SingHealth DukeNUS ACADEMIC MEDICAL CENTRE
National Dental Research Institute Singapore

GLOBICS
Global Consortium of Oral Health Birth Cohort Studies

Global Oral Health Agenda for Birth Cohort Studies: a DELPHI Study

Edited by GLOBICS team: Karen G Peres, Ashish Kalhan, Gustavo G Nascimento, Shilpa Sarawagi,
a GLOBICS initiative: Global Consortium of Oral Health Birth Cohort Studies

Singapore, June, 2023
Global Oral Health Agenda for Birth Cohort Studies: a DELPHI Study

Participants

Cohort	Country	Cohort	Country
Aarhus Birth Cohort		Northern Plains AI Birth Cohort	
Afzali and Kashani Public Hospital Study		Osaka Maternal and Child Health Study	
Australian Wide Twin Study		Pacific Islands Families Study	
BRISA Ribeirão Preto		Pelotas Birth Cohort Study (1982)	
1970 British Cohort Study		Pelotas Birth Cohort Study (1993)	
Chiang Mai		Pelotas Birth Cohort Study (2004)	
Christchurch Health and Development Study		Project Koshu	
County of Stockholm		Promise-EBF Trial	
Porto Alegre Early Life Nutrition and Health Study		RPS Ribeirão Preto	
Generation R Study		São Leopoldo Birth Cohort Study	
German Birth Cohort Study		BRISA São Luís	
Griffith University Environments for Healthy Living birth cohort study		Scottish Birth Cohort (1997-2009)	
Halland Health and Growth study		Study of Mothers' and Infants' Life Events Affecting Oral Health (SMILE)	
Growing Up in Singapore Towards Healthy Outcomes (GUSTO)		Prospective Cohort Study of Thai Children (PCTC)	
Haitian Health Foundation		The Dunedin Multidisciplinary Health and Development Study	
Hong Kong Children in 1997		The EDEN Mother-Child Cohort	
Healthy Smiles Healthy Kids study		Peri/postnatal Epigenetic Twins Study (PETS)	
IOWA Facial Growth Study		The Espoo Cohort Study	
IOWA Fluoride Study		The Finnish Family Competence Study	
Kobe Offspring Study		The Queensland Birth Cohort Study	
Longitudinal Study of Australian Children (LSAC)		Toddler Overweight and Tooth decay prevention Study (TOTS)	
Mater Mothers Hospital		TUMME Study	
Mother and Youth Access (MAYA) Trial		The VicGeneration (VicGen) Study	
National Child and Development Study (NCDS)		Welsh Electronic Cohort for Children (WECC)	
Newcastle Thousand Families Study			

Oral health is a highly relevant area to apply the lifecourse approach as most oral diseases and conditions are chronic; hence they need time to develop and are relatively prevalent in the population [Crall & Forrest 2018]. Prevention of oral diseases requires extensive knowledge of its causes, such as socioeconomic inequalities [Peres et al. 2009], nutrition and dietary aspects [Peres et al. 2017], access to fluoride [Ha et al. 2019], and appropriate dental care [Camargo et al. 2012], all of which may start early in life.

The multidisciplinary nature of birth cohort studies and their perspective of being long-standing studies allow the investigation of the effect of early-life exposures on outcomes developed later in life, such as the relationship between general and oral health. For instance, the effect of detrimental health behaviors and conditions, including overweight and obesity, during the life cycle on the risk of periodontitis in adults [Nascimento et al. 2017] or the protective effect of exclusive breastfeeding up to six months of age on dental malocclusion [Peres et al. 2015].

In 2019, we organised a workshop in Bangkok, which involved more than 10 coordinators of some of the longest-running oral health birth cohort studies **(OHBCS)** in low- middle-and, high-income countries, such as Australia, Brazil, Germany, Hong Kong, New Zealand, Thailand, Uganda, and the USA. Insights from multi-country data are particularly useful for this type of research as exposures between countries, including social and environmental conditions, are likely to vary more than exposures within countries. The outcome of this meeting was published in a leading journal in dental research [Peres et al. 2020] as a strategy to discuss the future of studies of this kind.

