Tuesday December 14, 2021, 1 pm GMT+1

Nick YOUNG[1,2*], Richard A. SHARPE[1,2,3], Rosa BARCIELA[1,2,4], Gordon NICHOLS[2], Keith DAVIDSON[5], Elisa BERDALET[6], Lora E. FLEMING[1,2]

Marine harmful algal blooms and observed human health effects – what is the evidence?

[1] European Centre for Environment and Human Health, Truro, UK
[2] University of Exeter Medical School, Exeter, UK
[3] Public Health, Cornwall, Truro, UK
[4] Met Office, Exeter, UK
[5] Scottish Association for Marine Science, Scottish Marine Institute, Oban, UK
[6] Institute of Marine Sciences (CSIC), Passeig Marítim de la Barceloneta, Barcelona, Spain
* Ny252@exeter.ac.uk

Exposure to harmful algal blooms (HABs) can lead to well recognised acute patterns of illness in humans. We carried out a scoping review using established methodology to map the evidence for associations between marine HABs and observed both acute and chronic human health effects. A systematic and reproducible search of publications from 1985 until May 2019 was conducted using diverse electronic databases. Following de-duplication, 5301 records were identified, of which 380 were included in the final qualitative synthesis. Most studies (220; 57.9%) related to Ciguatera Poisoning. Anecdotal and case reports were the most frequent study types (242; 63.7%), whereas there were fewer formal epidemiological studies (35; 9.2%). Only four studies related to chronic exposure to HABs. Few studies reported the use of human specimens for confirmation of the cause of illness (32; 8.4%). This study highlighted gaps in the evidence base including a lack of formal surveillance and epidemiological studies, limited use of toxin measurements in human samples, and a scarcity of studies of chronic exposure. Future research and policy should provide a baseline understanding of the burden of human disease to inform the evaluation of the current and future impacts of climate change and HABs on human health.

Marine harmful algal blooms and human health:

A systematic scoping review

Nick Young 14.12.21 ny252@exeter.ac.uk

University of Exeter Medical School

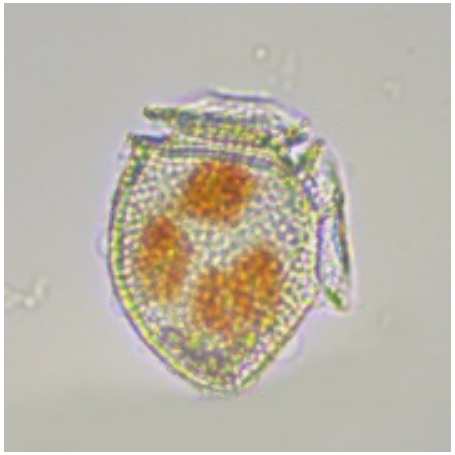
European Centre for Environment & Human Health

Met Office

NERC Science of the Environment

My background

- Natural Environment Research Council and Met Office – funded PhD student *"**Understanding of the connections between weather and climate, Marine Harmful Algal Blooms and Human Health for the UK**"*
- *Part-time epidemiologist (medical doctor) with UK Health Security Agency*
- *MScs in Epidemiology and Oceanography*



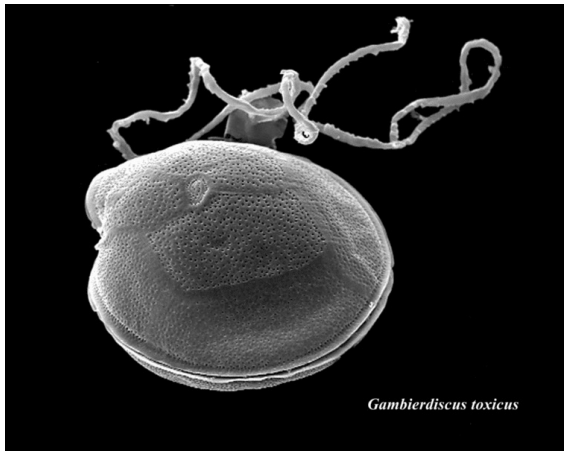
Contents

Scoping review

1. Aims
2. What is a scoping review?
3. Methods
4. Results
5. Limitations and insights
6. Recommendations
7. Acknowledgements

1. Aims

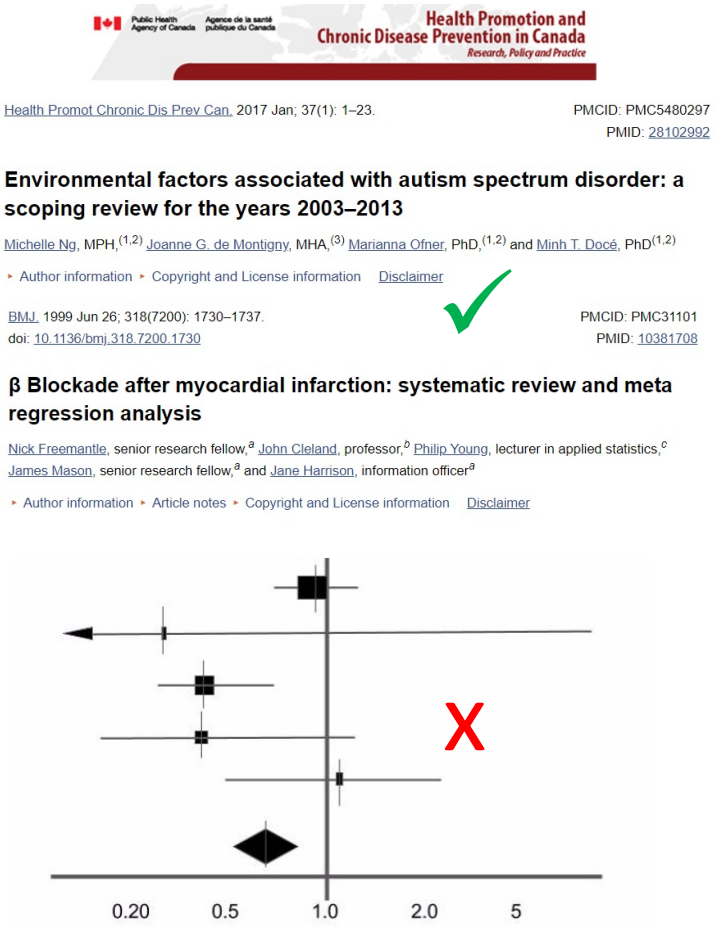
- Map existing evidence for the associations between exposure to marine HABs and observed human health effects
- Identify existing gaps in the evidence base
- Highlight research and policy directions and priorities.



