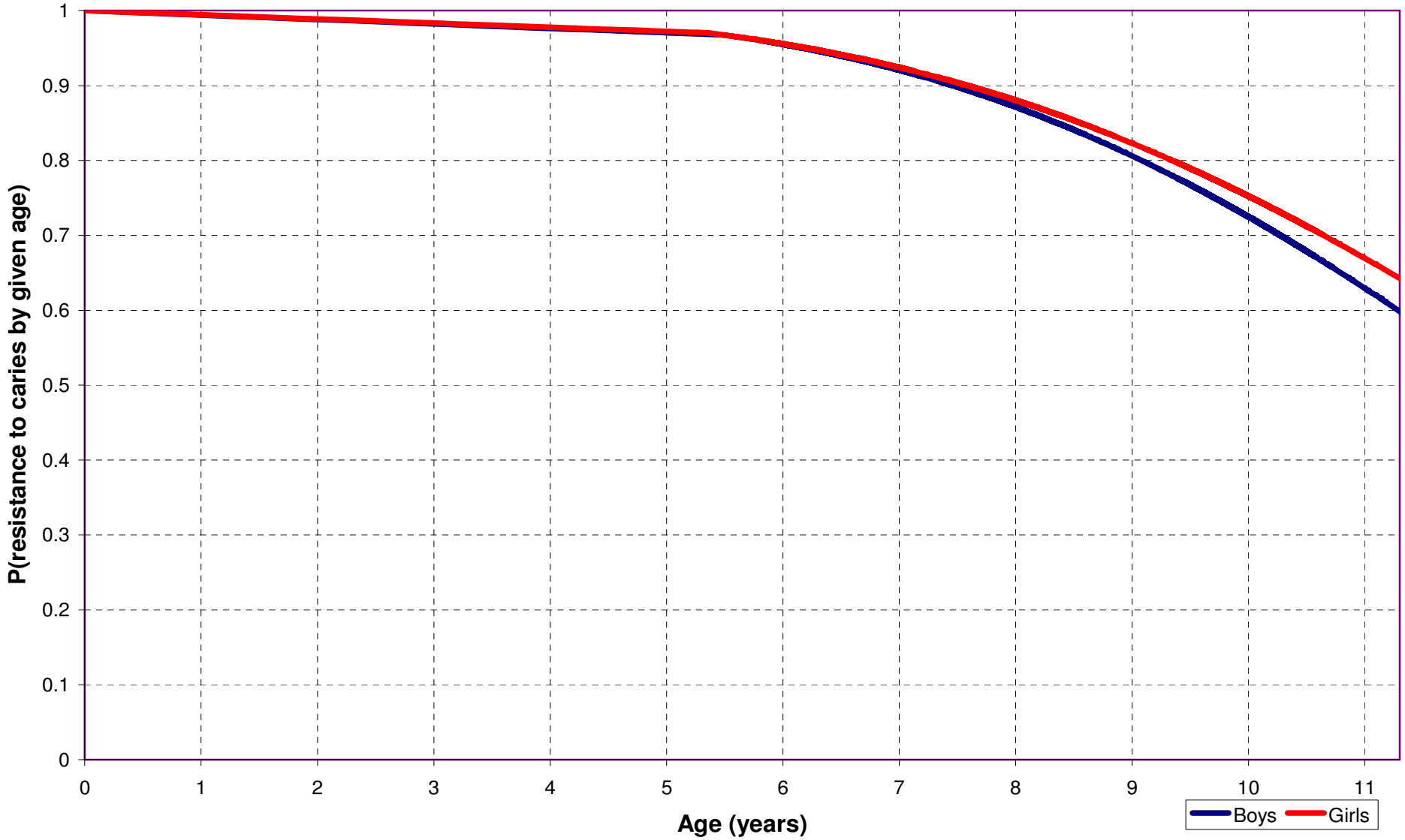
Phase 2 analysis: effect of grouping data on resistance to caries - molar teeth



Phase 2 analysis: comparison of resistance to caries for molar teeth across regions



Phase 2 analysis: comparison of survival against caries for molar teeth between genders



