


Awareness of infant safe sleep messages and associated care practices: findings from an Australian cohort of families with young infants

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To cite: Cole R, Young J, Kearney L, *et al.* Awareness of infant safe sleep messages and associated care practices: findings from an Australian cohort of families with young infants. *BMJ Paediatrics Open* 2021;**5**:e000972. doi:10.1136/bmjpo-2020-000972

► Additional material is published online only. To view, please visit the journal online (<http://dx.doi.org/10.1136/bmjpo-2020-000972>).

Received 1 December 2020
Revised 26 January 2021
Accepted 1 February 2021



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ABSTRACT

Objective To investigate primary infant caregiver awareness of the current national public health safe sleep messages and the associations of awareness with care practices.

Design and setting A cross-sectional survey in Queensland, Australia. All families with live babies birthed during April–May 2017 were eligible. Questionnaires were distributed when infants were approximately 3 months old.

Participants Of the 10 200 eligible families, 3341 (33%) primary caregivers participated.

Main outcome measures Participants were asked: to recall key safe sleeping messages they were aware of (unprompted); questions about their infant care practices; and to select the current, national six safe sleeping messages (prompted multi-choice).

Results Overall, the majority of families are aware of sleep-related infant mortality and sudden infant death (3178/3317, 96%); however, approximately one in four caregivers (867/3292, 26%) could not identify the current six messages to promote safer infant sleep in a multi-choice question. Despite being aware of the six key messages, some caregiver practices did not always align with advice (336/2423, 14% were not smoke-free; 349/2423, 14% were not usually supine for sleep; 649/2339, 28% employed practices which may increase risk of head or face covering; 426/2423, 18% were not receiving breastmilk).

Conclusions There is considerable scope for improvement in parent awareness and ability to recall key safe sleep messages. Awareness of advice does not always translate into safe infant care. Health promotion messaging to encourage safer infant sleep, ultimately aimed at reducing sudden unexpected infant deaths, needs more effective supportive strategies and dissemination if future campaigns are to be successful.

INTRODUCTION

Modifiable infant care practices remain the focus of sudden unexpected death in infancy (SUDI) safe sleep public health campaigns.^{1–4} However, uptake of safe sleep advice remains suboptimal.^{5–6} In Australia, a recent study of caregivers with young babies found only 13% of families routinely adopted all six

What this study adds?

- One in four families could not identify the current six key recommendations to reduce risk of sleep-related infant death.
- Caregiver awareness of safe sleep messages usually translated into safer infant sleep practices being employed; however not in all cases.
- Concerted efforts to provide consistent messaging along with practical strategies aimed at improving message recall and practice uptake are required.

What is known about the subject?

- Caregivers who employ safe sleep strategies into infant care reduce the risk of sudden unexpected death in infancy.
- The uptake of infant safe sleep advice is suboptimal with unsafe sleep practices persisting in sleep-related infant mortality cases.
- Little is known about primary infant caregiver awareness of contemporary safe sleep messages and if caregiver awareness influences care practices.

contemporary nationally supported ‘Safe Sleeping’ messages.⁷ Another local report found all sleep-related infant mortality cases had at least one contributory unsafe sleep practice, with most (86.4%) having two or more at the time of death.⁸ The major risk factors of non-supine sleep positioning, smoking, surface-sharing, not breast feeding and use of excess bedding persist,^{8,9} despite ongoing public health programmes which aim to reduce SUDI.

Emerging literature suggests explanations for suboptimal uptake of messages may include limited dissemination of safe sleep messages to new parents; large volumes of information that can be overwhelming; culturally inappropriate or insensitive messaging for priority populations; and practical difficulties

Box 1 Australia's national 'Safe Sleeping' campaign messages.⁴

Six ways to sleep baby safely and reduce the risk of sudden and unexpected death in infancy:

1. Sleep baby on back.
2. Keep head and face uncovered.
3. Keep baby smoke-free before and after birth.
4. Safe sleeping environment night and day.
5. Sleep baby in safe cot in parents' room.
6. Breast feed baby.

implementing messages into family routines.^{5,10} There is a paucity of literature exploring primary caregivers' awareness of current safe sleep messages, with no published studies evaluating parent awareness of the most recent Australian 'Safe Sleeping' campaign, comprising six key messages (box 1), since its launch in 2012.⁴

The objectives of this paper are to explore infant caregiver awareness of Australia's current safe sleep messages and if parent awareness influences practice.