2. What is a scoping review?

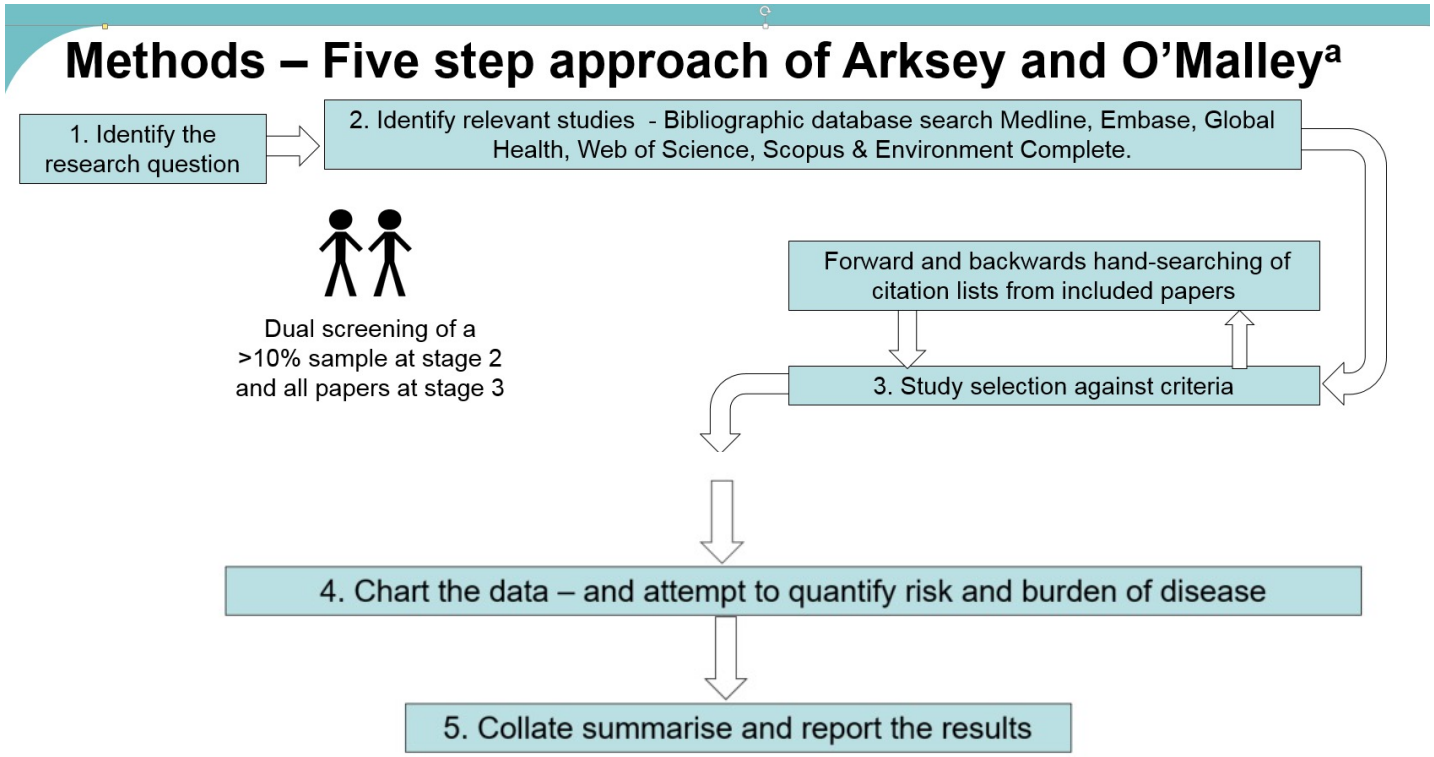
- A comprehensive, systematic and reproducible review
- Establish the range of the evidence
- Address a broad question across varied study types and disciplines
- Highlight research agenda
- Do not focus on a single research outcome - thematic description rather than a formal synthesis

Arksey, H., O'Malley, L., 2005. Scoping studies: towards a methodological framework. Int. J. Soc. Res. Methodol. 8(1), 19-32



Where is Step 1?

3. Methods - Step. 2



1985 to date

Arksey, H., O'Malley, L., 2005. Scoping studies: towards a methodological framework. Int. J. Soc. Res. Methodol. 8(1), 19-32

Inclusion and Exclusion criteria

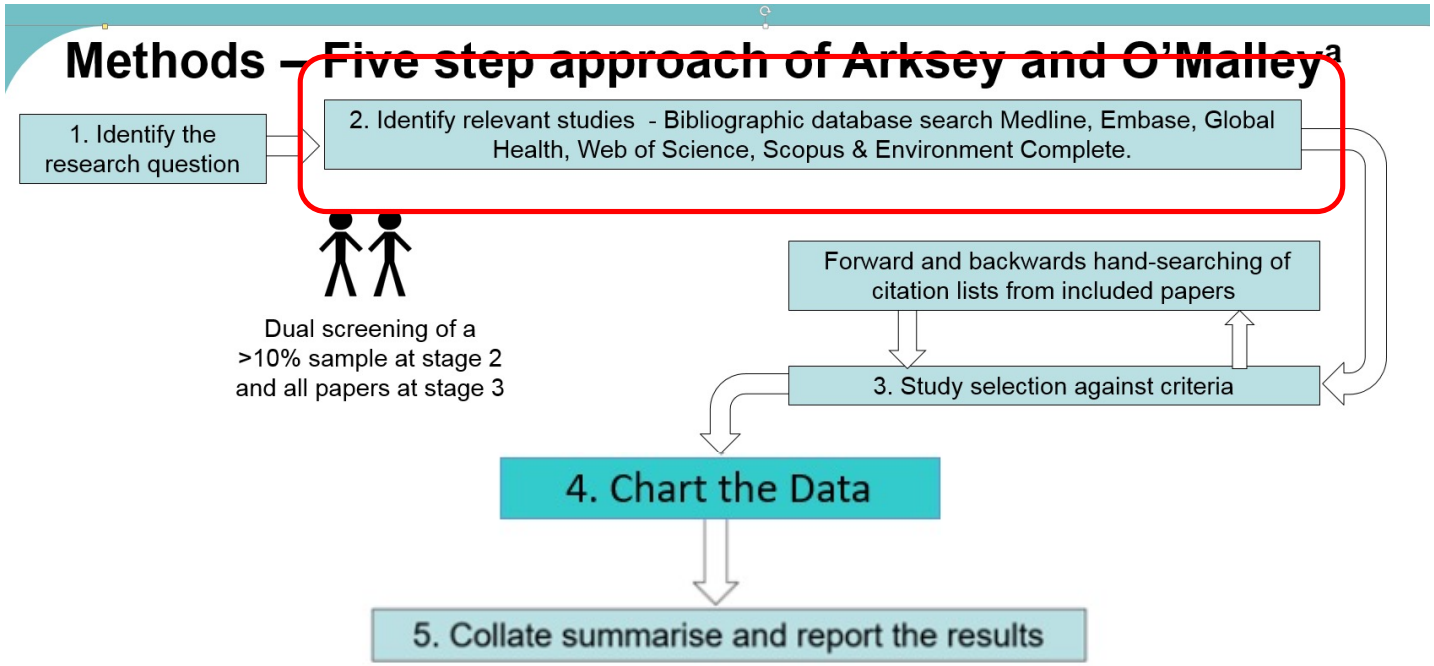
(PECO - Population Exclosure Context Outcome)

