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Generalised Linear Modelling of Childhood Caries

ongoing work presented as part of study for PhD by

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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

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)		
	1 st examination	2 nd examination	3 rd 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%

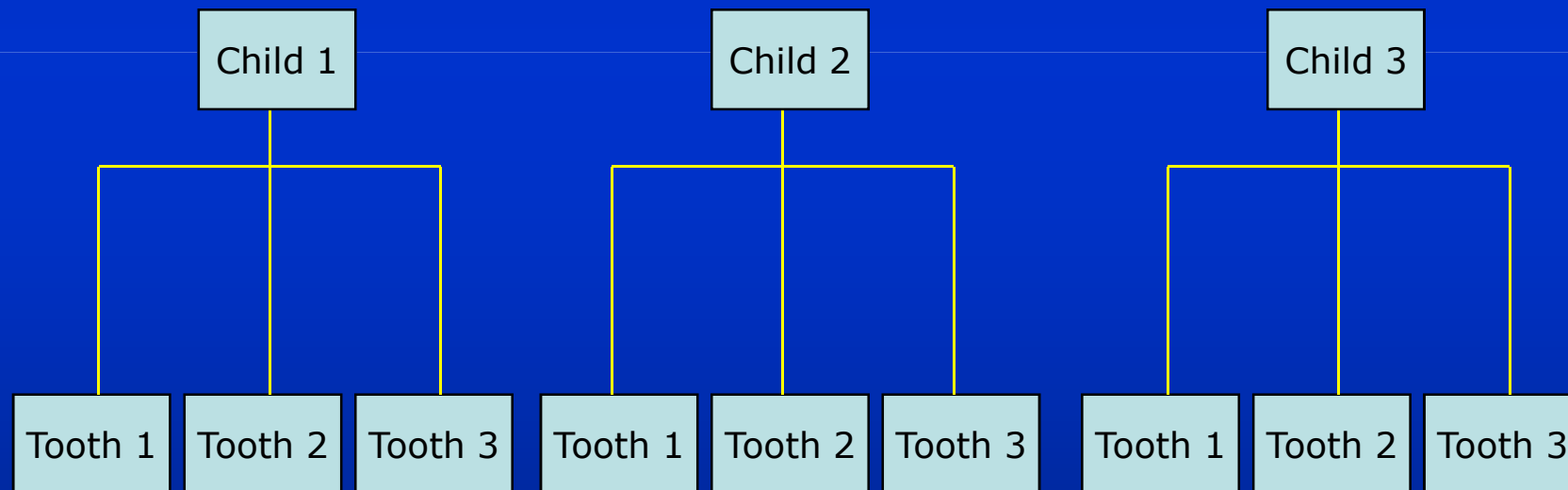
Hierarchical Data Structure

- 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

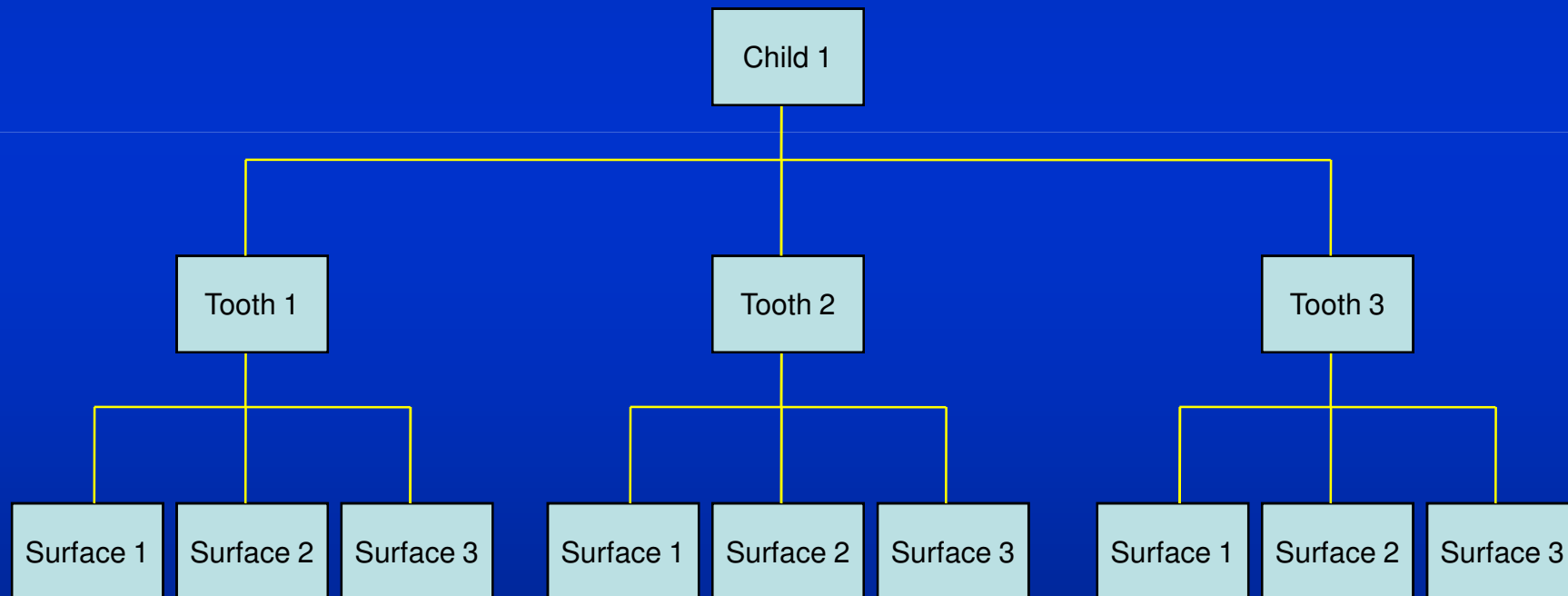
Responses at tooth level



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 *surface*, *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 1 st 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 1 st 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 1 st 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	<i>p</i> -value	Odds ratio	Inference
Gender	0.000	0.76 (0.65, 0.88)	Significant
Age at 1 st examination	0.001	1.30 (1.06, 1.60)	Significant
SEC	0.000	1.10 (1.08, 1.13)	Significant
<i>F</i> - 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	<i>p</i> -value	Odds ratio	Inference
Gender	0.000	0.63 (0.52, 0.77)	Significant
Age at 1 st exam	0.065	1.30 (0.98, 1.71)	Not significant
SEC	0.000	1.13 (1.09, 1.17)	Significant
<i>F</i> - 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

