INT J TUBERC LUNG DIS 14(8):1059–1065

The impact of the method of consent on response rates in the ISAAC time trends study

P. Ellwood,* M. I. Asher,* A. W. Stewart† and the ISAAC Phase III Study Group‡

***Department of Paediatrics, Child and Youth Health, The University of Auckland, Auckland, †School of Population Health, The University of Auckland, Auckland, New Zealand**

SUMMARY

BACKGROUND: Centres in Phases I and III of the International Study of Asthma and Allergies in Childhood (ISAAC) programme used the method of consent (passive or active) required by local ethics committees.

METHODS: Retrospectively, relationships between achieved response rates and method of consent for 13–14 and 6–7-year-olds (adolescents and children, respectively), were examined between phases and between English and non-English language centres.

RESULTS: Information was obtained for 113 of 115 centres for adolescents and 72/72 centres for children. Both age groups: most centres using passive consent achieved high response rates (>80% adolescents and >70% children). English language centres using active consent showed a larger decrease in response rate. Adolescents: seven centres changed from passive consent in Phase I to active consent in Phase III (median decrease of 13%), with five centres showing lower response rates (as low as 34%). Children: no centre changed consent method between phases. Centres using active consent had lower median response rates (lowest response rate 45%).

CONCLUSION: The requirement for active consent for population school-based questionnaire studies can impact negatively on response rates, particularly English language centres, thus adversely affecting the validity of the data. Ethics committees need to consider this issue carefully.

KEY WORDS: ISAAC; consent; epidemiology; children; asthma

QUESTIONNAIRE SURVEYS are used extensively in epidemiological research, particularly in school-based studies. The International Study of Asthma and Allergies in Childhood (ISAAC), the largest epidemiological questionnaire study in children ever undertaken,[1] begun in 1991, has completed three phases and has provided new information on the prevalence of asthma, rhinitis and eczema in schoolchildren throughout the world.[2–17] Briefly, ISAAC Phases I (1991–1996) and III (2001–2005) were cross-sectional, school-based questionnaire surveys, self-completed by 13–14-year-olds (adolescents) and by parents of 6–7-year-olds (children).[2,18] Schools were randomly selected from a defined geographical area. ISAAC Phase I involved 155 centres from 56 countries for the adolescent group and 91 centres from 38 countries for the children.[5] ISAAC Phase III was designed to examine time trends in symptom prevalence (involving 106 centres in 56 countries for the adolescent group and 66 centres in 37 countries for the children); in addition, due to the demand by new centres wishing to participate, the world map was enlarged.[16,17] Phase II was a more in-depth study involving 8–12-year-olds to identify determinants of the differences in symptom prevalence seen in Phase I.[3,4] The ISAAC Steering Committee recommended passive consent for Phases I and III (this decision ultimately remained with ethics committees); however, active consent was mandatory for Phase II. The study reported here concerns Phases I and III.

Important aspects of repeated cross-sectional surveys are comparability and replication of the study design,[19] and adherence to a high standard of methodology. ISAAC time trend centres followed a standardised protocol for field work, and completed a Centre Report for each phase that contained detailed questions about the ISAAC study characteristics. The Centre Report submitted to the ISAAC International Data Centre (IIDC) for review at the time of data submission was examined for adherence to protocol and consistency between phases. When the data and methodology checking process had been completed, a small number of centres was excluded from the Phase I or III analyses. Reasons for exclusion were failure to

‡See Acknowledgements.

Correspondence to: Philippa Ellwood, Department of Paediatrics, Child and Youth Health, The University of Auckland, Private Bag 92019, Auckland 1142, New Zealand. Tel: (+64) 9 373 7599, ext 86451. Fax: (+64) 9 373 7602. e-mail: p.ellwood@auckland.ac.nz

Article submitted 20 October 2009. Final version accepted 22 February 2010.

complete the data checks or Centre Report, having fewer than 1000 participants, low response rates of children within schools (<70% for adolescents and <60% for children) or changing the methodology significantly between phases. A small number of centres deviated from protocol; however, if these deviations were considered minor by the ISAAC Steering Committee and if the rest of the methodology was sound, these centres were included in the analyses and identified in the publications by the use of a footnote to indicate the departure from protocol.[9]

One major check undertaken by the IIDC was to identify the response rate of centres to ensure that the minimum response rate (set by the Steering Committee) was achieved. These were ⩾80% for adolescents and ⩾70% for children. Centres with response rates of between 70% and 80% for adolescents and 60% and 70% for children were included in the time trends analyses if all other aspects of the methodology met the criteria of the Steering Committee and these centres were identified in the first time trends publication by the use of a footnote.[12] Centres with response rates <70% for adolescents and <60% for children were excluded from the analyses, as it was considered that this level of response allowed too much bias. Due to the observation that the percentage of eligible respondents that participated varied between phases in the centres, a retrospective investigation was undertaken. The present study examined the effect of the method of consent used on response rates for centres that achieved the required response rate and that were included in the ISAAC Phase III time trends analyses and those that did not achieve the required response rate and were excluded. The differences in response rates and the consent method used in English and non-English language centres was also examined. This is a unique study; we were unable to locate any other epidemiological studies that have examined whether the method of consent could alter response rates, and what effect this may have on studies conducted over time.

METHODS

The study was approved by local ethics committees, or by another appropriate approving body such as the Ministry of Health in the case of the minority of centres that did not have an ethics committee. The Centre Report contained two questions about ethical approval; however, as information on the method of consent (active or passive) had not been requested, this was collected retrospectively. These two methods are described as applied in ISAAC Phases I and III:

Active consent: for both age groups, an information letter about the proposed research, with an attached consent form, was sent home from school via the pupils for parents/guardians to sign and return to the researcher before the research commenced.

Passive consent: for both age groups, an information letter about the proposed research was sent home to parents/guardians via the pupils. For adolescents, letters were sent out 2 weeks prior to the research taking place in the school and parents/guardians were requested to contact the researcher if they (and/or their adolescent) did not wish to participate (lack of response assumed willingness to participate). For children, questionnaires were sent home with the letter requesting completion and return of the questionnaire to the school.

Following the completion of Phase III, the Principal Investigators (PIs) were contacted and the methods described to them. They identified which method had been approved by their ethics committee for each age group and each phase. The medians of the within-centre changes in proportion of participants responding (response rates) were calculated for each combination of consent method for both age groups. These same median values were calculated for the English language and non-English language centres. Differences between these medians were tested using the Kruskal-Wallis test.