PECO criteria	Include		Exclude
Population	✓ Human	×	Human Cell lines
		×	In vitro
Exposure	✓ Direct or indirect exposure to microalgae or micro-algal derived toxins	×	Tetrodotoxin, cyanobacteria
		×	Chelonitoxin
		×	Scombroid
	✓ Bloom event not-required	×	Exposure via desalinated water
	✓ Exposure routes include: ingestion; inhalation; skin contact; sexual transmission; eye contact; other	×	Experimental exposure
		×	Food supplements
		×	*Lyngbya*
		×	*Pfiesteria*
	✓ Routes include consumption through a vector such as seafood	×	Exposure to palytoxin via coral/cnidarians/zoanthids
Context	✓ Marine/Estuarine/Coastal	×	Freshwater including lakes
	✓ Worldwide		

PECO criteria	Include		Exclude
Outcomes	✓ Adverse health effects including but not exclusively: Death, ASP, NSP, PSP, DSP, CP, AZP, Effects of Palytoxin-like toxins or "Ostreopsis spp. algal syndrome, gastrointestinal illness, respiratory illness, neurological illness, hospital admissions	×	Economic impacts
		×	Wider societal impacts – tourism/beach closure.
		×	Haff disease
		×	Exposure data only
	✓ Wellbeing impact – if estimates of adverse wellbeing		
	✓ Treatment if cases reported		
Study type	✓ English language	×	Non-English language
	✓ 1985 – search date	×	Pre-1985
	✓ Case reports	×	Editorials
	✓ Epidemiological studies	×	Review papers
	✓ Surveys	×	"No illness reported"
	✓ Published surveillance data	×	Conference abstracts
	✓ Incidence studies		
	✓ Modelling studies estimating incidence		

Where is Step 1, 3 or ...?

Methods - Step. 2



1985 to date

Step 2. Identifying relevant studies

12th May 2019 search of:

- ✓ MEDLINE
- ✓ PubMed
- ✓ Global Health
- ✓ SCOPUS
- ✓ Environment Complete
- ✓ Web of Science

Search Strategy

Exposure

[[Amnesic Shellfish Poisoning OR Pseudo-nitzschia OR Azaspiracid shellfish poisoning OR amphidoma* OR Ciguat* OR Gambierdiscus OR Diarrhetic shellfish poisoning OR dinophysis* OR Neurotoxic shellfish poisoning OR Karenia OR ostreopsis OR Paralytic shellfish poisoning OR alexandrium OR algal bloom* OR red tide* OR dinoflag* OR phytoplankton bloom* OR marine biotoxin* OR toxic microalga*]

OR

[[algal bloom* OR red tide* OR dinoflag* OR phytoplankton bloom* OR marine biotoxin* OR toxic microalga* OR shellfish OR mussels OR bivalve* OR clam OR scallop OR oyster OR gastropod*OR crustacean OR crab OR mollusc* OR Fish OR consum* OR seafood]

AND

[Pectenotoxin* OR Yessotoxin* OR Cyclic Imine* OR Spirolide* OR Gymnodin*OR Pinnatoxin* OR pteriatoxin* OR saxitoxin* OR Domoic acid OR Azaspiracid* OR Brevetox* OR palytox* OR okadaic acid*]]]

AND

Outcome

[[epidem* OR outbreak* OR inciden* OR admission* OR admitted* OR hospitalisation* OR hospitalization* OR fatal* OR case report* OR case-control OR cohort]

OR

[[Case* OR man OR woman OR men OR women OR individual* OR resident* OR consumer* OR Asthmatic* OR patient* OR child* OR neonate* OR lifeguard* OR occupational OR population*]

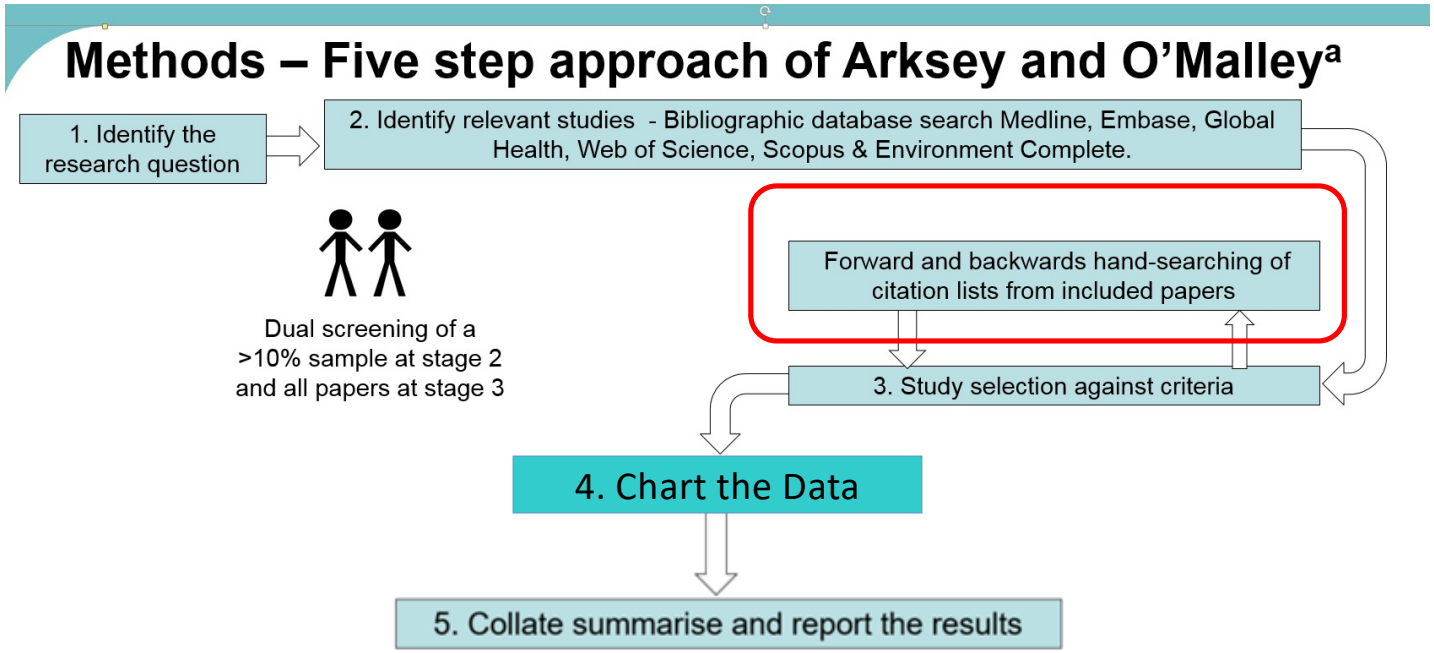
AND

[Death* OR illness* OR intoxication* OR poisoning* OR respiratory OR gastrointestinal OR neurological OR neurodegen* OR ocular OR eye OR derma* OR skin OR paraly* OR cardiovascular OR symptom* OR sexually transm* OR sexual transm*]]]