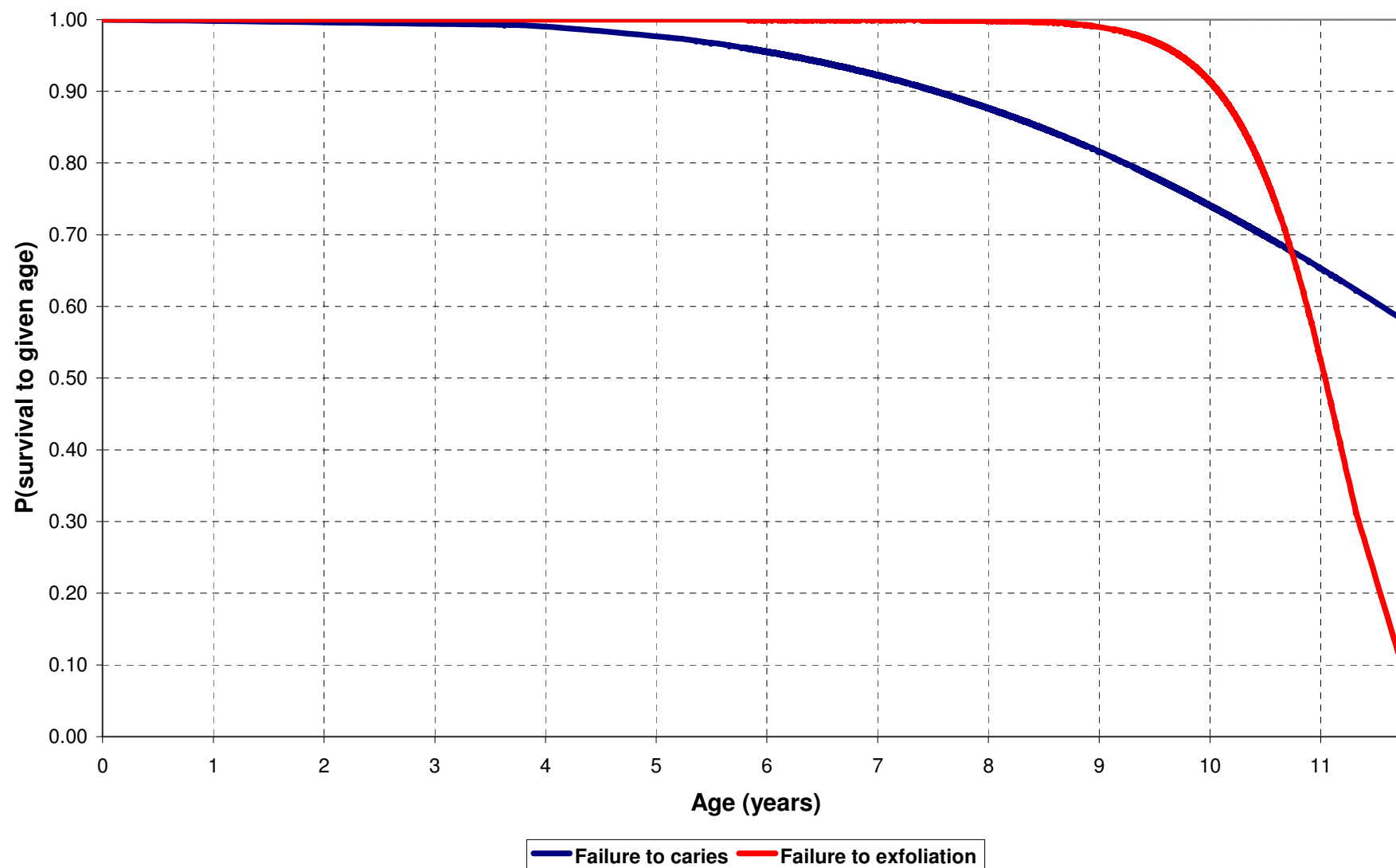
Phase 2 analysis

- 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