The key points emerging from the workshop were: i) broad engagement to build a joint research agenda for the future of OHBCS; ii) ensuring high-quality technical standards through systematic literature reviews and focused analytic work on OHBCS; iii) performing pooled data analyses to increase sample size and consequently the statistical power of the findings, iv) the training of the next generation of researchers; and v) wide dissemination of the evidence produced by the collective work and advocacy based on its recommendations.

Creating a consortium was the strategy adopted to reach the objectives foreseen in the workshop more productively while maintaining scientific validity. GLOBICS - Global Consortium of Oral Health Birth Cohort Studies - was founded with funding support from the Borrow Foundation, UK. Currently, the headquarter of GLOBICS is at the National Dental Centre, Singapore, and further research grants have been secured to ensure GLOBICS' future sustainability.

Based on the workshop outcomes, priority should be given to the elaboration of a research agenda to maximise resources and engage several OHBCS in joint efforts. Establishing a solid collaborative network that combines the interest of the OHBCS and research questions relevant to the scientific community and population is crucial for solidifying the consortium.

Accordingly, this report aims to present an overview of collaborative work to respond to the first theme mentioned above, detailing the findings of a DELPHI Study developed to set up a global research agenda for the future of the OHBCS. We hope this publication will stimulate further debate and establish a long-lasting collaborative work among researchers from OHBCS worldwide.

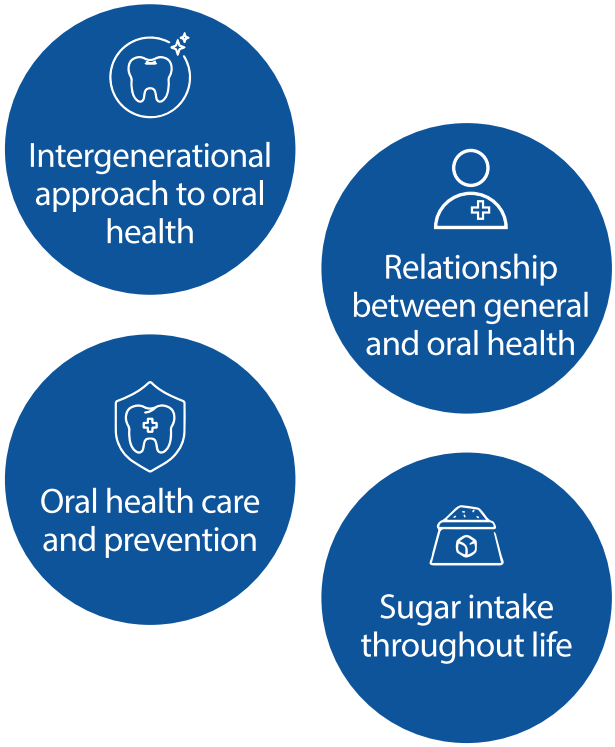
To seek potential collaborators for the GLOBICS Consortium, a scoping review was conducted to identify and map the published literature on OHBCS and describe the data on oral health and their respective methodological aspects. We mapped 120 OHBCS distributed in 34 countries across all continents.

These included literature from the mid-1940s to the early 21st century, revealing how early birth cohorts expanded worldwide (Peres et al. 2022). The map below displays the distribution of the identified birth cohort studies (Peres et al. 2022).

The GLOBICS team has done substantial qualitative work to understand patterns applied to longitudinal oral health studies. Titles and abstracts of over 1400 articles captured by the scoping review were read and organised into themes.

Thus, it was possible to group the articles into

four main thematic areas:



Birth cohorts

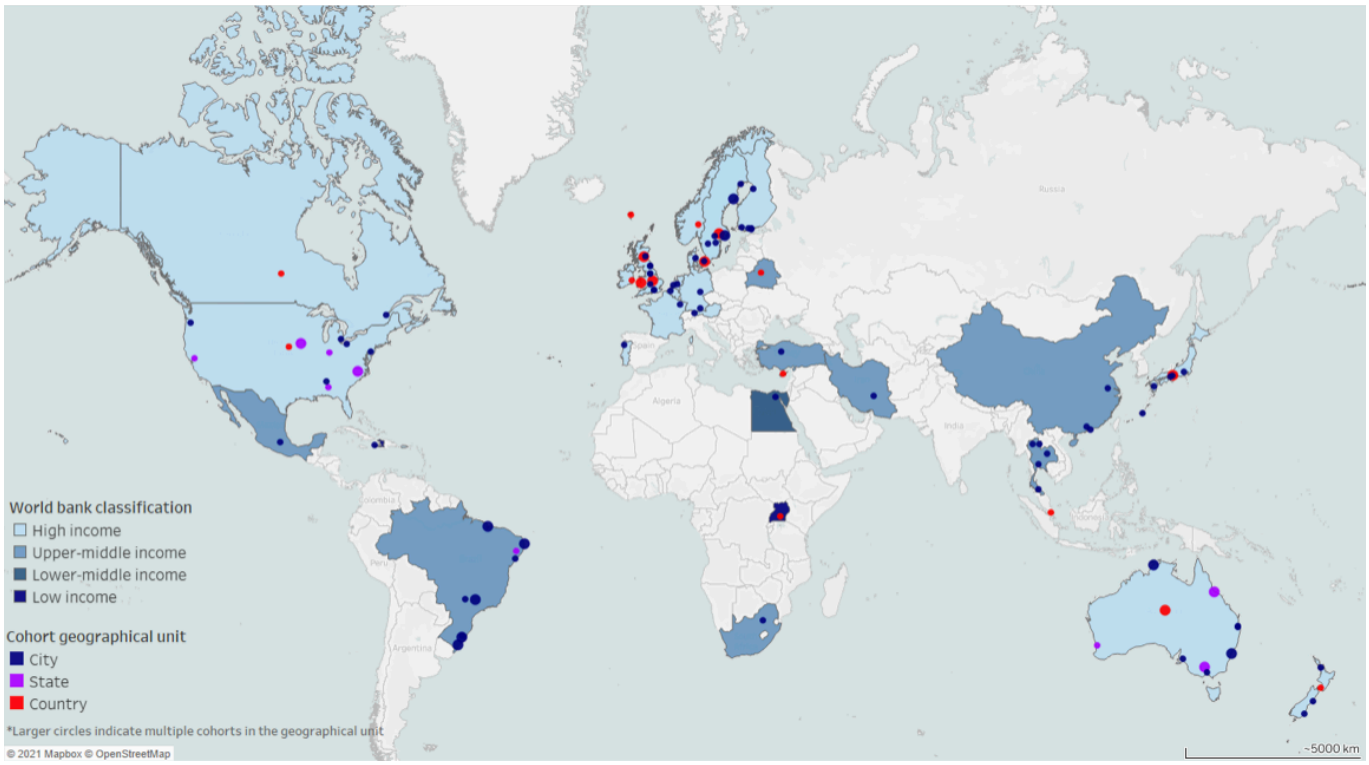


Figure 1: Potential collaborators for the GLOBICS consortium (Peres et al. 2022).

A DELPHI study was the method of choice to reach a consensus for a global OHBCS agenda. The study was conducted between June 2022 and January 2023 and consisted of 2 rounds. The target participants were oral investigators from the 120 OHBCS found through the scoping review [Peres et al. 2022] and key opinion leaders in population health.

The goal:

Find one expert from each identified birth cohort.

Potential participants were retrieved from the scientific publications included in our scoping review database, the authors' networks, and via LinkedIn. The call was disseminated through the participants' institutional e-mails, and reminders were sent fortnightly for approximately two months.

We identified 114 cohort coordinators or experts involved in these studies and invited them to contribute to the study. Figure 2 shows the participation rate over the two rounds of the DELPHI study and the final pool of participants who contributed to the research agenda.