RESULTS

Adolescents

For adolescents, information about the method of consent was obtained from 113 of 115 (98%) centres. For one centre, the PI was seriously ill and unable to be contacted; for the other, the PI left following the Phase III data collection and the new PI was unable to locate the information. In Phase I, 97/113 centres (86%) used passive consent and 16 (14%) used active consent. In Phase III, 93 (82%) used passive consent and 20 (18%) used active consent. Ten centres changed the method of consent between phases (Table 1). Seven of these centres changed from passive consent in Phase I to active consent in Phase III, showing a median decrease of 13% in response rate (Table 2). Three centres changed from active con-sent in Phase I to passive consent in Phase III, showing no change in median response rate (0%). Little change in the median response rate was seen in the 90 centres that used passive consent in both phases (−1%) and in the 13 centres that used active consent for both phases (−2%). Eight centres were excluded from the Phase III time trends publication due to response rates of <70%. Six of these centres used active consent and two used passive consent. Thirteen centres were footnoted for low response rates between 70% and 80%; of these, five used active consent and eight passive consent (Appendix Table A1).[12]* For centres using passive consent that

*Appendix available in the online version of this article at http://www.ingentaconnect.com/content/iuatld/ijtld/2010/00000014/00000008/art00022

Table 1 ISAAC 13–14 year age group: centres that changed their method of consent between Phase I and Phase III

	Phase I			Phase III		
Name of centre	Form of consent	Response %	Comment	Form of consent	Response %	Comment
Bay of Plenty, New Zealand*	Passive	89		Active	76	Footnoted
Buenos Aires, Argentina	Passive	88		Active	42	Excluded from analyses
Cape Town, South Africa	Passive	83		Active	83	
Jersey, Channel Islands	Passive	90		Active	78	Footnoted
Melbourne, Australia*	Passive	97		Active	<40	Excluded from analyses
Seattle, WA, USA*	Passive	80		Active	87	
Sydney, Australia*	Passive	90		Active	34	Excluded from analyses
Barcelona, Spain	Active	91		Passive	88	
Chapel Hill, NC, USA*	Active	32	Excluded from analyses	Passive	75	Excluded from analyses
Riga, Latvia	Active	95		Passive	95	

* English language countries.
ISAAC = International Study of Asthma and Allergies in Childhood.

Table 2 Median response rates and changes in rates for age groups 13–14 and 6–7 years in Phases I and III of ISAAC classified by method of consent

		13–14 years			6–7 years		
	Type of consent	Centres *n*	Median response rate %	Probability*	Centres *n*	Median response rate %	Probability*
Phase I	Passive	97	93		60	91	
	Active	16	94.5	0.68	12	84	0.018
Phase III	Passive	93	93		60	86	
	Active	20	86	<0.001	12	78	0.27
			Median change %			Median change %	
Change	Passive-passive†	90	−1		60	−2.5	
	Passive-active†	7	−13		0		
	Active-passive†	3	0		0		
	Active-active†	13	−2	0.035	12	−5.5	0.48

* Probability of a difference between the categories.
† For Phases I and III, respectively.
ISAAC = International Study of Asthma and Allergies in Childhood.

were excluded or footnoted, the reasons for low response rates included serious financial difficulty, absenteeism from school between many scheduled holidays, tense political situations resulting in school absenteeism, difficulty in recruitment of schools and within schools, lack of support from teaching staff and a high degree of illiteracy among parents.

Children

For children, information on the method of consent was obtained from all 72 centres (100%) in both phases (Appendix Table A2). The method of consent did not change for any centre between phases. Passive consent was used by 60 centres (83%) and active consent in 12 centres (17%). Centres that used passive consent showed a median decrease in response rate of 2.5%, and those that used active consent a median decrease in response rate of 5.5% between phases (Table 2). Six centres were excluded from the worldwide time trends publications due to Phase III response rates <60%. Three centres used active consent and three used passive consent (Table A2). Seven centres were footnoted for low response rates (60–70%), of which one used active consent and six passive consent. For centres using passive consent that were excluded or footnoted, the reasons for low response rates were the same as those described for the adolescent group.

English language centres and non-English language centres

Among adolescents, active consent generally resulted in lower response rates in English language centres. From Phases I to III, a median response rate decrease of 13% ($n = 9$) was found in English language centres compared to a decrease in the non-English language centres of 2% ($n = 11$, $P = 0.29$). Five English language centres that used active consent were excluded from the time trends publications due to low response rates. These were Chapel Hill, NC, USA,

response rate 32%; Hamilton, ON, Canada, 44%; Saskatoon, Canada, 54%; Sydney, Australia, 34%; and Melbourne, Australia, <40%. A lower response rate in Phase III was observed in Jersey, Channel Islands, which changed from passive consent in Phase I (90%) to active consent in Phase III (78%). Passive consent was less commonly associated with very low response rates (<70%) in non-English language than in English language centres, with two non-English languages centres excluded, Mumbai [16], India, response rate 63% and Tbilisi, Georgia, 46%.

Among children, active consent in English language centres also affected response rates. From Phase I to Phase III, a median response rate decrease of 15% ($n = 4$) was found in English language centres compared with non-English language centres, which had a median response rate decrease of 2.5% ($n = 8$, $P = 0.30$). For centres that used active consent, two English language centres (Hamilton, ON, Canada, response rate 54% and Seattle, WA, USA, 32%) were excluded. One non-English language centre using active consent with a low response rate (Valencia, Spain, 64%) was footnoted in the first publication. For English language centres using passive consent, one centre was excluded (Wellington, New Zealand, response rate 47%), and Saskatoon, Canada (63%) was footnoted. For non-English language centres using passive consent, two centres were excluded: Chennai, India, response rate 40% and Tbilisi, Georgia, 56%.

DISCUSSION

Cross-sectional studies are relatively easy, economical and useful for measuring prevalence of disease and investigating exposures that are fixed characteristics. Exposure and effect are measured at the same time and research of this type is often the first step in assessing the health needs of countries. Bias and sources of error in epidemiological studies must be minimised to have confidence in the results, and it is important to assess the importance of each potential source of bias or error when interpreting data.[20] In studies such as ISAAC, true differences in prevalence values between centres and countries can be detected, but these can also be modified by the effect of differences in survey methods. If cross-sectional studies are repeated, it is important that methods used on each occasion are as similar as possible.[21]

A high response rate from participants is essential in epidemiological research, particularly when estimating prevalence to minimise systematic error.[20] The measure that is most important for assessing the extent to which a sample is representative is the percentage of randomly selected subjects that provide data for a study. If the method of consent used has a negative impact on the response rate, this has serious implications.