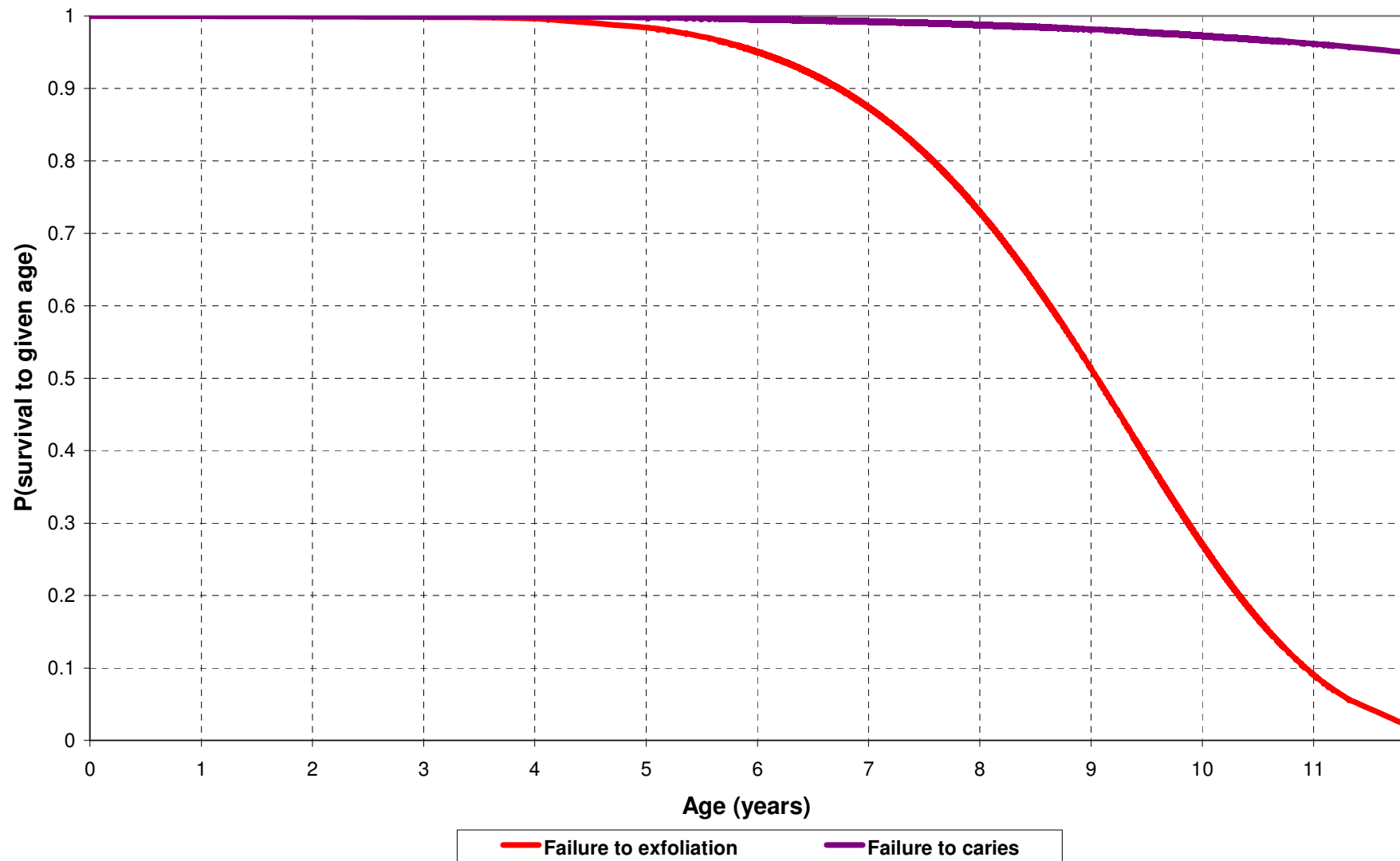
Phase 2 analysis: method

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