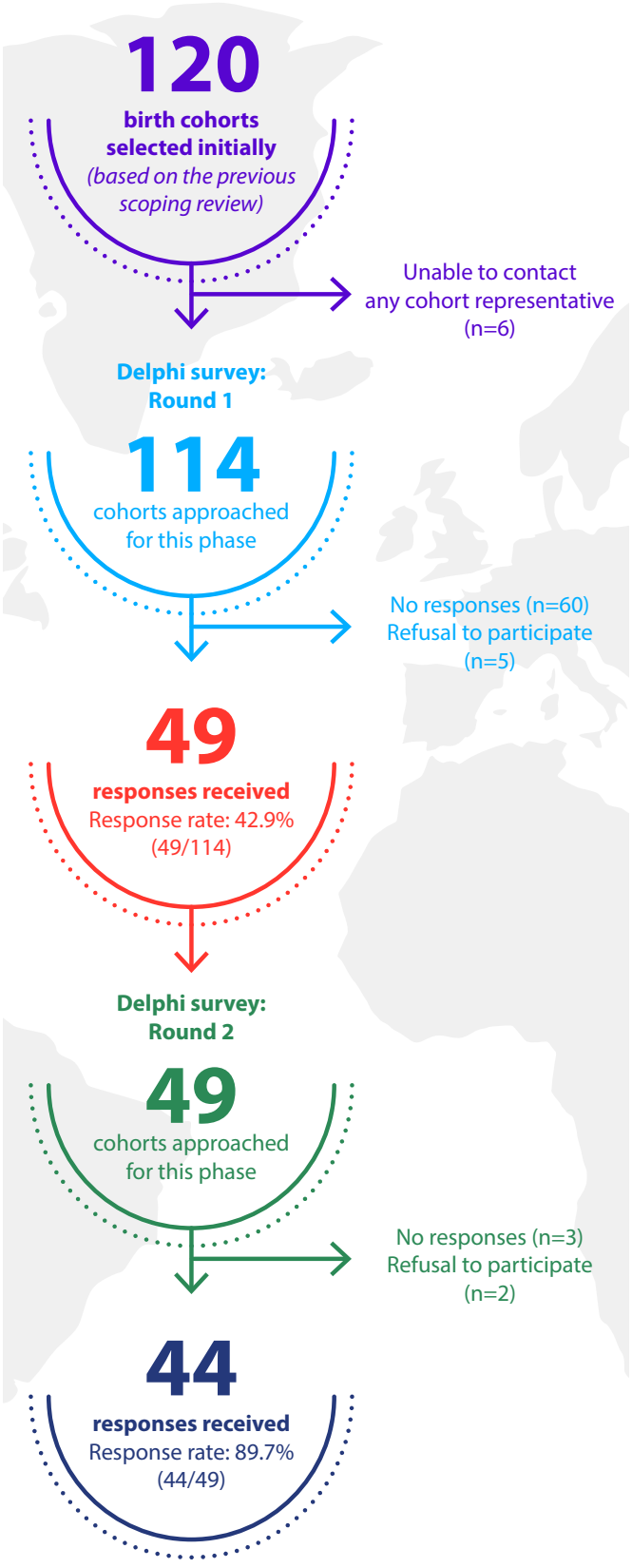


Figure 2: Flowchart illustrating the Delphi study design and response rate.

The first round of the DELPHI started with an overview of 16 research questions distributed in four thematic areas, as defined earlier. The questions were created based on the research hypotheses that most appeared in the articles of the cohorts included in the scoping review (Peres et al. 2021) and then discussed with the GLOBICS executive group before being included in the DELPHI study (Figure 3A).

Experts gave opinions on how important for a global agenda is each question using a Likert-type scale with nine categories from 'highest priority' to 'lowest priority'.

In addition to the pre-established questions, space for including new questions, comments, and suggestions was also available.

Themes	Research Questions
1 Intergenerational approach to oral health	1. Is smoking during pregnancy associated with the risk of offspring's early childhood caries? 2. Is there an association between maternal caries experience and early childhood caries patterns of their offspring? 3. Does maternal sugar intake affect the offspring's oral health? 4. Is maternal oral health-related quality of life (OHQoL) positively associated with the OHQoL of their offspring?
2 Relationship between general and oral health	5. Do birth weight and infant growth during the first year of life affect the occurrence of dental defects of enamel in permanent dentition? 6. Is there an association between childhood obesity and dental caries in permanent teeth? 7. What is the impact of the lifecourse trajectory of obesity on periodontal disease in adulthood? 8. What is the effect of prolonged breastfeeding on early childhood caries?
3 Oral health care and prevention	9. What is the short-term impact of a dental visit in the child's first year of life on early childhood caries? 10. Does a favourable pattern of dental visits in early life have a positive effect on oral health over the lifecourse? 11. Does fluoride exposure modify the association between early childhood caries and exposure to sugar during the first year of the child's life? 12. Are socioeconomic inequalities in dental caries in primary and permanent teeth mitigated by exposure to fluoride sources?
4 Sugar intake in the lifecourse	13. What is the effect of sugar intake during the child's first year of life on early childhood caries? 14. Does the oral microbiome modify the effect of prolonged breastfeeding on early childhood caries? 15. How do sugar consumption trajectories affect the increment of dental caries from childhood to adolescence? 16. Does restriction of sugar intake at the levels proposed by the WHO reduce childhood dental caries?