Deduplication – The Bramer method

- *Bramer, W.M., Giustini, D., de Jonge, G.B., Holland, L., Bekhuis, T., 2016. De-duplication of database search results for systematic reviews in EndNote. J. Med. Libr. Assoc. 104(3), 240.*

Methods - Step. 2



1985 to date

Backwards and Forwards citation searching

- **Backwards** - hand search reference lists from *included* papers

2. European Commission. Regulation (EC) No. 853/2004 of the European Parliament and of the Council 29 April 2004 laying down specific hygiene rules for on the hygiene of foodstuffs. 30.4.2004: L 139/55. [Accessed 7 Aug 2019]. Available from: https://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2004:139:0055:0205:en:PDF

3. Valdiglesias V, Prego-Faraldo MV, Pásaro E, Méndez J, Laffon B. Okadaic acid: more than a diarrheic toxin. Mar Drugs. 2013;11(11):4328-49. https://doi.org/10.3390/md11114328 PMID: 24184795

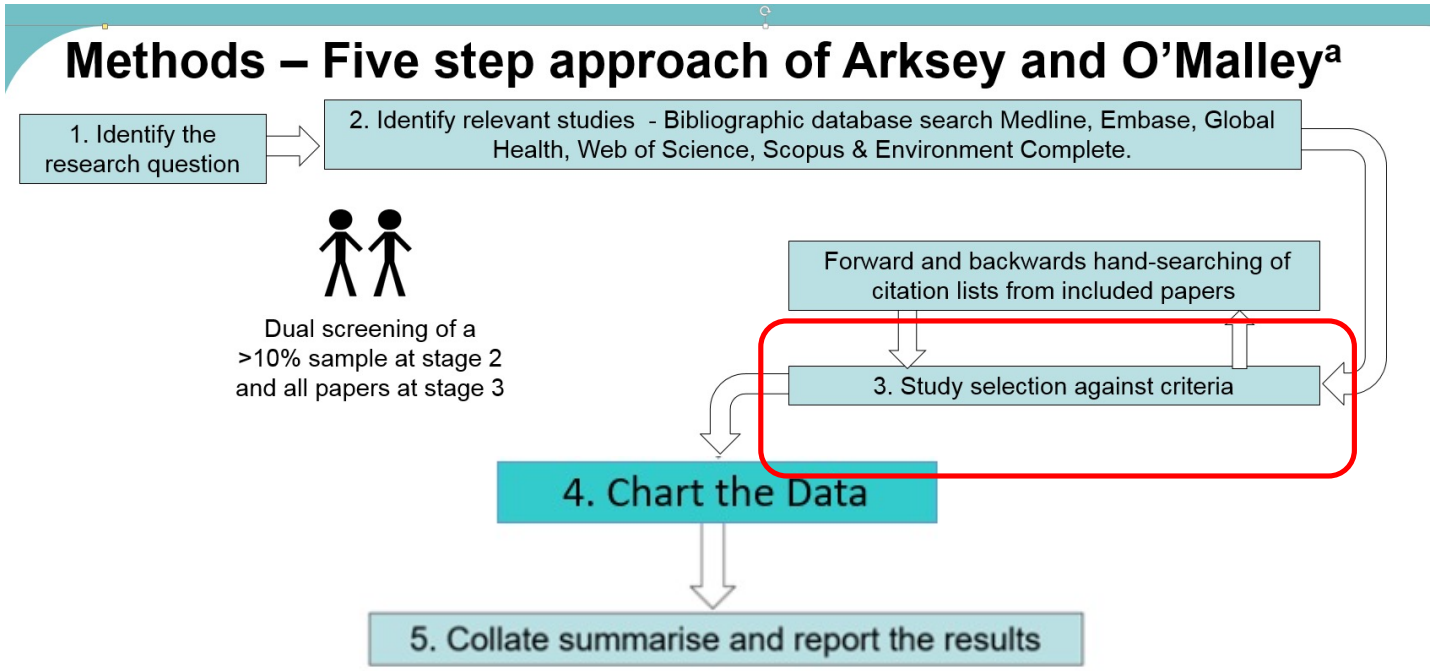
4. Hossen V, Jourdan-da Silva N, Guillois-Bécel Y, Marchal J, Krys S. Food poisoning outbreaks linked to mussels contaminated with okadaic acid and ester dinophysistoxin-3 in France, June 2009. Euro Surveill. 2011;16(46):20020. https://doi.org/10.2807/ese.16.46.20020-en PMID: 22115047

- **Forwards**
- Any study that has cited an included paper was considered using Web of Science