METHODS

A cross-sectional survey design was used to measure safe sleep message awareness and infant care practices used by primary caregivers whose babies birthed during April–May 2017 (n=10 200) in Queensland, Australia. Questionnaires (see online supplemental appendix A) were distributed by the Queensland Registry of Births, Deaths and Marriages to mothers via postal mail when infants were approximately 3 months old. No incentives were provided for study participation. An estimated response rate of 30% was expected given Queensland survey participation rates using a similar sample frame.¹¹ Survey development and study methodology used in the 'I-CARE Queensland' Study have been reported previously in detail, together with prevalence of key infant care practices associated with Australia's current SUDI risk reduction programme.^{7,12}

Caregiver recall and awareness of the six key safe sleep messages comprising the current national campaign (herein referred to as the 'key messages') were assessed through an unprompted question (free-text responses) and prompted (multiple-choice) question. The unprompted recall question was asked first to reduce undue influence from the remaining survey questions (it is acknowledged participants may have returned to this question on the paper questionnaires). For questions where no response was provided, these were considered to be missing data and are reflected in reported denominators.

Free-text responses were analysed thematically and coded numerically using predetermined criteria, guided by current safe sleep messages,⁴ by two authors (RC, JY) to enable quantitative summary analysis, following familiarisation with the data. Differences or uncertainty in coding

of responses were evaluated by a third reviewer (LK), prior to consensus being reached. Responses were coded as accurate (consistent with key messages); inconsistent (not part of key messages but practice/behaviour may be part of previous campaigns or a recommendation from another country); and hazardous (inaccurate and potentially unsafe, for example, prone sleep position). Due to the complexity of, and debate in literature regarding bed-sharing^{6,13–15} resulting in differing national and international guidelines, a fourth category was included to capture responses where strategies to reduce risk in shared sleeping environments, consistent with the Red Nose risk minimisation approach,¹⁶ were listed.

Data analysis

Univariable and multivariable analyses were undertaken to examine the relationships between caregiver awareness of safe sleep messages and reported infant care practices with family sociodemographic, antenatal, birth and environmental characteristics. Univariable associations were assessed using χ^2 tests. Multivariable ORs were estimated using logistic regression and a backward stepwise reduction process until all variables remained significant at the 5% level. Analyses were performed using SAS V.9.4 (SAS Institute). Statistical significance was defined at 5%.

Patient and public involvement

While neither study participants nor the public were involved in study design, the questionnaire was modelled on the 2002 Queensland Infant Care Practice Study¹⁷ with the addition of contemporary questions, and piloted by 30 mothers. This process, detailed elsewhere,^{7,12} facilitated questions that were well defined, clearly understood and presented in a consistent understandable manner for parents/carers.

RESULTS

Participant characteristics and awareness of safe infant sleep messages

A response rate of 33% (3341/10 200) was achieved. Median age of caregivers was 32 years (IQR 28.7–35.1) with a median infant age of 3.7 months (IQR 2.8–4.1). When compared with the target population, participant caregivers were more likely to be partnered, born in Australia, be primiparous and less likely to be a younger mother (≤ 24 years), or identify as Aboriginal and/or Torres Strait Islander. Most participants (2439, 73%) returned the questionnaire via reply-paid postage. Caregiver characteristics and care practices used did not differ between electronic and paper completion with the exception of maternal smoking (participant characteristics have been described in detail elsewhere).⁷

While some caregivers did not recall hearing the term SUDI, which includes sudden infant death syndrome (SIDS) and fatal sleeping accidents (139/3317, 4.2%), most remembered receiving advice about safe infant sleep (3235/3325, 97%), with healthcare professionals reported