Main findings

In Phase III, the requirement for active consent in 20 (18%) centres for adolescents and 12 (17%) centres for children resulted in only five of these centres for the adolescents and two for the children being excluded from the worldwide time trends analyses. Of the centres that used passive consent, three were excluded in each age group; however, the explanations for low response rates given by investigators were related to reasons other than the use of passive consent.

Strengths and limitations of this study

In this study of consent, which included a large number of locations in the world, all centres with children as participants responded. For the adolescent group, all but two of the centres approached provided data, and these two centres were excluded from this consent study. Although the information was obtained retrospectively, the data are very likely to be reliable because each PI provided the information directly.

Ethics committees and consent

Most countries now have accredited ethics committees to review research projects to protect participants, particularly if children are involved. The process used by researchers to enrol participants and obtain consent is closely examined. The literature is consistent in the view that active consent is mandatory to protect children involved in invasive medical research such as clinical trials.[22–24] However, the ethical issue of using passive consent with school-based questionnaire surveys (epidemiological studies) using children (or parents of the children) as participants is contentious. Some believe active consent is required at all times,[25] while others believe different types of research projects require different approaches to consent.[22,26] This is the first study that we are aware of that examines the possible effect of the method of consent on response rates, and it is thus an important addition to the literature on methodology.

The role of ethics committees in ISAAC

In 1991, before the start of Phase I, the Steering Committee recommended using passive consent, recognising that higher response rates would be achieved and expense reduced by removing one step from the research process. They acknowledged, however, that the consent method used by centres would be determined by local ethics committees. Following Phase I, for unknown reasons, some countries adopted policies requiring active consent for all research involving human participants. Importantly, some ethics committees are beginning to distinguish between the types of research that have differing potential risks for participants (e.g., clinical trials vs. epidemiological research). Some countries are developing new standards allowing the use of passive consent. For example,

guidelines recently published by the National Ethics Advisory Committee of New Zealand[27] state: 'Questionnaires are often innocuous and may even be offered by mail. Completion of the questionnaire can be taken as consent, provided that the letter of invitation expressly leaves the participant free of obligation'. However, these projects still require ethics committee review to ensure that the questionnaires are appropriate for passive consent use.

CONCLUSION

We found in this investigation that a higher response rate in questionnaire-based epidemiological studies is more likely if parents are not required to give active consent. A universal standardised model for the type of consent to be used for each type of research would be the ideal—a consistent methodology allowing passive consent for epidemiological research which ethics committees considered would 'do no harm'. Some ethics committees are now actively reviewing this issue. Our study underlines the importance of such examination, as it suggests that the stringent ethical requirement of active consent reduces participation (to the extent of exclusion) and thereby undermines one of the central tenets of the ethical process.[28] In requiring active consent when it is not necessary, which in turn can lead to results with questionable validity, are ethics committees themselves acting in an unethical manner?

Acknowledgements

The authors are grateful to the children and parents who participated in ISAAC Phase III and for the coordination and assistance by the school staff. The authors also acknowledge and thank the many funding bodies throughout the world that supported the individual ISAAC centres and collaborators and their meetings. The current main source of funding for the ISAAC International Data Centre (IIDC) is the BUPA Foundation (grant number: RBF0065). Many New Zealand funding bodies have contributed support for the IIDC during the periods of fieldwork and data compilation (the Health Research Council of New Zealand, the Asthma and Respiratory Foundation of New Zealand, the Child Health Research Foundation, the Hawke's Bay Medical Research Foundation, the Waikato Medical Research Foundation, Glaxo Wellcome New Zealand, the NZ Lottery Board and Astra Zeneca New Zealand). Glaxo Wellcome International Medical Affairs supported the regional coordination for Phase III and the IIDC. Without help from all of the above, ISAAC would not have been such a global success.

The ISAAC Phase III Time Trends Study Group

ISAAC Steering Committee

N Aït-Khaled* (International Union Against Tuberculosis and Lung Disease, Paris, France); H R Anderson (Division of Community Health Sciences, St Georges, University of London, London, UK); M I Asher (Department of Paediatrics: Child and Youth Health, Faculty of Medical and Health Sciences, The University of Auckland, Auckland, New Zealand); R Beasley* (Medical Research Institute of New Zealand, Wellington, New Zealand); B Björkstén* (Institute of Environmental Medicine, Karolinska Institutet, Stockholm, Sweden); B Brunekreef (Institute of Risk Assessment Sciences, Universiteit Utrecht, Utrecht, The Netherlands); J Crane (Wellington Asthma Research Group, Wellington School of Medicine, Wellington, New Zealand); P Ellwood (Department of Paediatrics: Child and Youth Health, Faculty of Medical and Health Sciences, The University of Auckland, Auckland, New Zealand); C Flohr (St John's Institute of Dermatology, St Thomas' Hospital, London, UK); S Foliaki* (Centre for Public Health Research, Massey University, Wellington, New Zealand); F Forastiere (Department of Epidemiology, Rome E Health Authority, Rome, Italy); L García-Marcos (Instituto de Salud Respiratoria, Universidad de Murcia, Murcia, Spain); U Keil* (Institut für Epidemiologie und Sozialmedizin, Universität Münster, Münster, Germany); C K W Lai* (Department of Medicine and Therapeutics, The Chinese University of Hong Kong, Hong Kong, SAR China); J Mallol* (Department of Respiratory Medicine, University of Santiago de Chile, Santiago, Chile); E A Mitchell (Department of Paediatrics: Child and Youth Health, Faculty of Medical and Health Sciences, The University of Auckland, Auckland, New Zealand); S Montefort* (Department of Medicine, University of Malta, Malta), J Odhiambo* (Centre Respiratory Diseases Research Unit, Kenya Medical Research Institute, Nairobi, Kenya); N Pearce (Centre for Public Health Research, Massey University, Wellington, New Zealand); C F Robertson (Murdoch Children's Research Institute, Melbourne, Australia); A W Stewart (Epidemiology and Biostatistics, School of Population Health, The University of Auckland, Auckland, New Zealand); D Strachan (Division of Community Health Sciences, St Georges, University of London, London, UK); E von Mutius (Dr von Haunerschen Kinderklinik de Universität München, Munich, Germany); S K Weiland (deceased) (Institute of Epidemiology, University of Ulm, Ulm, Germany); G Weinmayr (Institute of Epidemiology, University of Ulm, Ulm, Germany); H Williams (Centre for Evidence Based Dermatology, Queen's Medical Centre, University Hospital, Nottingham, UK); G Wong (Department of Paediatrics, Prince of Wales Hospital, Hong Kong, SAR China).