Figure 3A: Proposed research question for round 1.

After round 1, three questions reached the consensus threshold for agreement, and three had been given extremely low priority. The content of round 2 was adjusted based on the results from round 1 and the experts' comments.

Round 2 included ten original research questions and four new research questions suggested by the participants in round 1 (Figure 3B), which were put to the vote again using the same criteria.

1 Intergenerational approach to oral health

1. What is the impact of maternal micronutrients intake on the risk of tooth development and early childhood caries?

2 Relationship between general and oral health

2. What is the role of gut-oral microbiome axis in the progression of dental caries?
3. Do childhood oral infections increase the risk of developing chronic systemic diseases in adulthood?
4. What is the impact of early childhood nutritional status on risk of dental hypoplasia and dental caries?

Figure 3B Additional questions included in Round 2 based on suggestions from Round 1.

A total of

7 research questions satisfied the three following criteria:

- **>51%** Responding to the categories 8 and 9 (highest priority) of the Likert scale
- **<2.5** Interquartile range (IQR)
- Standard deviation (SD) **<1.7 or >75%** Responses between 2 points above and below the mean score

One question which reached borderline consensus (50% agreement) was also included. Hence, the final global agenda included 8 research questions (Figure 4).

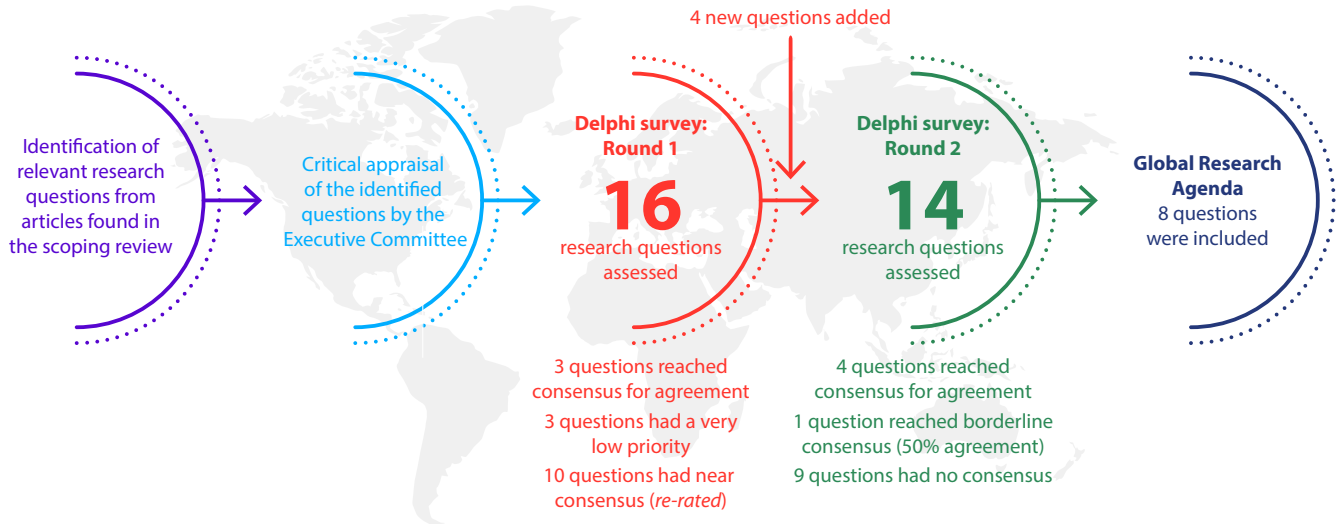
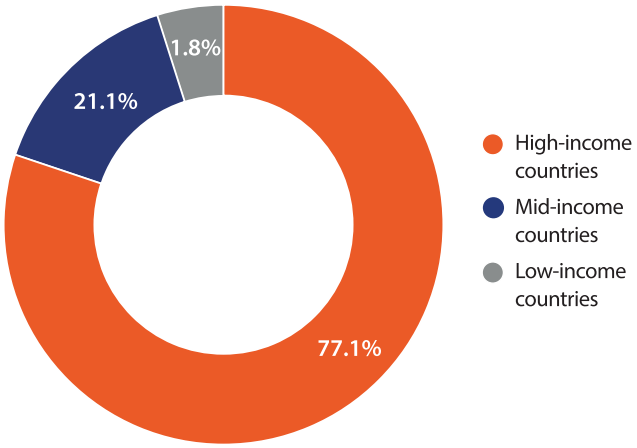


Figure 4: Flow chart of the questions comprising the global research agenda.