Table 1 Awareness of key safe sleeping programme messages

Responses	Total number of times response listed* or selected n (%)	Number of caregivers who provided a response within each category† n (%)
Unprompted recall question: accurate responses (ie, consistent with strategies or key messages in the current safe sleep campaign) ⁴		
<i>Message 1: sleep baby on back</i>		2791 (83.4)
Baby on back	2741 (82.7)	
No prone sleep	68 (2.0)	
<i>Message 2: keep head and face uncovered</i>		2146 (64.2)
Head and face uncovered	952 (28.5)	
Don't sleep with hats	287 (8.6)	
Feet to foot	1251 (37.5)	
Use sleeping bag	182 (5.5)	
Blankets tucked in	1137 (34.0)	
<i>Message 3: keep baby smoke-free before and after birth</i>		1111 (33.3)
Smoke-free	1101 (33.0)	
No alcohol	99 (3.0)	
No drugs	46 (1.4)	
<i>Message 4: safe sleeping environment night and day</i>		2666 (79.8)
Safe cot (ie, meets current standards)	114 (3.4)	
Safe mattress (ie, firm, flat, right size for cot)	460 (13.8)	
Nothing in cot (ie, safe bedding—no soft surfaces or bulky bedding)	1424 (42.6)	
No pillow	862 (25.8)	
No cot bumper	606 (18.1)	
No toys	1714 (51.3)	
No bulky blankets/duonas	125 (3.7)	
No sheepskin	14 (0.4)	
<i>Message 5: sleep baby in safe cot in parents' room</i>		1590 (47.6)
Room-share	888 (26.6)	
Sleep in cot/own bed (ie, don't bed-share)	1092 (32.7)	
Cot in parents' room (those who listed both Room-share and Sleep in cot/own bed)	426 (12.8)	
Not sleeping on couch with or without another person	57 (1.7)	
Not sleeping on a person/chest	23 (0.7)	
Not sleeping in sitting devices (eg, bouncer/car seat)	22 (0.7)	
<i>Message 6: breast feed baby</i>		321 (9.6)
Breast feed	321 (9.6)	
Unprompted recall question: inconsistent responses (ie, not a listed strategy or key message but not necessarily incorrect or unsafe)		
Thermoregulation	648 (19.4)	1535 (45.9)
Swaddle/wrapping	493 (14.8)	
No blankets/not too many blankets	354 (10.6)	
Dummy use	140 (4.2)	
Room/cot ventilation	107 (3.2)	
Use a baby monitor	47 (1.4)	
Immunise baby	24 (0.7)	
Other	224 (6.7)	

Continued



Table 1 Continued

Responses	Total number of times response listed* or selected n (%)	Number of caregivers who provided a response within each category† n (%)
Unprompted recall question: shared sleeping responses		163 (4.9)
Factor(s) listed to reduce risk while sharing sleep surface	163 (4.9)	
Unprompted recall question: hazardous responses		60 (1.8)
Practice(s) known to potentially increase risk	60 (1.8)	
Prompted multi-choice question: responses		3292 (98.5)
Correct selection of the current 6 key safe sleep messages	2425 (73.7)	
Incorrect multi-choice selection	745 (22.6)	
Unsure	122 (3.7)	

*Multiple responses could be listed in free-text recall question.

†For accurate responses, caregiver number was measured by recall of at least one or more responses related to the key message and/or associated strategies promulgated to support the key message.

as the most common source of advice (1978/3228, 61%). More than 1 in 10 (380/3305, 12%) parents would have liked to have received more information about safe sleep. Co-sleeping, strategies to support settling baby supine to sleep, thermoregulation and swaddling/wrapping were the most common topics where more information was sought.

Comparison of online versus postal responses for the unprompted recall question demonstrated there was either no difference or a slightly higher response prevalence for key messages among online participants (unable to go back in survey after advancing from a question), when compared with postal participants (had ability to amend responses).

A small proportion of caregivers indicated they did not know any (unprompted) recommendations to reduce SUDI (182/3295, 5.5%). Table 1 provides caregiver recall of safe sleep messages measured by unprompted recall of key messages and/or one or more associated strategies to support the key message. Of the 3113 participants who indicated they could identify a key message, less than half listed four or more accurate messages or strategies (1419, 43%); with the most common being: baby on back, no toys, safe bedding and 'feet to foot'.

Univariable analysis identified a number of family characteristics to be significantly associated with a positive awareness of the current safe sleep messages (online supplemental table). In the multivariable model, a number of variables remained independently associated after controlling for potential confounders (table 2). Analyses indicated mothers aged 25 years or older, being partnered, Australian born, and having completed tertiary education, a private antenatal model of care and awareness of terms relating to sudden infant death were independently associated with correct selection of the six key messages (prompted).

While the majority of caregivers (2425/3292, 74%) selected the correct response with the six key messages

(prompted multi-choice question), a considerable proportion were incorrect (745, 23%) or unsure (122, 3.7%).

Relationship between message awareness and practice implementation

When a correct response was recalled (unprompted), it was associated with the caregiver being significantly more likely to usually employ that practice (table 3). Similarly, families in the prompted question who correctly selected the six key messages were significantly more likely to use practices consistent with the key messages (table 4).