ISAAC International Data Centre

M I Asher, T O Clayton, P Ellwood, E A Mitchell, Department of Paediatrics: Child and Youth Health, and A W Stewart, School of Population Health, Faculty of Medical and Health Sciences, The University of Auckland, New Zealand.

ISAAC Phase III collaborators

Africa: Algeria: B Benhabylès (Wilaya of Algiers); Kenya: F O Esamai (Eldoret), L Ng'ang'a† (Nairobi); Morocco: Z Bouayad† (Casablanca, Marrakech); Nigeria: B O Onadeko (Ibadan); South Africa: H J Zar† (Cape Town); Tunisia: M Jerray (Sousse); **Asia-Pacific:** China: Y Z Chen† (Beijing), N-S Zhong (Guangzhou); SAR China: Y L Lau (Hong Kong 6–7 years), G Wong (Hong Kong 13–14 years); Indonesia: C B Kartasasmita (Bandung); Japan: H Odajima (Fukuoka); Malaysia: K H Teh (Alor Setar), J de Bruyne† (Klang Valley), B S Quah (Kota Bharu); Philippines: F Cua-Lim†

*Regional coordinator.

†National coordinator.

(Metro Manila); Singapore: D Y T Goh (Singapore); South Korea: H-B Lee† (Provincial Korea, Seoul); Taiwan: J-L Huang† (Taipei); Thailand: P Vichyanond† (Bangkok), M Trakultivakom (Chiang Mai); **Eastern Mediterranean:** Iran: M-R Masjedi† (Rasht, Tehran); Kuwait: J A al-Momen (Kuwait); Malta: S Montefort† (Malta); Pakistan: N Mahmood† (Karachi); Sultanate of Oman: O Al-Rawas† (Al-Khod); **Indian sub-continent:** India: V A Khatav (Borivali), L Kumar (Chandigarh), G Setty (Chennai), K C Jain (Jodphur), T U Sukumaran (Kottayam), M K Joshi (Mumbai [16]‡), A V Pherwani (Mumbai [18]), S K Sharma, (New Delhi [7]), N M Hanumante (Pune); **Latin America:** Argentina: I M E Guimaraes (Buenos Aires), C E Baena-Cagnani† (Córdoba); Brazil: N Rosário (Curitiba), G B Fischer (Porto Alegre), M de Britto (Recife), L de Freitas Souza (Salvador), D Solé† (São Paulo); Chile: L Amarales, (Punta Arenas), P Aguilar, (South Santiago) M A Calvo (Valdivia); Costa Rica: M E Soto-Quirós† (Costa Rica); Mexico: I Romieu (Cuernavaca); Panama: G Cukier† (David-Panamá); Paraguay: J A Guggiari-Chase† (Asunción); Peru: P Chiarella† (Lima); Uruguay: D Holgado† (Montevideo); **North America:** Barbados: M E Howitt† (Barbados); Canada: M Sears† (Hamilton), D Rennie (Saskatoon); USA: K Yeatts (Chapel Hill, NC), G J Redding (Seattle, WA); **Northern and Eastern Europe:** Albania: A Priftanji† (Tiranë); Estonia: M-A Riikjärv† (Tallin); Finland: J Pekkanen† (Kuopio County); Georgia: M Gotua† (Kutaisi, Tbilisi); Latvia: V Svabe (Riga); Lithuania: J Kudzyte† (Kaunas); Poland: G Lis† (Kraków), A Breborowicz (Poznan); Romania: D Deleanu (Cluj); Russia: E G Kondiourina (Novosibirsk); Sweden: H Vogt (Linköping); Ukraine: V Ognev† (Kharkiv); **Oceania:** Australia: C F Robertson† (Melbourne), G Marks (Sydney); New Zealand: M I Asher† (Auckland), C Moyes (Bay of Plenty), P Pattemore (Christchurch), R Mackay (Nelson), N Pearce (Wellington); **Western Europe**: Austria: G Haidinger† (Kärnten, Urfahr-Umgebung); Belgium, J Weyler (Antwerp); Channel Islands, P Standring (Guernsey), R Goulding (Jersey); Germany: U Keil† (Münster); Isle of Man: A Steriu (Isle of Man); Italy: E Bonci (Cosenza), C Galassi (Emilia-Romagna), M G Petronio, (Empoli), E Chellini (Firenze), L Bisanti (Milano), F Forastiere† (Roma), P Sestini (Siena), G Ciccone (Torino), S Piffer (Trento); Portugal: R Camâra (Funchal), J E Rosado Pinto† (Lisboa), C Nunes, (Portimao) J M Lopes dos Santos (Porto); Republic of Ireland: L Clancy (Republic of Ireland); Spain: R M Busquets (Barcelona), C González Díaz (Bilbao), L García-Marcos† (Cartagena), A Arnedo-Pena (Castellón), G Garcia Hernández (Madrid), F Guillén-Grima, (Pamplona), M M Morales-Suarez-Varela (Valencia), A Blanco Quirós (Vallodolid); UK: H R Anderson† (North Thames, South Thames), J B Austin (Scotland), M H Shamssain (Sunderland), D Strachan (Surrey/Sussex), M Burr (Wales).

ISAAC Phase III national coordinators not identified above

H R Anderson (Channel Islands), J Mallol (Chile), C Lai (SAR China), H R Anderson (Isle of Man), J Shah (India), K Baratawidjaja (Indonesia), S Nishima (Japan), M Baeza-Bacab (Mexico), P Manning (Republic of Ireland), R M Khaitov (Russia), B Lee (Singapore), L Nilsson (Sweden).

* Regional coordinator.
† National coordinator.
‡ Numbers in brackets indicate centre numbers.