The final group of participants who voted on the research agenda, illustrated in Figure 4, included a global representation of birth cohorts

predominantly from high-income countries (77.1%) but also some from lower and middle-income (21.1%) and low-income countries (1.8%).



Of the 24 lower and upper-middle participants in Round 1, 45.8% completed Round 2. Invited cohorts from low-income countries fulfilled both DELPHI rounds (Figure 5).

Cohorts participating in Delphi Process

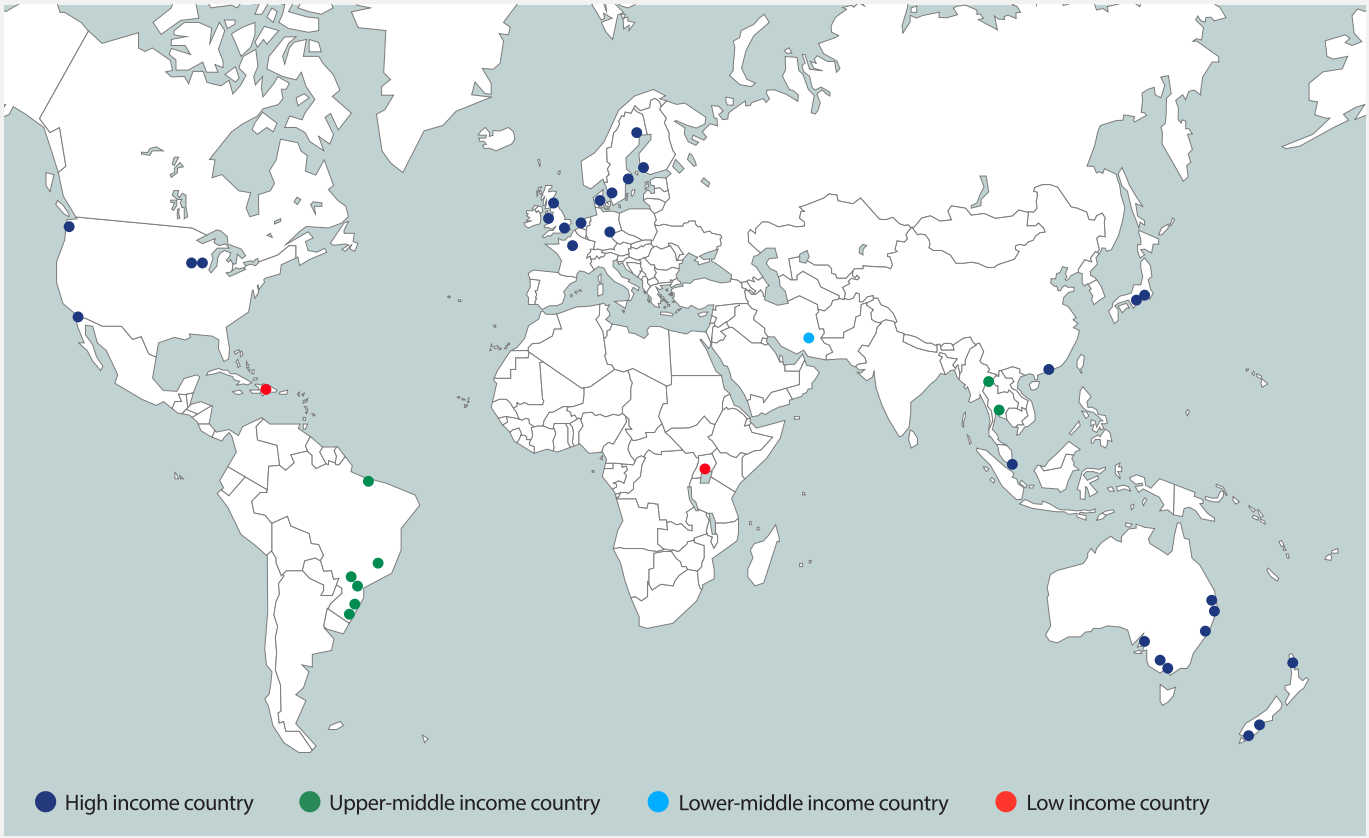


Figure 5: Countries of origin of cohorts participating in both rounds 1 and 2.