Placing baby on their back on a firm, flat surface was correctly identified as the safest sleep position for a healthy baby by most caregivers (2823/3288, 86%), however, only 13% (414/3286) identified that supine sleep on a flat surface was safest for a baby with reflux, while a quarter (821/3286, 25%) were unsure or did not know. A considerable proportion incorrectly selected elevating baby's head (1955/3286, 60%) and/or placing baby prone or side lying (360/3286, 11%) as the recommended sleep position for a baby with reflux. Caregivers who incorrectly identified *supine with head elevation* as the recommended sleep position for healthy babies (279/3325, 8.4%) were significantly more likely to use pillows ($p<0.0001$), rolled towels/blankets ($p=0.004$) or positioning devices (eg, wedges) ($p=0.001$), when compared with caregivers who selected *supine on a firm, flat surface* as the recommended sleep position.

Where a caregiver listed *room-sharing* in the unprompted recall, the proportion of caregivers who room-shared with baby was nearly twice the proportion of caregivers who slept their baby in a separate room (572/883, 65% vs 311/883, 35%). Of babies usually placed to sleep alone in a separate room (1251/3305, 38%), a quarter (311/1251, 25%) had listed room-sharing as a key message, and a considerable proportion used a baby monitor compared with those who slept baby in a separate room and did

Table 2 Characteristics remaining significantly associated with awareness of safe sleeping programme messages in multivariable analysis

	Prompted awareness Correct multi-choice selection of the current 6 key messages OR (95% CI)
Maternal age	
24 years or younger	1.00
25 years or older	1.88 (1.41 to 2.52)
Marital status	
Single (never married, separated, widowed)	1.00
Partnered (married/de facto)	1.55 (1.07 to 2.24)
Country of birth	
Overseas born	1.00
Australian born	1.36 (1.11 to 1.67)
Education level*	
Less than tertiary completed	1.00
Tertiary completed	2.13 (1.75 to 2.58)
Model of maternity care†	
Public	1.00
Private	1.35 (1.13 to 1.63)
Heard of terms SUDI and SIDS	
No	1.00
Yes	2.04 (1.36 to 3.07)

*Tertiary education in Australia includes training completed in both higher education (including universities leading to a Bachelor, Master or Doctoral degree) or vocational education and training (providing certificate and diploma qualifications).

†Australia's healthcare system has two models: the public health system where Australian public access care for free or at a lower cost via a tax-funded scheme, and the private health system where health service providers are owned and managed privately and services provided at the expense of the client.

SIDS, sudden infant death syndrome; SUDI, sudden unexpected death in infancy.

not use a monitor (757/1242, 61% vs 485/1242, 39%). Although almost one-third of caregivers (1061/3267, 33%) listed *sleep baby in a cot or own bed* as a key message, over half (543/1061, 51%) had shared a sleep surface with their baby in the last 2 weeks.

Caregivers who listed *keep baby smoke-free* were proportionately less likely than families who did not list *keep baby smoke-free* to live in a household with one or more current smokers (126/1091, 12% vs 410/2200, 19% ($p<0.0001$)), or identify maternal smoking during pregnancy (26/1089, 2.4% vs 109/2192, 5.0% ($p=0.0004$)) or post partum (43/1091, 3.9% vs 148/2200, 6.7% ($p=0.0013$)). This is consistent with the prompted findings where caregivers who correctly selected the key messages, compared with those who were unsure or incorrect, were more likely to have a smoke-free household (2087/2423, 86% vs 669/869, 77% ($p<0.0001$)).

Information sources for safe sleep advice and message awareness

Most caregivers (3024/3233, 94%) received safe sleep advice from their nurse or midwife. Nearly half (1573/3228, 49%) indicated their nurse or midwife was their main source of safe sleep advice with the next most common sources being: previous experience, books/brochures, internet and family/friends (table 5). Prevalence of recall was statistically significantly lower among participants whose main source of advice was a health-care professional, compared with another advice source, for key messages: keeping baby smoke-free (633/1977, 32.0% vs 448/1250, 35.8% ($p=0.025$)), safe cot in parents' room (236/1978, 11.9% vs 182/1250, 14.6% ($p=0.0302$)) and breast feed baby (117/1977, 9.0% vs 142/1250, 11.4% ($p=0.026$)).

DISCUSSION

The I-CARE Queensland Study investigated parental awareness of Australia's current six 'Safe Sleeping' public health programme messages, launched in the 2012 'Safe Sleep, My Baby' campaign. Numerous campaigns have targeted SUDI reduction in Australia since 1991, and this study confirms the message is being shared, heard and applied.