References

1 Anonymous. Guinness world records. London, UK: Guinness World Records, 2004.
2 ISAAC Steering Committee. International Study of Asthma and Allergies in Childhood. Phase One manual. Auckland/Münster: ISAAC, 1993.
3 Weiland S K, Björkstén B, Brunekreef B, et al. Phase II of the International Study of Asthma and Allergies in Childhood (ISAAC II): rationale and methods. Eur Respir J 2004; 24: 406–412.
4 Weiland S K, Strachan D. Worldwide variations in prevalence of symptoms of allergic rhinoconjunctivitis in children: the International Study of Asthma and Allergies in Childhood (ISAAC). Clin Exp Allergy 1998; 28 (Suppl 5): 52–66; discussion 90–91.
5 ISAAC Steering Committee. Worldwide variations in the prevalence of asthma symptoms: the International Study of Asthma and Allergies in Childhood (ISAAC). Eur Respir J 1998; 12: 315–335.
6 Strachan D, Sibbald B, Weiland S, et al. Worldwide variations in prevalence of symptoms of allergic rhinoconjunctivitis in children: the International Study of Asthma and Allergies in Childhood (ISAAC). Pediatr Allergy Immunol 1997; 8: 161–176.
7 Williams H, Robertson C, Stewart A, et al. Worldwide variations in the prevalence of symptoms of atopic eczema in the International Study of Asthma and Allergies in Childhood. J Allergy Clin Immunol 1999; 103: 125–138.
8 ISAAC Steering Committee. Worldwide variation in prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and atopic eczema: ISAAC. Lancet 1998; 351: 1225–1232.
9 Crane J, Mallol J, Beasley R, et al. Agreement between written and video questions for comparing asthma symptoms in ISAAC. European Respir J 2003; 21: 455–461.
10 Weinmayr G, Weiland S, Björkstén B, et al. Atopic sensitization and the international variation of asthma symptom prevalence in children. Am J Respir Crit Care Med 2007; 176: 565–574.
11 Ellwood P, Asher M I, Beasley R, Clayton T O, Stewart A W, and the ISAAC Steering Committee. The international study of asthma and allergies in childhood (ISAAC): Phase Three rationale and methods. Int J Tuberc Lung Dis 2005; 9: 10–16.
12 Asher M I, Montefort S, Björkstén B, et al. Worldwide time trends in the prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and eczema in childhood: ISAAC Phases One and Three repeat multicountry cross-sectional surveys. Lancet 2006; 368: 733–743.
13 Pearce N, Aït-Khaled N, Beasley R, et al. Worldwide trends in the prevalence of asthma symptoms: Phase III of the International Study of Asthma and Allergies in Childhood (ISAAC). Thorax 2007; 62: 758–766.
14 Björkstén B, Clayton T, Ellwood P, Stewart A, Strachan D, Group IPIS. Worldwide time trends for symptoms of rhinitis and conjunctivitis: Phase III of the International Study of Asthma and Allergies in Childhood. Pediatr Allergy Immunol 2008; 19: 110–124.
15 Williams H, Stewart A, von Mutius E, et al. Is eczema really on the increase worldwide? J Allergy Clin Immunol 2008; 121: 947–954.e15.
16 Aït-Khaled N, Pearce N, Anderson H, et al. Global map of the prevalence of symptoms of rhinoconjunctivitis in children: the International Study of Asthma and Allergies in Childhood (ISAAC) Phase Three. Allergy 2009; 64: 123–148.
17 Lai K, Beasley R, Crane J, et al. Global variation in the prevalence and severity of asthma symptoms: Phase Three of the International Study of Asthma and Allergies in Childhood (ISAAC). Thorax 2009; 64: 476–483.
18 Ellwood P, Asher M I, Beasley R, Clayton T O, Stewart A W, on behalf of the ISAAC Steering Committee and the ISAAC Phase Three Study Group. ISAAC Phase Three manual. Auckland, New Zealand: ISAAC International Data Centre, 2000.

19 Pearce N, Douwes J. The global epidemiology of asthma in children. Int J Tuberc Lung Dis 2006; 10: 125–132.
20 Beaglehole R, Bonita R, Kjellström T. Basic epidemiology. Geneva, Switzerland: WHO, 1993.
21 Jessop E. Be the best—Copy EXACTLY! J Public Health Med 2003; 25: 87.
22 Hansson M O. Balancing the quality of consent. J Medical Ethics 1998; 24: 182–187.
23 Williams J R. The physician's role in the protection of human research subjects. Sci Eng Ethics 2006; 12: 5–12.
24 Steinbrook R. Protecting research subjects—the crisis at Johns Hopkins. N Engl J Med 2002; 346: 716–720 [erratum 346: 1678].
25 Peart N, Holdaway D. Ethical guidelines for health research with children. N Z Bioethics J 2000; 1: 3–9.
26 Esbensen F A, Deschenes E P, Vogel R E, West J, Arboit K, Harris L. Active parental consent in school-based research. An examination of ethical and methodological issues. Eval Rev 1996; 20: 737–753.
27 National Ethics Advisory Committee. Ethics of observational research, audit and related activities: second discussion document. Wellington, New Zealand: Ministry of Health, 2004.
28 Council for International Organizations of Medical Sciences. International guidelines for biomedical research involving human subjects. Geneva, Switzerland: WHO, 2002.

RÉSUMÉ

CONTEXTE : Les centres situés aux Phases I et III du programme de l'International Study of Asthma and Allergies in Childhood (ISAAC) ont utilisé la méthode de consentement passif ou actif exigée par les comités locaux d'éthique.

MÉTHODES : On a examiné de manière rétrospective les relations entre les taux de réponses obtenus et les méthodes de consentement utilisées chez les adolescents de 13 à 14 ans et les enfants de 6 à 7 ans aussi bien entre les phases qu'entre les centres de langue anglaise ou non-anglaise.

RÉSULTATS : On a obtenu des informations en provenance de 113 des 115 centres pour adolescents et de 72/72 centres pour enfants. Les deux groupes d'âge : la plupart des centres utilisant le consentement passif ont obtenu des taux élevés de réponses (>80% chez les adolescents et >70% chez les enfants). La diminution du taux de réponse a été plus forte dans les centres de langue anglaise utilisant le consentement actif. Adolescents : dans sept centres, on est passé du consentement passif en Phase I au consentement actif en Phase III (décroissance médiane 13%) avec des taux de réponses plus faibles dans cinq centres (baissant jusqu'à 34%). Enfants : aucun des centres n'a modifié la méthode entre les phases. Les taux médians de réponses ont été plus faibles dans les centres utilisant le consentement actif (taux de réponses le plus faible : 45%).