This study started with 16 potential questions to be investigated using oral health data from birth cohort studies, of which 8 have been ranked as high priority to be included in the research agenda for OHBCS.

Through a DELPHI process, we prioritized four research studies on '*oral health care and prevention*' and three on the theme of '*lifetime sugar intake*'. The theme '*relationship between general and oral health*' was represented by one research question (Figure 6).

Theme	Qn. no.	Research Questions	Agreement (%) for highly important	IQR	SD	% of responses +/- 2 points of mean
Sugar intake in the lifecourse	Q13	What is the effect of sugar intake during the child's first year of life on early childhood caries?	62.0	2	1.57	96.0
	Q15	How do sugar consumption trajectories affect the increment of dental caries from childhood to adolescence?	64.0	2	1.57	92.0
	Q16	Does restriction of sugar intake at the levels proposed by the WHO reduce childhood dental caries?	61.4	2	1.37	93.2
Relationship between general and oral health	Q5	Do birth weight and infant growth during the first year of life affect the occurrence of dental defects of enamel in permanent dentition?	58.0	2	1.65	86.0
Oral health care and prevention	Q10	Does a favourable pattern of dental visits in early life have a positive effect on oral health over the lifecourse?	68.2	2	1.41	93.2
	Q12	Are socioeconomic inequalities in dental caries in primary and permanent teeth mitigated by exposure to fluoride sources?	63.6	1.5	1.65	84.1
	Q11	Does fluoride exposure modify the association between early childhood caries and exposure to sugar during the first year of the child's life?	54.6	1.5	1.71	88.6
	Q9	What is the short-term impact of a dental visit in the child's first year of life on early childhood caries?	50.0	1	1.46	88.6

Abbreviations: IQR = interquartile range; SD = standard deviation

Figure 6: Thresholds reached by the selected questions.

Figure 7: Questions included in the Global Research Agenda.

Although the theme 'intergenerational approach to oral health' was not included in the proposed final agenda, two main questions,

'Is there an association between maternal caries experience and early childhood caries patterns of their offspring?'

'Does maternal sugar intake affect the offspring's oral health?'

received scores for specific criteria very close to the established threshold. A more qualitative assessment of each question may lead to the perception that a larger sample or other methodological approaches could produce a different result. We also recognized that a diverse mix of stakeholders, a different set of activities for the consensus meeting, or an alternative approach to facilitating the process could show us a different outcome.

The following steps on our research agenda comprise the engagement of participants in a co-design approach to optimize these research questions to be answered by pooling OHBCS data from around the world. The results of our study identified that

'Does a favourable pattern of dental visits in early life have a positive effect on oral health throughout life?'

is the top research priority for OHBCS, followed by further research to investigate whether socioeconomic inequalities in dental caries in primary and permanent teeth are mitigated by exposure to fluoride sources. Therefore, we will be committed to setting up a collaborative network and, from now on, inviting all interested parties to keep in touch with GLOBICS via its webpage GLOBICS (https://www.ndcs.com.sg/research-innovation/ndris/globics/pages/home.aspx).

GLOBICS is an inclusive initiative open to new ideas, proposals, and collaborators. We are focused on an international and interdisciplinary collaboration necessary to improve oral health worldwide.

This research agenda represents a beginning, not an end, and we encourage regions and countries to work with local stakeholders to modify it as appropriate for their own needs.

We greatly appreciate your participation, ideas, and suggestions.

Welcome to GLOBICS!

SCAN ME

ACKNOWLEDGEMENT

The GLOBICS research team would like to express their thanks to The Borrow Foundation, UK, for their support in creating GLOBICS and producing this report.

We acknowledge funds from The Borrow Foundation and the National Medical Research Council (NMRC), Singapore, for supporting the continuation of the GLOBICS project.

SingHealth DukeNUS ACADEMIC MEDICAL CENTRE

National Dental Research Institute Singapore

GLOBICS
Global Consortium of Oral Health Birth Cohort Studies