Some caregivers noted they were less familiar with the term SUDI compared with SIDS. During the last decade, the term SUDI (inclusive of, but not limited to, SIDS, fatal sleeping accidents and deaths undetermined)

Table 3 Unprompted message awareness and practice implementation

Key safe sleep messages*	Infant care practices employed consistent with associated key message				P value
	Caregiver recalled message		Caregiver did not recall message		
	n	%	n	%	
Baby on back	2303/2735	84.2	442/574	77.0	<0.0001
Head and face uncovered	721/926	77.9	1426/2252	63.3	<0.0001
Keep baby smoke-free	965/1091	88.5	1790/2200	81.4	<0.0001
Sleep in cot in parents' room	162/421	38.5	909/2876	31.6	0.005
Breast feed baby	291/321	90.7	2275/3002	75.8	<0.0001

*Key message 'safe sleeping environment' excluded from analysis due to responses capturing part of, but not all, key components of the 'safe sleeping environment' message (ie, safe cot, safe mattress, safe bedding).

Table 4 Prompted message awareness and practice implementation

	Infant care practices employed consistent with associated key message				
	Correct selection of the current six key messages		Unsure or incorrect selection of the messages		P value
	n	%	n	%	
Safe sleep message					
Baby on back	2074/2423	85.6	672/887	75.8	<0.0001
Head and face uncovered	1690/2339	72.3	458/840	54.4	<0.0001
Keep baby smoke-free	2087/2423	86.1	669/869	77.0	<0.0001
Safe sleeping environment	876/2414	36.3	230/881	26.1	<0.0001
Sleep in cot in parents' room	849/2418	35.1	222/879	25.3	<0.0001
Breast feed baby	1997/2423	82.4	570/901	63.3	<0.0001

has become more widely used in Australian safe sleep messaging,^{4 18} in an effort to focus on modifiable risk and protective factors associated with potentially avoidable infant mortality^{19 20}; yet there remains substantial room for improvement. With continued inconsistency and confusion in these classification terms identified as an issue for pathologists and researchers working in the field,²¹ this poor knowledge and understanding of terms by the general public is not surprising.

Misinformation relating to optimal positioning for infants with mild oesophageal reflux appears to pervade in this Australian population. A concerning proportion of parents adopted inclined infant sleep positions or used hazardous practices²² despite national safe sleep recommendations to the contrary.^{4 23} These findings highlight the importance of caregivers understanding the evidence underpinning safe sleep messages, particularly relevant for families with infants born premature or with medical needs.

Significant associations between knowledge of safe infant sleep practices and application of these practices

were clearly evident in our study, affirming the value of clear public health campaigns. However, messages may not be reaching some vulnerable groups of the population. One in four families from a relatively socially advantaged population,⁷ could not identify the current six key recommendations to reduce risk of sleep-related infant death in a multi-choice question. This finding is important to inform future public health initiatives as social inequalities have widened in recent decades with infant deaths known to occur most frequently in the context of unsafe sleep environments^{6 24} among families experiencing socioeconomic disparities, with poorer access to healthcare and educational opportunities.²⁴⁻²⁷

Further, parent recall responses were inconsistent with key messages, illustrating limited awareness and highlighting misconceptions associated with suboptimal infant care practices. We propose that this is contributed to by the number and complexity of key messages in the current national safe sleeping programme. Specifically, the fourth key message 'safe sleeping environment' is broad and imprecise; simple,

Table 5 Sources of advice from where safe sleeping information received

	Main source of safe sleep advice			Any safe sleep advice received from source		
	Rank	n=3228	%	Rank	n=3233*	%
Nurse/midwife	1	1573	48.7	1	3024	93.5
Previous experience	2	314	9.7	5	1135	35.1
Books/brochures	3	256	7.9	2	1579	48.8
Internet	4	249	7.7	6	1099	34.0
Family/friends	5	249	7.7	7	1059	32.8
Antenatal classes	6	241	7.5	4	1303	40.3
Doctor/GP	7	164	5.1	3	1322	40.9
Other:	8	137	4.2	11	134	4.1
Social media (Facebook, Twitter)	9	33	1.0	8	571	17.7
Media (TV, radio, magazines)	10	11	0.3	9	235	7.3
Baby store/shop/expo	11	1	0.0	10	211	6.5

*Participants could list more than one source of advice.
GP, general practitioner.