CONCLUSION : L'exigence d'un consentement actif pour des études par questionnaire concernant la population scolaire peut avoir un impact négatif sur les taux de réponses, particulièrement dans les centres de langue anglaise, ce qui entraîne un effet défavorable sur la validité des données. Les comités d'éthique doivent prendre soigneusement ce problème en considération.

RESUMEN

MARCO DE REFERENCIA: Los centros que se encuentran en la Fase I y III del Estudio Internacional de Asma y Alergia en la Infancia (ISAAC) utilizaron un método activo o pasivo de obtención del consentimiento informado que exigen los comités locales de ética.

MÉTODO: Se examinó en forma retrospectiva la relación entre las tasas de respuesta alcanzadas y el método de obtención del consentimiento en adolescentes de 13 y 14 años de edad y niños de 6 y 7 años de edad en las diferentes fases del estudio y entre los centros anglohablantes y no anglohablantes.

RESULTADOS: Se obtuvo información de 113 de los 115 centros para adolescentes y de 72 de los 72 centros para niños. Análisis de ambos grupos de edad: la mayoría de los centros que usaron un método pasivo de obtención del consentimiento alcanzaron altas tasas de respuesta (superiores a 80% en los adolescentes y superiores a 70% en los niños). En los centros anglohablantes que aplicaron un método activo de obtención del consentimiento se observó una mayor disminución de la tasa de respuesta. Análisis de los adolescentes: siete centros cambiaron el método pasivo de obtención del consentimiento utilizado en la Fase I, por un consentimiento activo en la Fase III (mediana de la disminución 13%) y en cinco centros se observaron tasas muy bajas de respuesta (hasta de 34%). Análisis de los niños: ningún centro cambió el método de obtención del consentimiento entre las fases. La mediana de la tasa de respuesta en los centros que usaron consentimiento activo fue menor (la tasa de respuesta más baja fue 45%).

CONCLUSIÓN: La exigencia de un consentimiento activo en los estudios con cuestionarios administrados a una población de edad escolar puede tener una repercusión negativa en las tasas de respuesta, sobre todo en los centros anglohablantes, afectando así la validez de los datos. Los comités de ética deben considerar atentamente este aspecto.

APPENDIX

Table A1 ISAAC 13–14 year age group method of consent of Phase I and III centres

Centre name & language	Phase I Form of consent	Phase I Response %	Phase I Comment	Phase III Form of consent	Phase III Response %	Phase III Comment
Africa						
Algeria						
West Algiers (French)	Passive	97.8		Passive	89.6	
Kenya						
Eldoret (English)	Passive	100.0		Passive	100.0	
Nairobi (English)	Passive	99.0		Passive	99.7	
Morocco						
Casablanca (Arabic)	Passive	98.4		Passive	100.0	
Marrakech (Arabic)	Passive	89.7		Passive	99.9	
Nigeria						
Ibadan (English)	Passive	76.4	Footnote	Passive	99.7	
South Africa						
Cape Town (Xhosa 33%, English 41%, Africaans 26%)	Passive	82.8		Active	83.4	
Tunisia						
Sousse (Arabic)	Passive	100.0		Passive	99.9	
Asia-Pacific						
China						
Beijing (Chinese)	Passive	99.0		Passive	97.8	
Guangzhou (Chinese)	Passive	99.7		Passive	95.7	
Hong Kong						
Hong Kong (Chinese)	Passive	95.6		Passive	99.5	
Indonesia						
Bandung (Indonesian)	Passive	95.7		Passive	99.6	
Japan						
Fukuoka (Japanese)	Passive	94.1		Passive	94.6	
Malaysia						
Alor Setar (Malay)	Passive	91.0		Passive	91.3	
Klang Valley (Malay)	Passive	91.4		Passive	91.0	
Kota Bharu (Malay)	Passive	95.9		Passive	92.4	
Philippines						
Metro Manila (Tagalog)	Active	95.5		Active	77.5	Footnote
Singapore						
Singapore (English)	Passive	91.4		Passive	93.9	
South Korea						
Provincial Korea (Korean)	Active	98.3		Active	96.3	
Seoul (Korean)	Active	95.6		Active	96.7	
Taiwan						
Taipai (Chinese)	Passive	93.3		Passive	95.9	
Thailand						
Bangkok (Thai)	Passive	74.8	Footnote	Passive	93.8	
Chiang Mai (Thai)	Passive	94.7		Passive	95.7	
Eastern Mediterranean						
Iran						
Rasht (Persian)	Passive	99.0		Passive	99.8	
Tehran (Persian)	Passive	86.4		Passive	99.8	
Kuwait						
Kuwait (Arabic)	Passive	70.4	Footnote	Passive	91.6	
Malta						
Malta (Maltese 88%, English 12%)	Passive	88.7		Passive	90.0	
Pakistan						
Karachi (English 54%, Urdu 46%)	Passive	100.0		Passive	96.0	
Sultanate of Oman						
Al-Khod (Arabic)	Passive	94.0		Passive	97.2	
Indian Sub-Continent						
India						
Borivali (Marathi 60%, Hindi 30%, English 10%)	Passive	100.0		Passive	99.9	
Chandigarh (English)	Passive	97.4		Passive	99.4	
Chennai (Tamil 60%, English 40%)	Passive	96.2		Passive	94.8	
Jodphur (Hindi)	Passive	84.5		Passive	79.6	
Kottayam (Malyalam)	Passive	90.7		Passive	98.5	
Mumbai [16] (Marathi 80%, English 20%)	Passive	90.9		Passive	62.7	Excluded
Mumbai [18] (Marathi 70%, English 30%)	Passive	99.4		Passive	99.4	
New Delhi [7] (Hindi 64%, English 36%)	Passive	100.0		Passive	86.7	
Pune (Marathi 75%, English 25%)	Passive	99.8		Passive	70.8	Footnote