Phase 2 analysis: conclusions

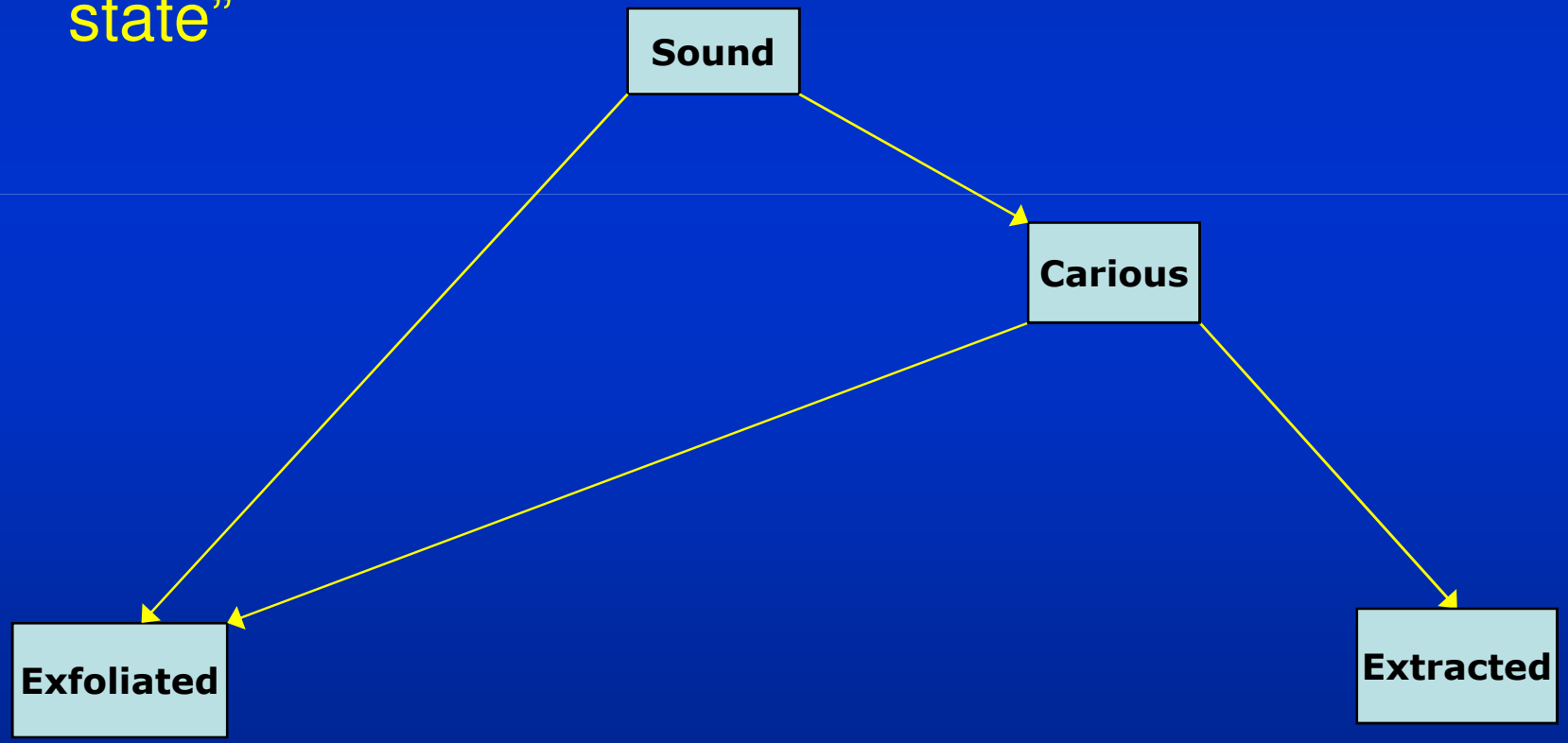
- Caries not life-limiting feature at any stage of lifetime of non-molar teeth
- Caries may limit lifetime of primary molar teeth surviving beyond ~10 years
- Grouping data by age of experimental unit does not significantly affect survival curve for primary molars
- Resistance to caries for primary molars distinct for children in fluoridated and non-fluoridated regions
- Resistance to caries for primary molars not significantly distinct between genders

Future work

- Future Phase 3 analysis: unit lifetime modelling
  - Models ultimate fate of sound, decayed and treated primary teeth
- Will incorporate additional treatment data from British Dental Practice Board (applies in ~51% of individuals)
- Will assume competing risks / multistate model with alternative “routes” to exfoliation possible
  - sound-exfoliation
  - sound-caries-exfoliation etc.
- Will assess effect of treatment on primary tooth survival and on subsequent state of permanent dentition

Future Work: Tooth lifetime model

- Competing risks multistate model
- Allows for extraction of carious teeth as “absorbing state”



Future Work: Tooth lifetime model (2)

- Competing risks multistate model
- Allows repeated transitions between carious and filled states