explicit and targeted message wording would be of benefit.^{28 29} However, oversimplified messaging may conversely lead to poor comprehension with parents not understanding how and/or why a recommendation is important, rendering the messaging ineffective. It has been suggested the rationale and justification for the mechanisms as to *how* the strategy works needs to be clearly communicated to parents,³⁰ as it has been demonstrated that when there is an understanding of a physiological link between advice and risk, implementation of practice is enhanced.¹⁰

Providing reliable and consistent safe infant sleep advice is a global public health problem and efforts at all system levels are recommended. While there was statistical significance on recall of messages based on sources of advice, this significance was relatively small and not considered to be of clinical significance. We live in an information-rich period where access and advice sources, such as the internet and social media, have no national boundaries or measures of accountability for accuracy.^{6 19} It is therefore understandable parental confusion exists when international, national and even local guidelines and policies are inconsistent.^{1 2 4 18 31} Similarly, if key messages appear non-specific or vague with multiple concepts (such as *safe sleeping environment*), without easily accessible adjunct information, this may be open to broader interpretation and the actual strategy of, for instance having no soft surfaces in the sleep space, is misplaced.

This study identified that despite parental awareness of a key message, it was not always followed. While it was beyond the scope of this study and the cross-sectional design used, to fully understand the reasons for low uptake of key messages into practice, previous studies have reported exhaustion, fatigue, cultural heritage, impractical advice and lack of understanding as influencing these choices.^{6 32 33} If socially advantaged parents, who are more likely to be aware of the advice and associated risks, are not always following the messages for every infant sleep, concerted efforts must be made to realise strategies and interventions, especially for families experiencing social vulnerabilities. Simply instructing families on 'what to do' and 'what not to do' is likely to be ineffective when families are presented with the complexities of parenting, particularly during the night; situational factors may strongly influence infant care choices and sleeping behaviours.⁶

A recent consensus forum which drew on international content expertise has prioritised strategies for stakeholder consideration in the revision of the next Australian safe sleep campaign³¹ which will aim to maximise reach to populations which experience vulnerabilities associated with the highest infant mortality. Directly informed by results of the I-CARE Study, the top four priority themes for future campaign messaging were identified as: sleep position, sleep space, smoking and surface-sharing.³⁴

Limitations

The aim of this study, to explore parental awareness of contemporary safe infant sleep messages and any associations with infant care practices used, was achieved in a large contemporary cohort of Australian families. As with any self-report cross-sectional study, social desirability bias and non-response bias must be considered when interpreting findings. Our sample, as reflected by our participant characteristics, comprised a relatively socially advantaged population, likely to have access to, and be more receptive of, health promotion opportunities.²⁴⁻²⁷ Furthermore, participants were from Queensland, an Australian state experiencing consistently higher infant mortality since the first national risk reduction campaign,³⁵ care is therefore required in generalising and interpreting information. Further investigation to explore caregiver practice and awareness in other Australian cohorts is recommended; particularly studies investigating challenges with implementing safe sleeping recommendations from parent perspectives.

Conclusion

This study has identified which public health messages aimed at reducing SUDI that caregivers are most likely to recall, and that the awareness of advice usually translates into safer practice; although, not in all cases. Understanding the difficulties parents experience in implementing safe sleep messages is an area recommended for further research in order to ensure future campaigns are founded on evidence-based strategies which are easy to understand, culturally acceptable and practical for parents to implement.

The mode of delivery, number and clarity of messages, along with consistency of message wording, may represent important modifiable factors in improving effectiveness of future public health campaigns. Safe, practical strategies to promote caregiver awareness and recall, together with promotion of understanding and value of the evidence underpinning safe sleep messages, need to be explored. Moreover, effective delivery of messaging requires ongoing evaluation and investigation to ensure future campaigns aimed at continuing to reduce infant mortality are successful and effective.

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Contributors RC, JY and LK conceptualised the study. RC and JY coordinated data collection, collating and processing data. RC, JY and JMDT analysed the results. JY, LK and JMDT provided expert guidance on the analysis plan. All authors contributed to the interpretation of results. RC prepared the manuscript with intellectual input from JY, LK and JMDT. All authors critically reviewed and have approved the manuscript.

Funding The I-CARE Queensland Study was supported by Wishlist and the USC 2017 Roberta M C Taylor Rural and Remote Nursing and Midwifery Scholarship.

Competing interests None declared.

Patient consent for publication Not required.

Ethics approval Ethical approval was obtained from the institution's Human Research Ethics Committee (S/17/1032) with governance approval provided by the Registry of Births, Deaths and Marriages. Informed consent was implied by the return of a completed questionnaire.



Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request.

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