Centre name & language	Phase I Form of consent	Phase I Response %	Phase I Comment	Phase III Form of consent	Phase III Response %	Phase III Comment
Latin America						
Argentina						
Buenos Aires (Spanish)	Passive	87.7		Active	42.0	Excluded
Córdoba (Spanish)	Passive	78.6	Footnote	Passive	99.4	
Brazil						
Curitiba (Portuguese)	Passive	93.9		Passive	90.5	
Porto Alegre (Portuguese)	Passive	96.8		Passive	97.0	
Recife (Portuguese)	Passive	97.6		Passive	95.5	
Salvador (Portuguese)	Passive	93.4		Passive	80.5	
São Paulo (Portuguese)	Passive	94.0		Passive	96.5	
Chile						
Punta Arenas (Spanish)	Passive	93.1		Passive	89.6	
South Santiago (Spanish)	Passive	96.5		Passive	84.8	
Valdivia (Spanish)	Passive	81.6		Passive	94.1	
Costa Rica						
Costa Rica (Spanish)	Passive	91.4		Passive	69.6	Footnote
Mexico						
Cuernavaca (Spanish)	Passive	92.3		Passive	85.9	
Panamá						
David-Panamá (Spanish)	Passive	96.2		Passive	92.9	
Paraguay						
Asunción (Spanish)	Passive	93.2		Passive	99.3	
Peru						
Lima (Spanish)	Passive	96.6		Passive	99.2	
Uruguay						
Montevideo (Spanish)	Passive	93.1		Passive	90.8	
North America						
Barbados						
Barbados (English)	Active	87.9		Active	70.6	Footnote
Canada						
Hamilton (English)	Active	67.4	Footnote	Active	43.9	Excluded
Saskatoon (English)	Active	70.5	Footnote	Active	53.7	Excluded
USA						
Chapel Hill (English)	Active	32.0	Excluded	Passive	75.2	Excluded
Seattle (English)	Passive	80.3		Active	86.6	
Northern & Eastern Europe						
Albania						
Tiranë (Albanian)	Passive	96.8		Passive	86.6	
Estonia						
Tallinn (Estonian)	Passive	85.3		Passive	93.3	
Finland						
Kuopio County (Finnish)	Passive	96.5		Passive	98.8	
Georgia						
Kutaisi (Georgian)	Passive	89.6		Passive	88.9	
Tbilisi (Georgian)	Passive	90.8		Passive	45.9	Excluded
Latvia						
Riga (Russian 55%, Latvian 45%)	Active	95.3		Passive	94.8	
Lithuania						
Kaunas (Lithuanian)	Passive	88.9		Passive	90.5	
Poland						
Krakow (Polish)	Passive	92.5		Passive	95.4	
Poznan (Polish)	Passive	89.2		Passive	84.5	
Romania						
Cluj (Romanian)	Passive	99.0		Passive	92.8	
Russia						
Novosibirsk (Russian)	Active	95.9		Active	97.2	
Sweden						
Linköping (Swedish)	Passive	93.9		Passive	81.2	
Ukraine						
Kharkiv (Russian)	Passive	98.9		Passive	98.9	
Oceania						
Australia						
Melbourne (English)	Passive	97.3		Active	<40	Excluded
Sydney (English)	Passive	90.1		Active	34.0	Excluded
New Zealand						
Auckland (English)	Passive	94.6		Passive	92.3	
Bay of Plenty (English)	Passive	88.5		Active	76.2	Footnote
Christchurch (English)	Passive	95.5		Passive	88.2	
Nelson (English)	Passive	92.4		Passive	90.5	
Wellington (English)	Passive	88.9		Passive	96.9	

Appendix – 3

Centre name & language	Phase I Form of consent	Phase I Response %	Phase I Comment	Phase III Form of consent	Phase III Response %	Phase III Comment
Western Europe						
Austria						
Urfahr-Umgebung (German)	Active	92.6		Active	86.0	
Belgium						
Antwerp (Dutch)	Active	97.4		Active	96.6	
Channel Islands						
Guernsey (English)	Passive	91.2		Passive	90.2	
Jersey (English)	Passive	89.7		Active	78.1	Footnote
Germany						
Münster (German)	Passive	94.0		Passive	93.9	
Isle of Man						
Isle of Man (English)	Passive	91.1		Passive	88.7	
Italy						
Cosenza (Italian)	Passive	89.4		Passive	88.1	
Emilia-Romagna (Italian)	Passive	97.7		Passive	94.9	
Empoli (Italian)	Passive	97.7		Passive	91.7	
Firenze (Italian)	Passive	96.7		Passive	88.4	
Milano (Italian)	Passive	96.8		Passive	96.6	
Roma (Italian)	Passive	94.2		Passive	93.3	
Siena (Italian)	Passive	97.4		Passive	91.6	
Torino (Italian)	Passive	97.5		Passive	98.5	
Trento (Italian)	Passive	94.4		Passive	87.5	
Portugal						
Funchal (Portuguese)	Passive	96.5		Passive	73.2	Footnote
Lisboa (Portuguese)	Passive	93.1		Passive	77.5	Footnote
Portimao (Portuguese)	Passive	99.6		Passive	85.6	
Porto (Portuguese)	Passive	81.9		Passive	89.7	
Republic of Ireland						
Republic of Ireland (English)	Passive	92.1		Passive	90.9	
Spain						
Barcelona (Spanish)	Active	91.2		Passive	87.6	
Bilbao (Spanish)	Active	89.8		Active	89.4	
Cartagena (Spanish)	Passive	95.1		Passive	79.6	
Castellón (Spanish)	Passive	93.6		Passive	91.2	
Madrid (Spanish)	Passive	90.2		Passive	93.2	
Pamplona (Spanish)	Active	94.0		Active	82.6	
Valencia (Spanish)	Active	99.9		Active	78.3	Footnote
Valladolid (Spanish)	Passive	99.8		Passive	91.0	
United Kingdom						
North Thames (English)	Passive	85.4		Passive	87.7	
Scotland (English)	Passive	84.6		Passive	88.9	
South Thames (English)	Passive	86.9		Passive	84.5	
Sunderland (English)	Active	89.9		Active	91.0	
Surrey/Sussex (English)	Passive	91.0		Passive	90.8	
Wales (English)	Passive	86.1		Passive	85.2	