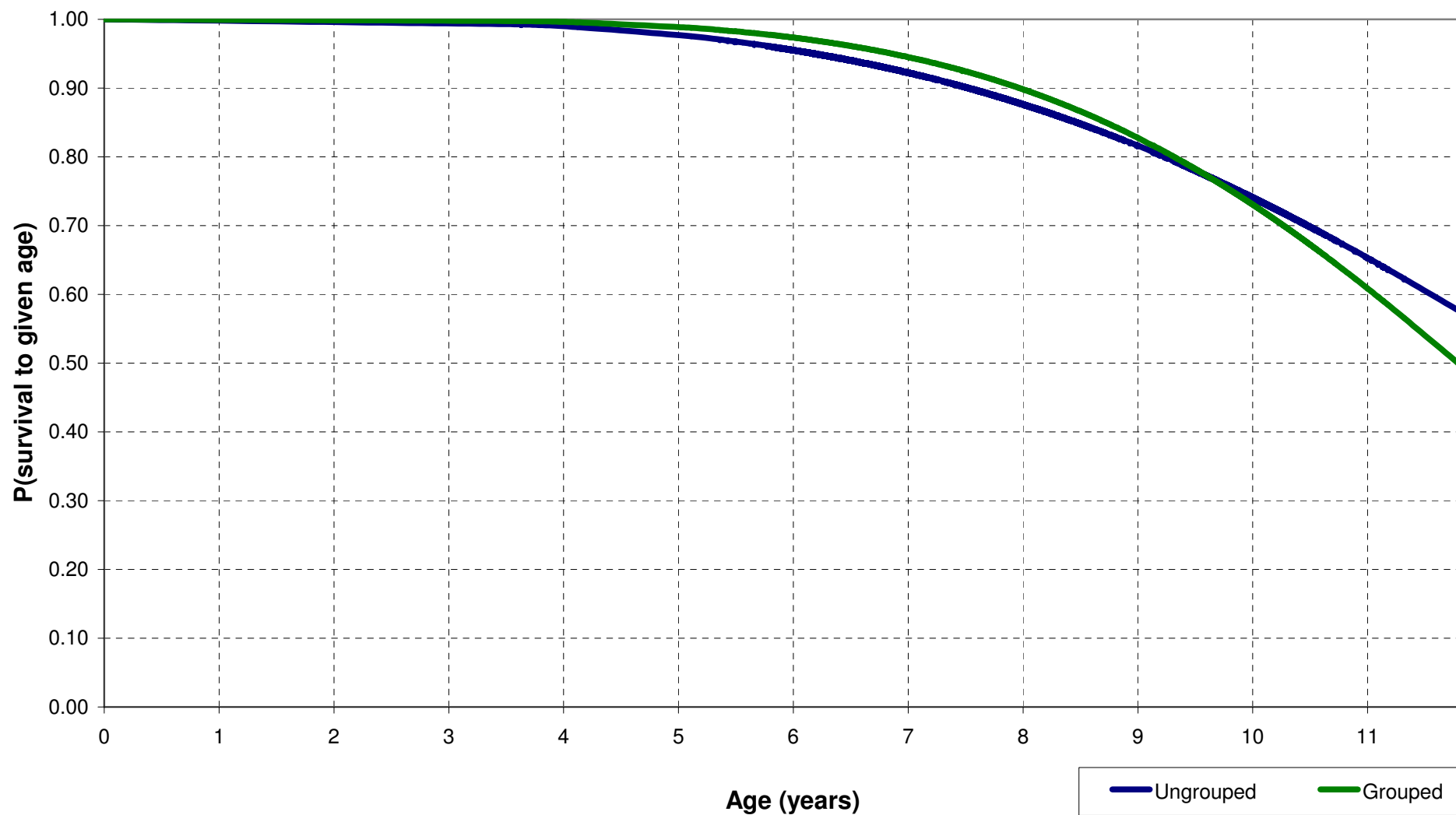
Phase 2 analysis: resistance to caries and exfoliation - molar teeth