6
Citations

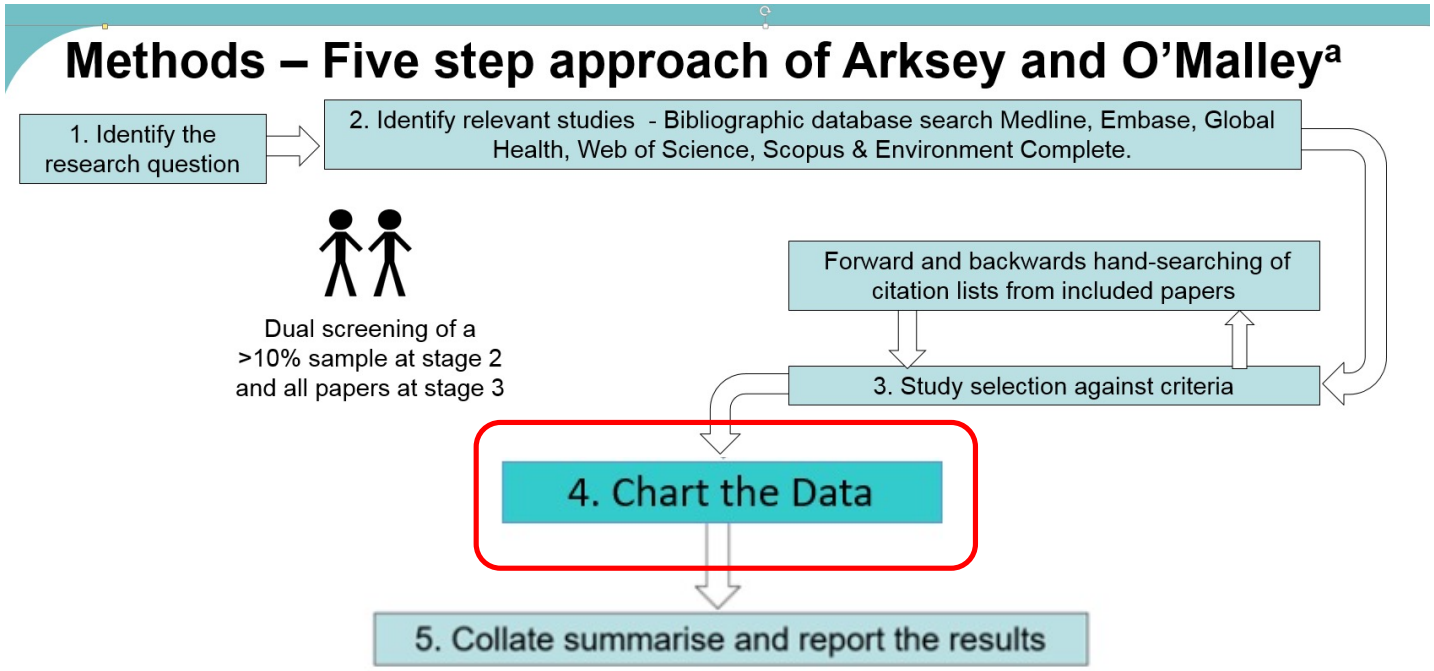
38
References

Methods - Step. 2



1985 to date

Methods - Step. 2

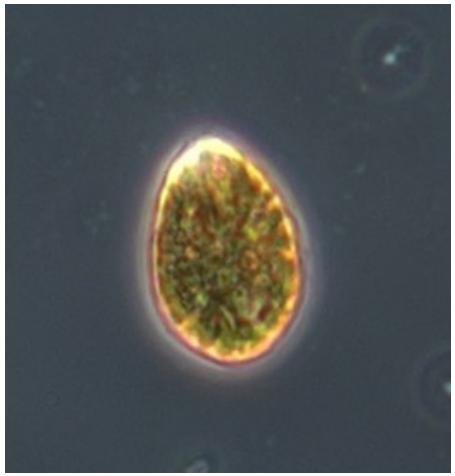


1985 to date

Charting the data

Clinical Syndrome	HAB toxin*	Notes
Amnesic Shellfish Poisoning (ASP)	Domoic acid	
Azaspiracid Shellfish Poisoning (AZP)	Azaspiracid	
Ciguatera Poisoning (CP)	Ciguatoxin	
Diarrhetic (Diarrheic) Shellfish Poisoning (DSP)	Okadaic acid (dinophysistoxins)	
Neurotoxic Shellfish Poisoning (NSP) and brevetoxin associated respiratory irritation	Brevetoxins	
Palytoxicosis	Palytoxin	Refers to seafood intoxication only
Effects of Palytoxin-like toxins or "*Ostreopsis* spp. algal syndrome"	Attributed to Palytoxin-analogues.	Respiratory and cutaneous irritation after postulated exposure to seawater and/or aerosol during *Ostreopsis* spp. blooms
Paralytic Shellfish Poisoning (PSP)	Saxitoxin	

Exposure and outcome - Acute *versus* chronic



Charting the data – study types

- anecdotal mention of cases
- case reports
- routine surveillance data,
- formal epidemiologic studies designs
- auxiliary studies
- trials of treatment
- biological marker/genomic

Charting the data - Confirmation

Toxin detected in **remnants** of food consumed.	Toxin detected in **same batch** food consumed.	**Toxin** in **same area** of food production/exposure **within one week** of harvesting/exposure.	Harmful algal **species** in **same area** of food production/exposure **within one week** of harvesting/exposure.	**Toxin** in **same area** of food production/exposure **outside of one week** of harvesting/exposure.
Harmful algal **species** in **same area** of food production/exposure **outside of one week** of harvesting/exposure.	**Direct measure of exposure** – for example personal or ambient air monitoring.	Based on **clinical symptoms only**.	Toxin or metabolites detected in **human specimens**.	**Human samples negative** for toxin or metabolites.

Adapted from Tubaro, A., Durando, P., Del Favero, G., Ansaldi, F., Icardi, G., Deeds, J., Sosa, S., 2011. Case definitions for human poisonings postulated to palytoxins exposure. Toxicon 57(3), 478-495.