Table A2 ISAAC 6–7 year age group, method of consent of Phase I and III centres

	Phase I			Phase III		
Centre name and language	**Form of consent**	**Response %**	**Comment**	**Form of consent**	**Response %**	**Comment**
Africa						
Nigeria						
Ibadan (English)	Passive	72.9		Passive	86.2	
Asia-Pacific						
Hong Kong						
Hong Kong (Chinese)	Passive	97.2		Passive	96.0	
Indonesia						
Bandung (Indonesian)	Passive	92.7		Passive	88.1	
Japan						
Fukuoka (Japanese)	Passive	91.3		Passive	90.7	
Malaysia						
Alor Setar (Malay)	Passive	85.1		Passive	84.1	
Klang Valley (Malay 99%, Chinese 1%)	Passive	74.0		Passive	78.0	
Kota Bharu (Malay)	Passive	92.8		Passive	91.0	
Philippines						
Metro Manila (Tagalog)	Active	87.7		Active	45.1	Excluded
Singapore						
Singapore (English 82%, Chinese 11%, Malay 7%)	Passive	94.1		Passive	92.0	
South Korea						
Provincial Korea (Korean)	Active	90.0		Active	93.8	
Seoul (Korean)	Active	98.2		Active	97.0	
Taiwan						
Taipai (Chinese)	Passive	92.2		Passive	96.8	
Thailand						
Bangkok (Thai)	Passive	90.8		Passive	72.8	
Chiang Mai (Thai)	Passive	87.7		Passive	83.9	
Eastern Mediterranean						
Iran						
Rasht (Persian)	Passive	98.8		Passive	97.4	
Tehran (Persian)	Passive	83.0		Passive	80.9	
Malta						
Malta (Maltese 93%, English 7%)	Passive	78.2		Passive	79.7	
Sultanate of Oman						
Al-Khod (Arabic)	Passive	99.2		Passive	97.5	
Indian Sub-Continent						
India						
Chennai (Tamil 60%, English 40%)	Passive	94.6		Passive	40.1	Excluded
Jodphur (English)	Passive	76.0		Passive	70.5	
Kottayam (Malyalam)	Passive	78.1		Passive	96.4	
Mumbai [16] (Marathi 80%, English 20%)	Passive	89.7		Passive	95.5	
Mumbai [18] (Marathi 60%, English 40%)	Passive	96.0		Passive	99.2	
New Delhi [7] (English 53%, Hindi 47%)	Passive	99.2		Passive	82.4	
Pune (Marathi 75%, English 25%)	Passive	99.6		Passive	90.4	
Latin America						
Brazil						
São Paulo (Portuguese)	Passive	72.0		Passive	68.2	Footnote
Chile						
Punta Arenas (Spanish)	Passive	86.7		Passive	87.1	
South Santiago (Spanish)	Passive	74.0		Passive	90.4	
Valdivia (Spanish)	Passive	88.4		Passive	89.2	
Costa Rica						
Costa Rica (Spanish)	Passive	84.1		Passive	80.9	
Mexico						
Cuernavaca (Spanish)	Passive	94.2		Passive	84.3	
Panamá						
David-Panamá (Spanish)	Passive	97.9		Passive	92.5	
North America						
Barbados						
Barbados (English)	Active	82.2		Active	85.9	
Canada						
Hamilton (English)	Active	73.1		Active	53.8	Excluded
Saskatoon (English)	Passive	78.2		Passive	63.3	Footnote
USA						
Seattle (English)	Active	37.3	Excluded	Active	87%	

Centre name and language	Phase I Form of consent	Phase I Response %	Phase I Comment	Phase III Form of consent	Phase III Response %	Phase III Comment
Northern & Eastern Europe						
Albania						
Tiranë (Albanian)	Passive	90.5		Passive	87.6	
Estonia						
Tallinn (Estonian)	Passive	88.9		Passive	85.6	
Georgia						
Kutaisi (Georgian)	Passive	94.3		Passive	92.9	
Tbilisi (Georgian)	Passive	93.9		Passive	56.1	Excluded
Lithuania						
Kaunas (Lithuanian)	Passive	93.9		Passive	92.0	
Poland						
Krakow (Polish)	Passive	93.7		Passive	81.3	
Poznan (Polish)	Passive	85.7		Passive	82.8	
Russia						
Novosibirsk (Russian)	Active	95.8		Active	95.2	
Sweden						
Linköping (Swedish)	Passive	80.0		Passive	63.8	Footnote
Ukraine						
Kharkiv (Russian)	Passive	98.5		Passive	99.1	
Oceania						
Australia						
Melbourne (English)	Passive	90.0		Passive	81.9	
New Zealand						
Auckland (English)	Passive	90.2		Passive	84.6	
Bay of Plenty (English)	Passive	86.8		Passive	79.9	
Christchurch (English)	Passive	90.5		Passive	86.0	
Nelson (English)	Passive	97.4		Passive	92.0	
Wellington (English)	Passive	92.2		Passive	47.2	Excluded
Western Europe						
Austria						
Kärnten	Passive	97.5		Passive	86.0	
Urfahr-Umgebung (German)	Passive	95.5		Passive	92.6	
Belgium						
Antwerp (Dutch 98.1%, Turkish 0.9%, Hebrew, 0.7%, Arabic 0.3%)	Active	85.8		Active	77.8	
Germany						
Münster (German)	Active	81.2		Active	82.4	
Italy						
Emilia-Romagna (Italian)	Passive	98.2		Passive	97.0	
Empoli (Italian)	Passive	91.0		Passive	91.4	
Firenze (Italian)	Passive	96.2		Passive	83.9	
Milano (Italian)	Passive	96.1		Passive	96.6	
Roma (Italian)	Passive	94.5		Passive	86.2	
Torino (Italian)	Passive	96.9		Passive	95.9	
Portugal						
Funchal (Portuguese)	Passive	74.1		Passive	63.5	Footnote
Lisboa (Portuguese)	Passive	95.5		Passive	60.4	Footnote
Portimao (Portuguese)	Passive	95.7		Passive	83.6	
Spain						
Bilbao (Spanish)	Active	78.3		Active	77.3	
Cartagena (Spanish)	Passive	68.5	Footnote	Passive	72.3	
Castellón (Spanish)	Passive	79.8		Passive	88.1	
Madrid (Spanish)	Passive	89.8		Passive	89.0	
Pamplona (Spanish)	Passive	73.3		Passive	78.7	
Valencia (Spanish)	Active	70.5		Active	64.5	Footnote
United Kingdom						
Sunderland (English)	Active	70.0		Active	91.9	