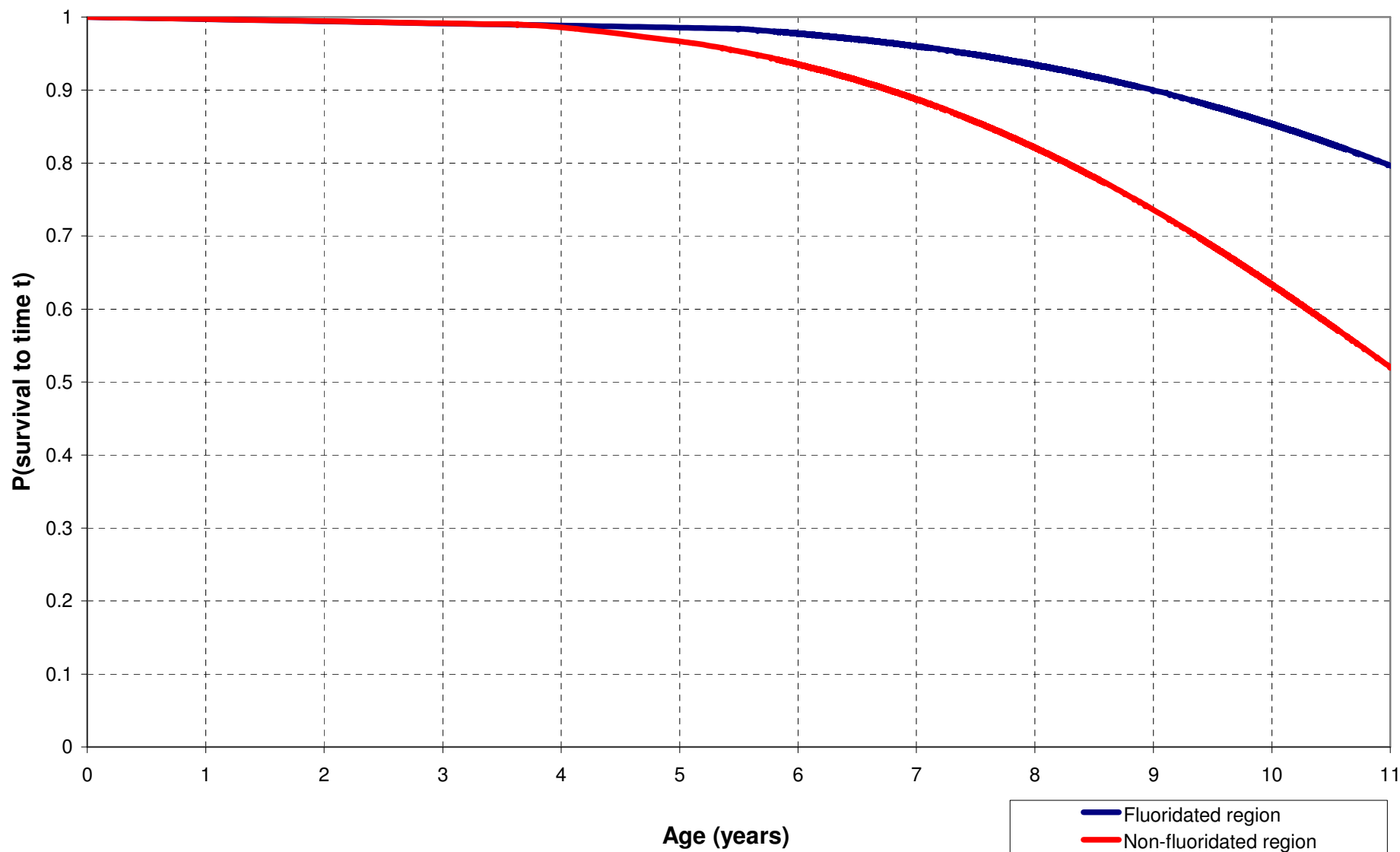
Phase 2 analysis: resistance to caries and exfoliation -non-molar teeth