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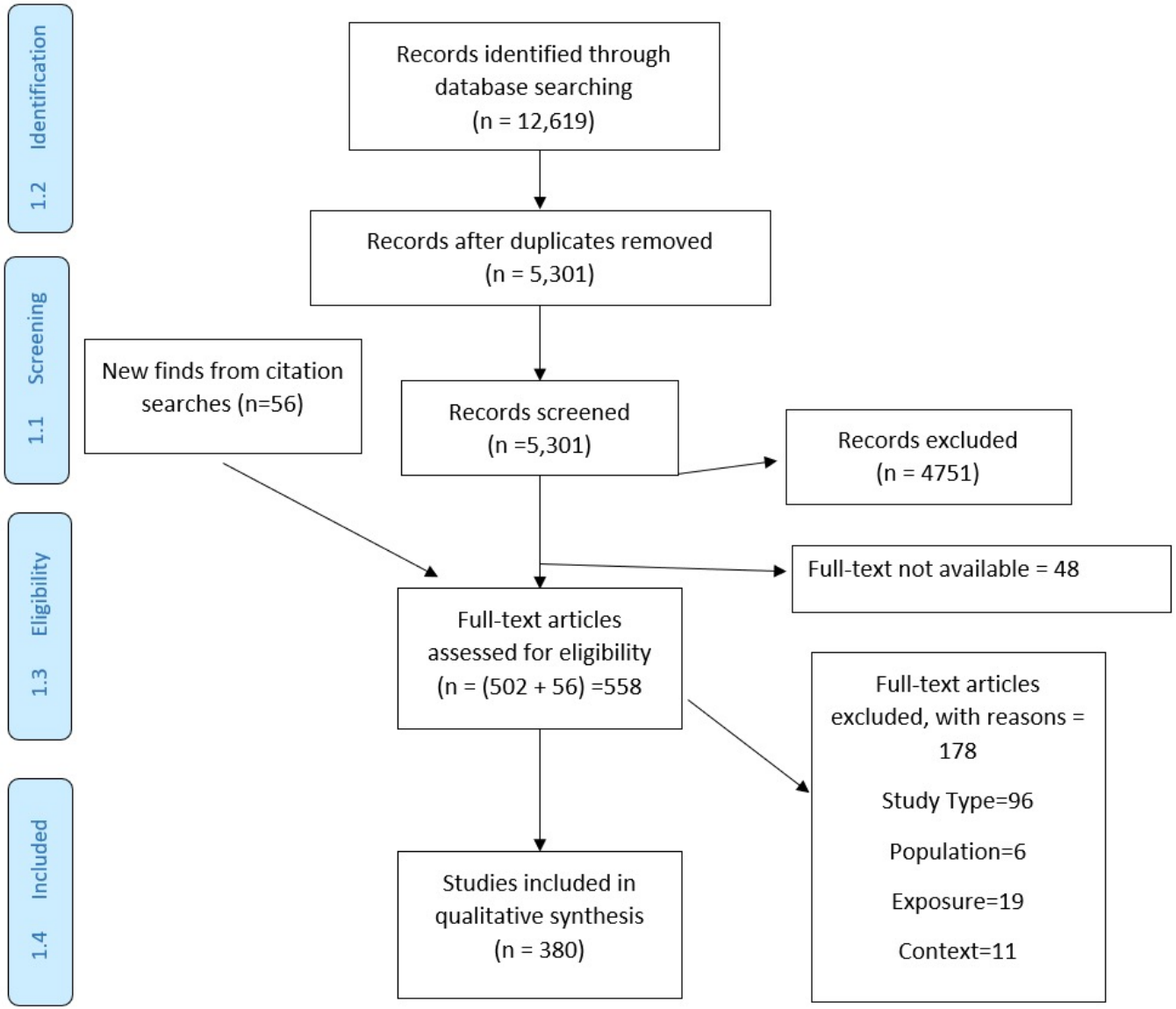
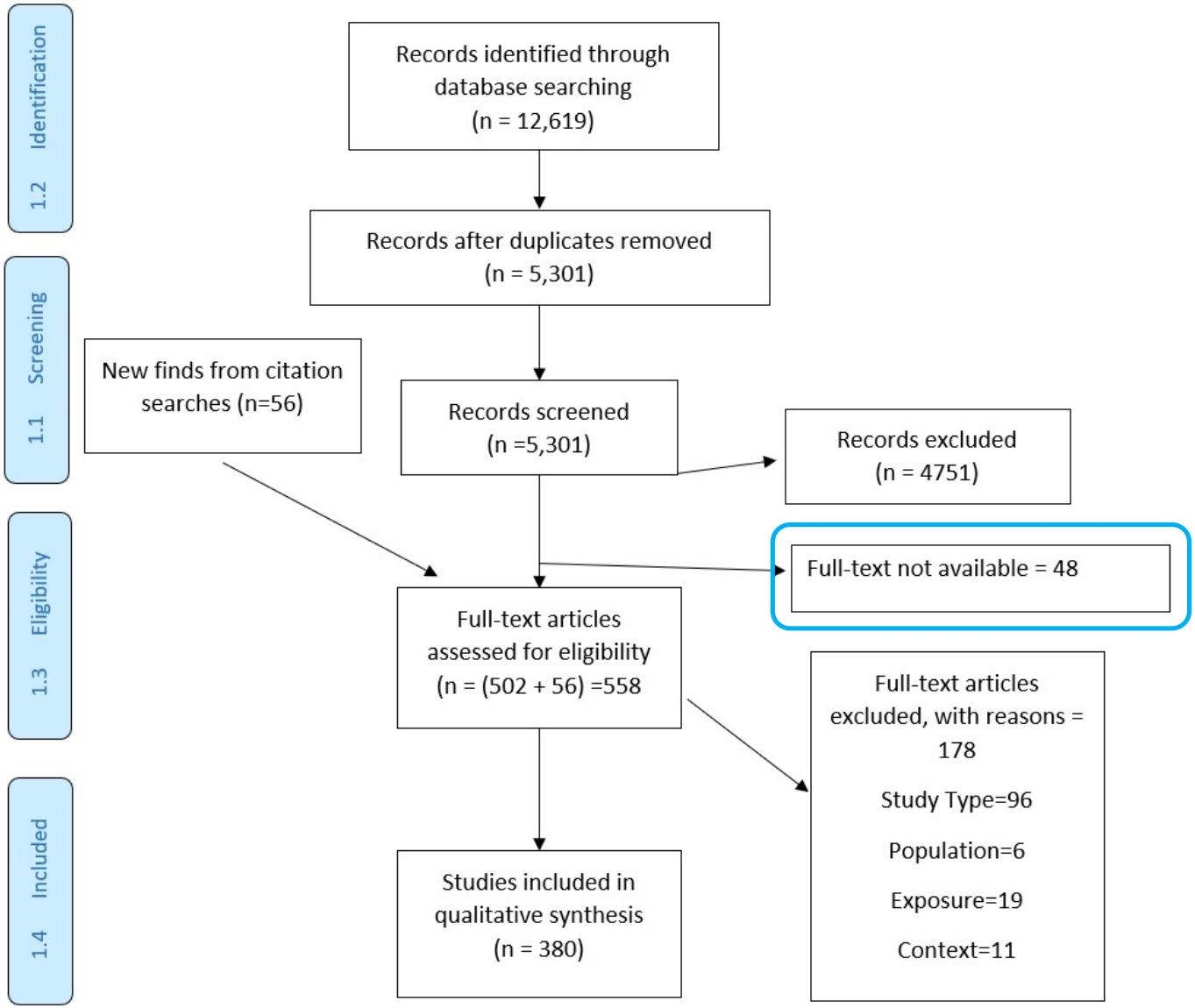
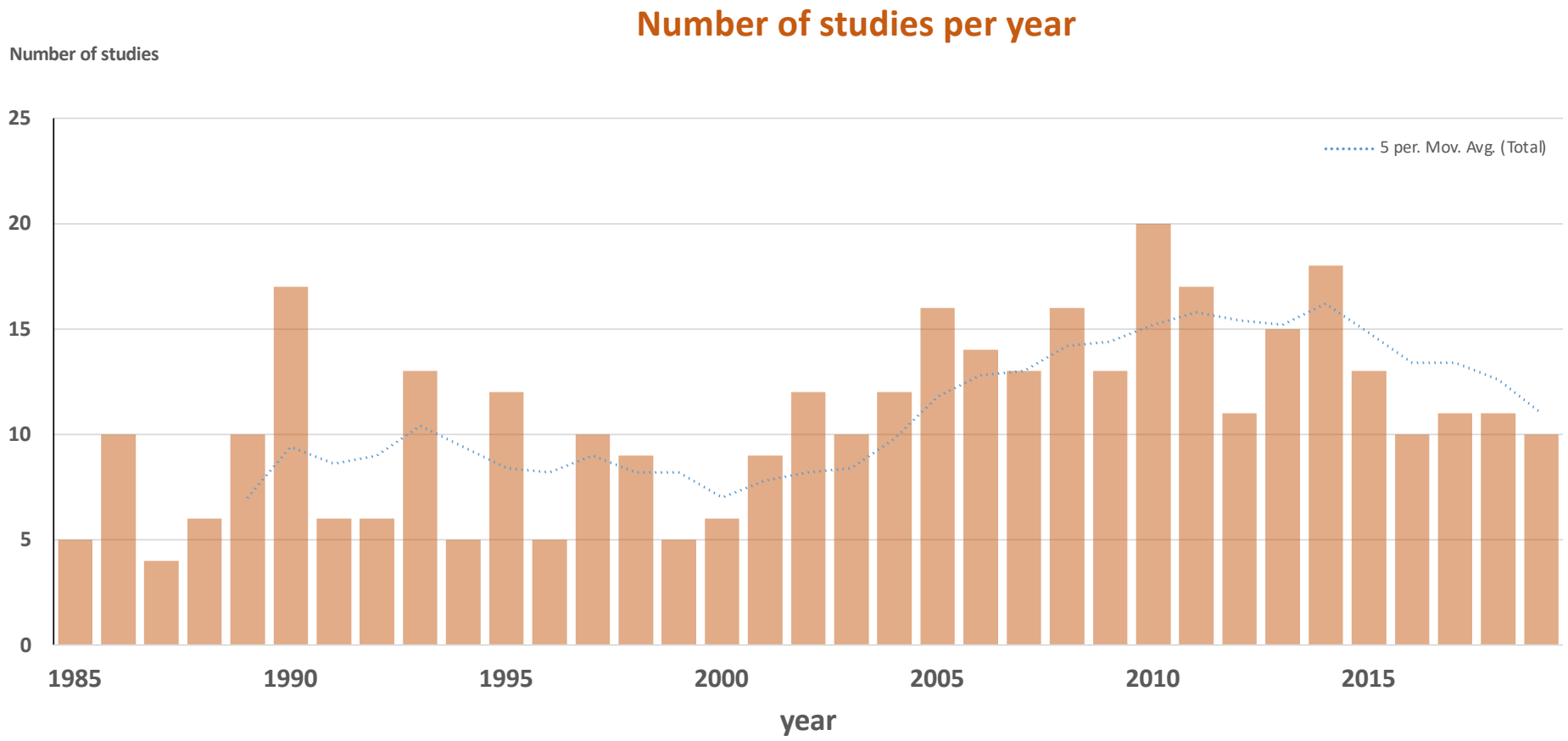
Results

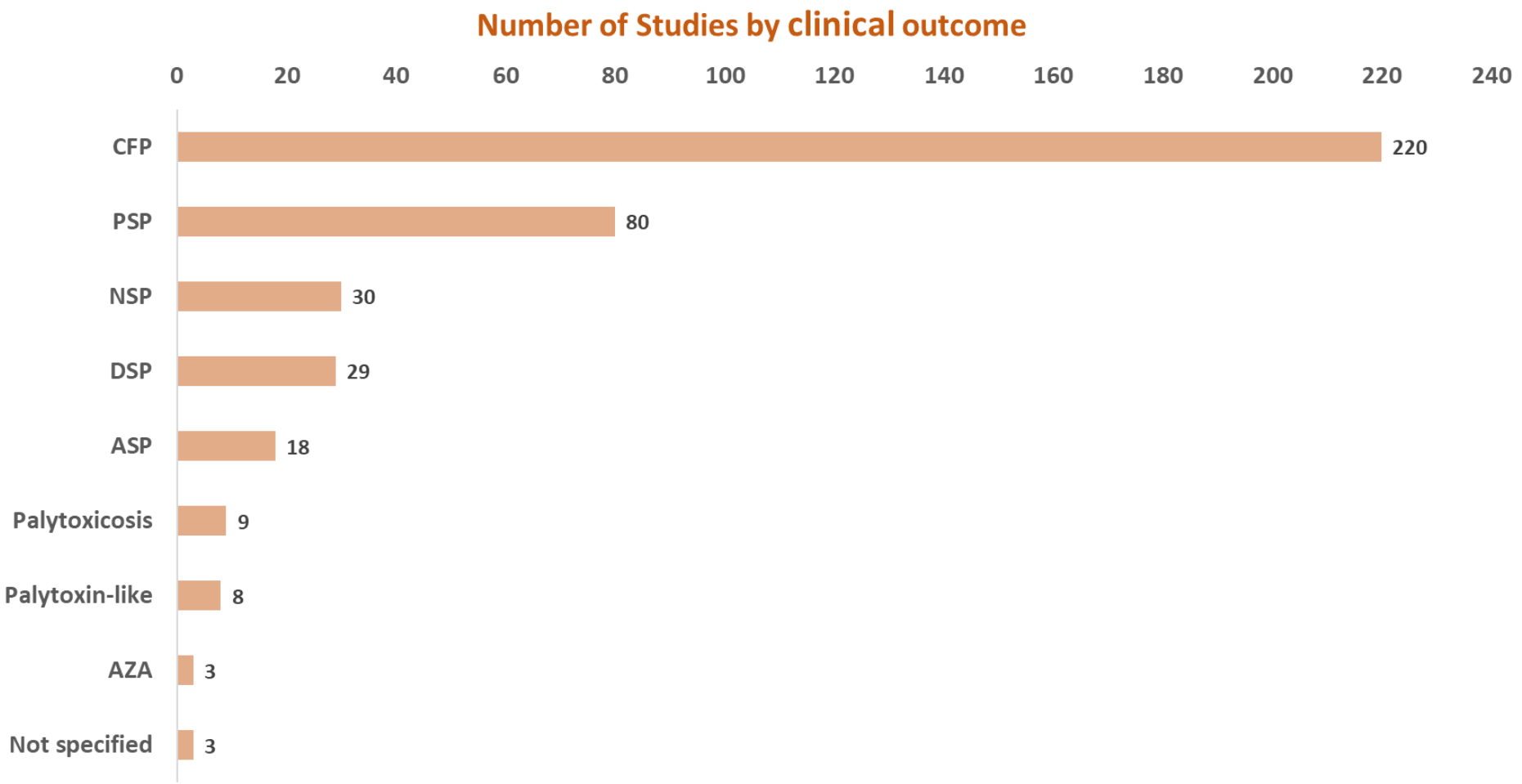
4. Results (PRISMA)