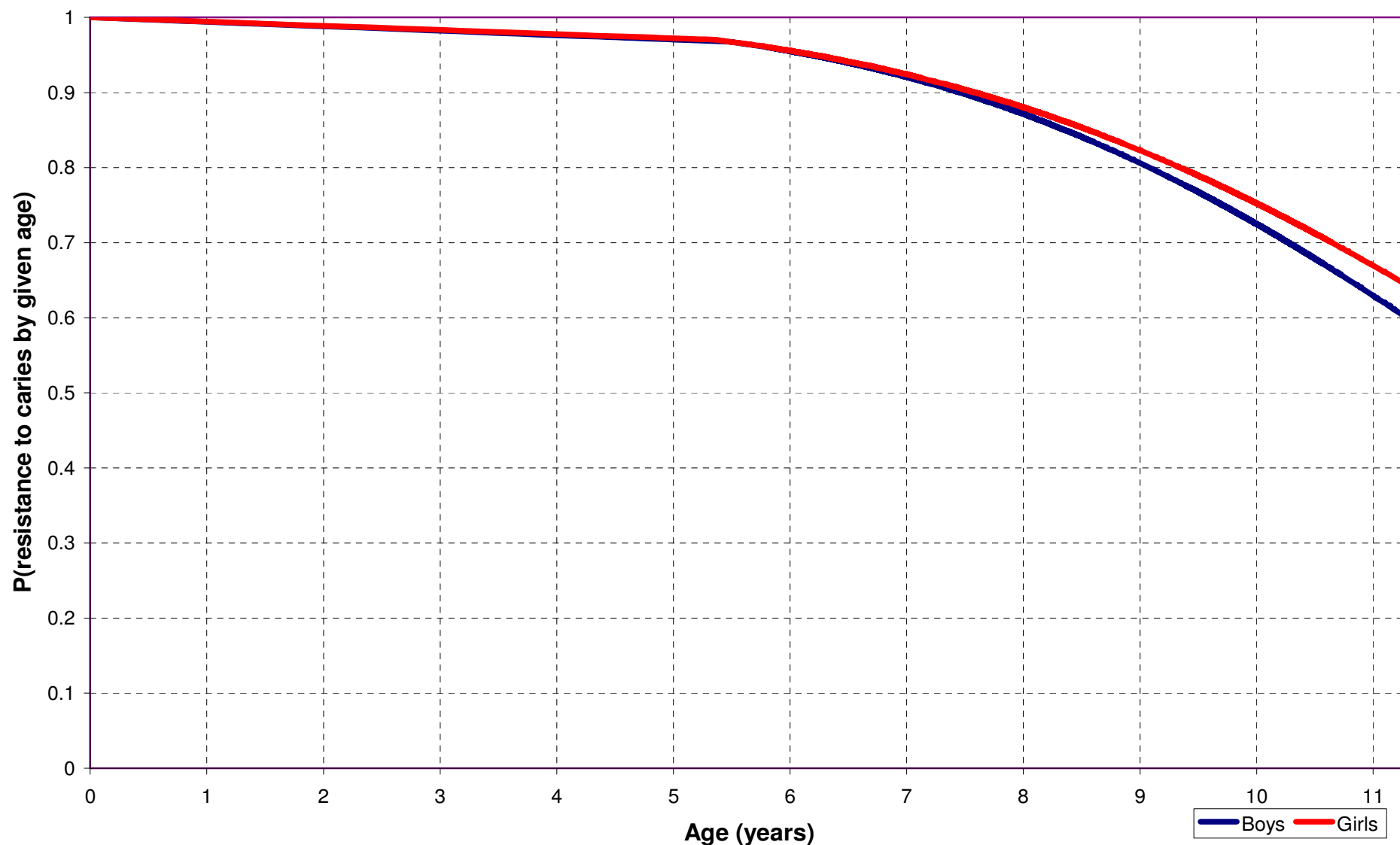
Phase 2 analysis: effect of grouping data on resistance to caries - molar teeth



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

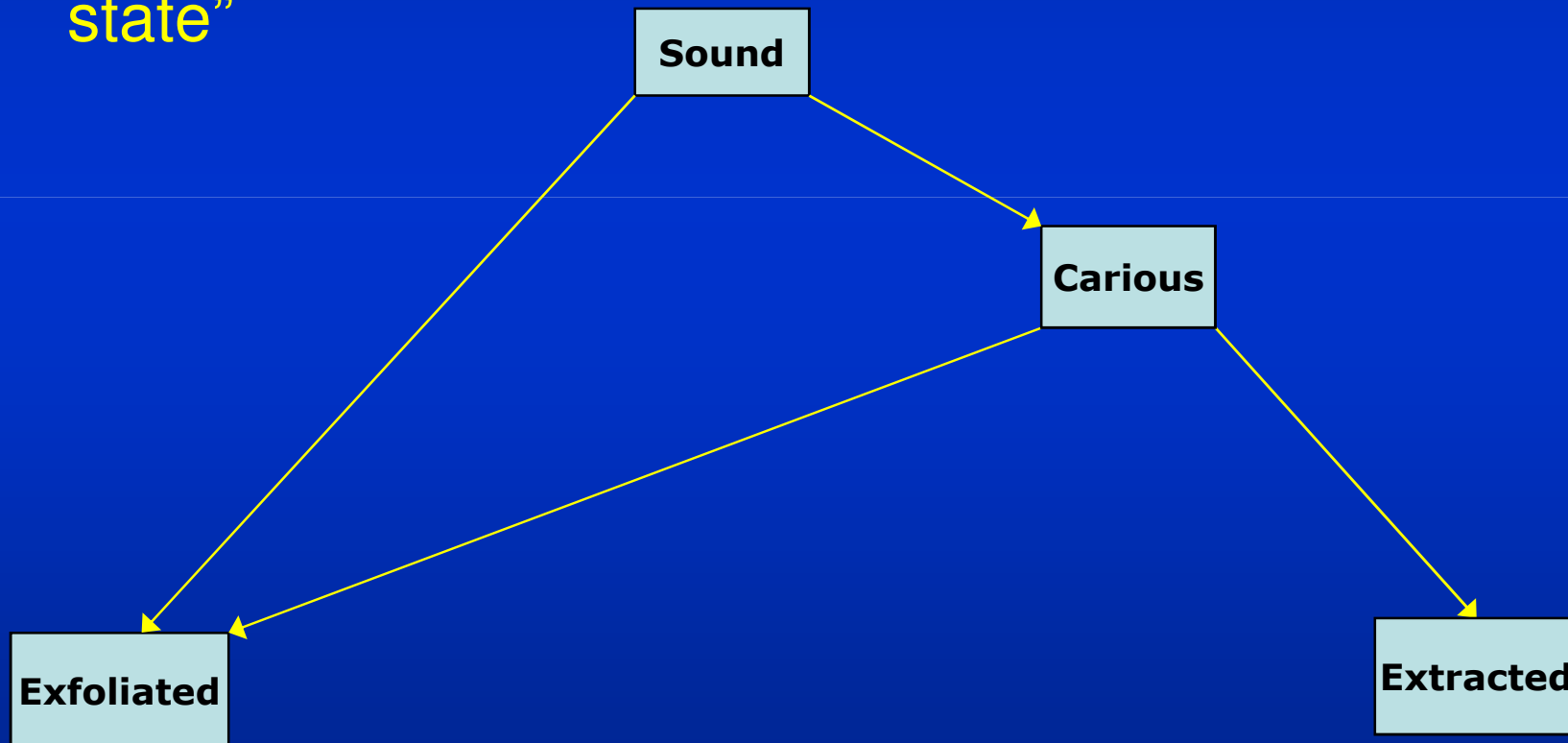
- Caries not life-limiting feature at any stage of lifetime of non-molar teeth
- Caries may limit lifetime of primary molar teeth surviving beyond ~10 years
- Grouping data by age of experimental unit does not significantly affect survival curve for primary molars
- Resistance to caries for primary molars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