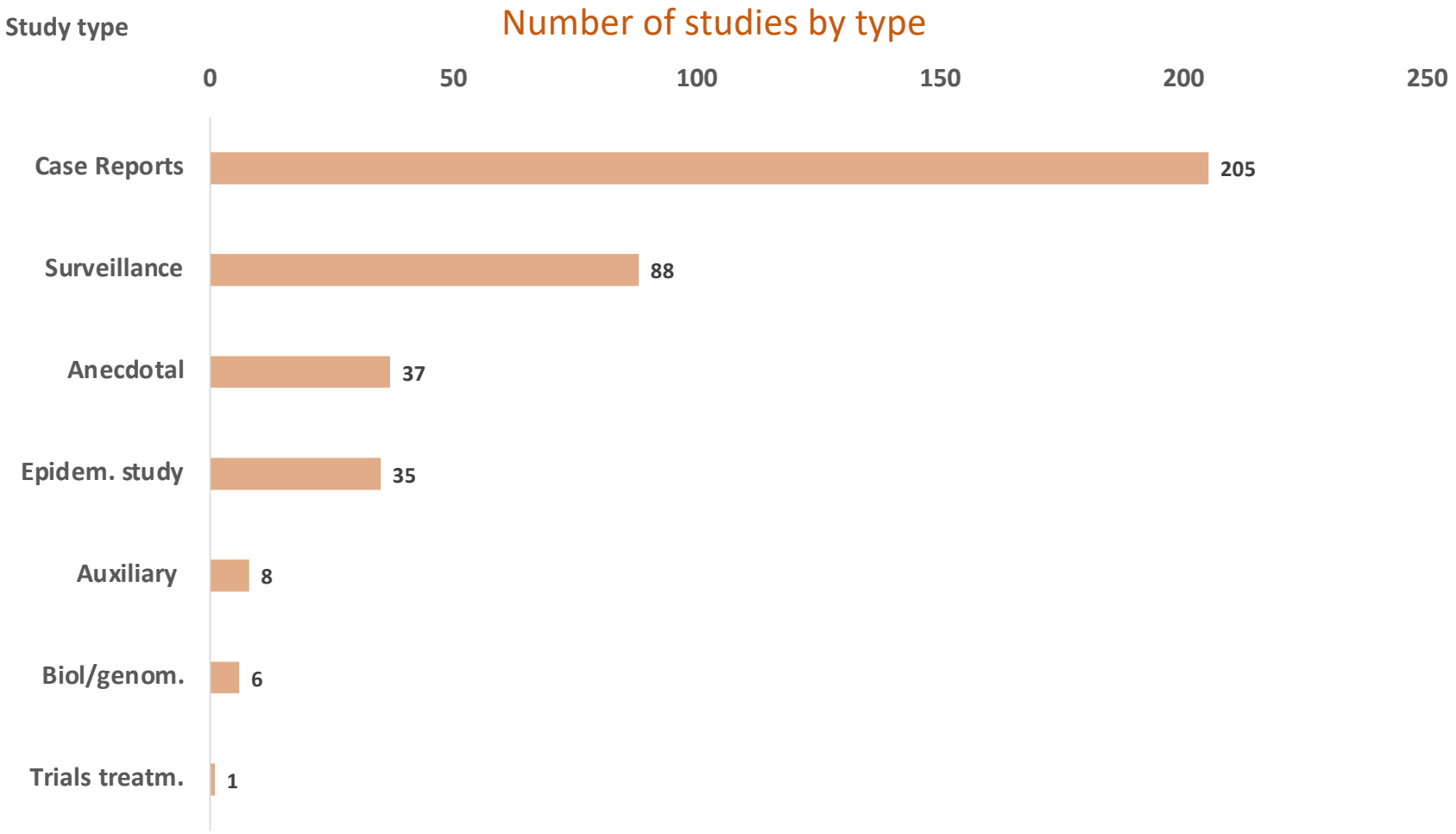


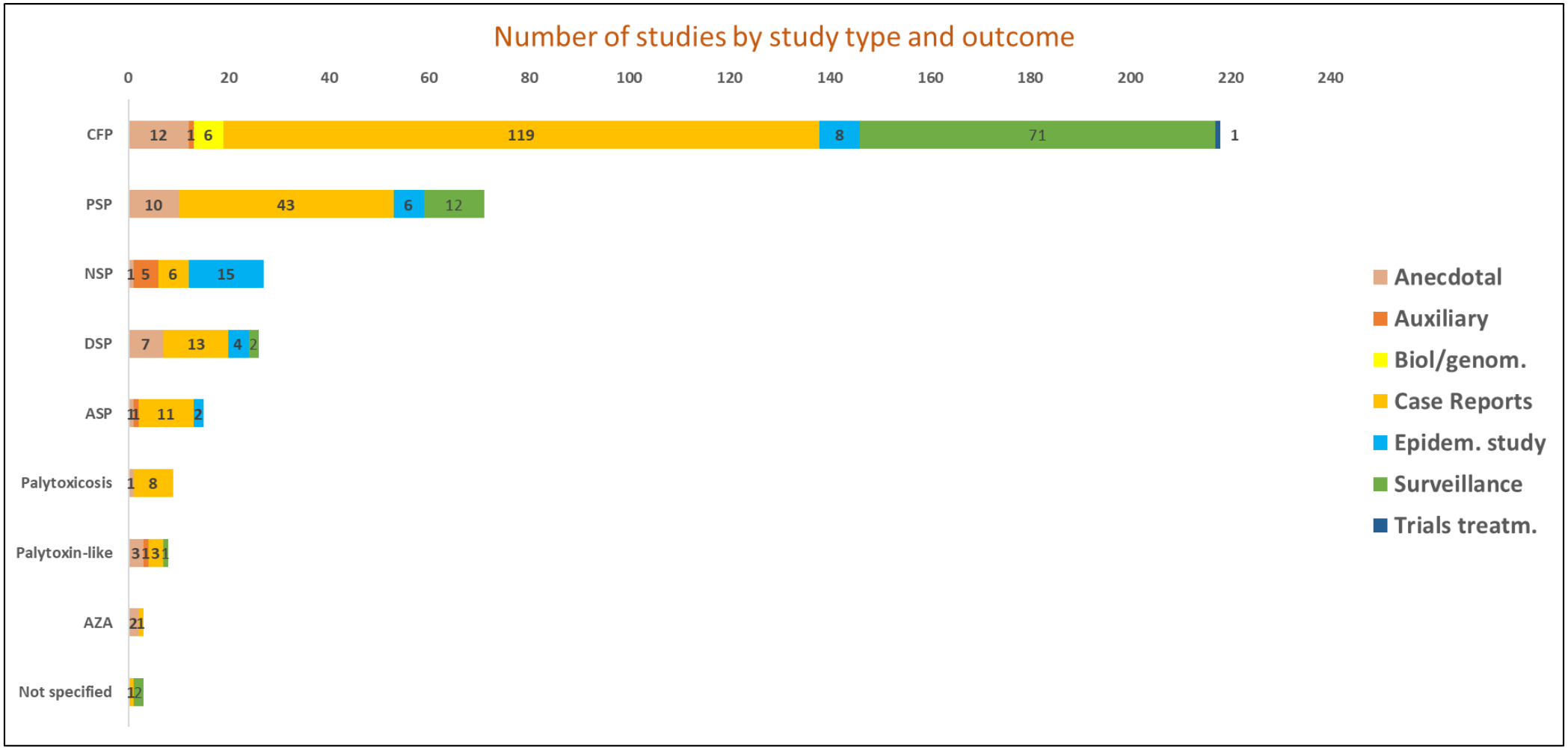
Results (PRISMA)




Number of studies per year
Number of studies
25
20
15
10
5
0
5 per. Mov. Avg. (Total)
1985
1990
1995
2000
2005
2010
2015
year


Number of Studies by clinical outcome
0
20
40
60
80
100
120
140
160
180
200
220
240
CFP
220
PSP
80
NSP
30
DSP
29
ASP
18
Palytoxicosis
9
Palytoxin-like
8
AZA
3
Not specified
3


Study type
Number of studies by type
0
50
100
150
200
250
Case Reports
205
Surveillance
88
Anecdotal
37
Epidem. study
35
Auxiliary
8
Biol/genom.
6
Trials treatm.
1


Number of studies by study type and outcome
0
20
40
60
80
100
120
140
160
180
200
220
240
CFP
12
1
6
119
8
71
1
PSP
10
43
6
12
NSP
1
5
6
15
DSP
7
13
4
2
ASP
1
1
11
2
Palytoxicosis
1
8
Palytoxin-like
3
1
3
1
AZA
2
1
Not specified
1
2
Anecdotal
Auxiliary
Biol/genom.
Case Reports
Epidem. study
Surveillance
Trials treatm.

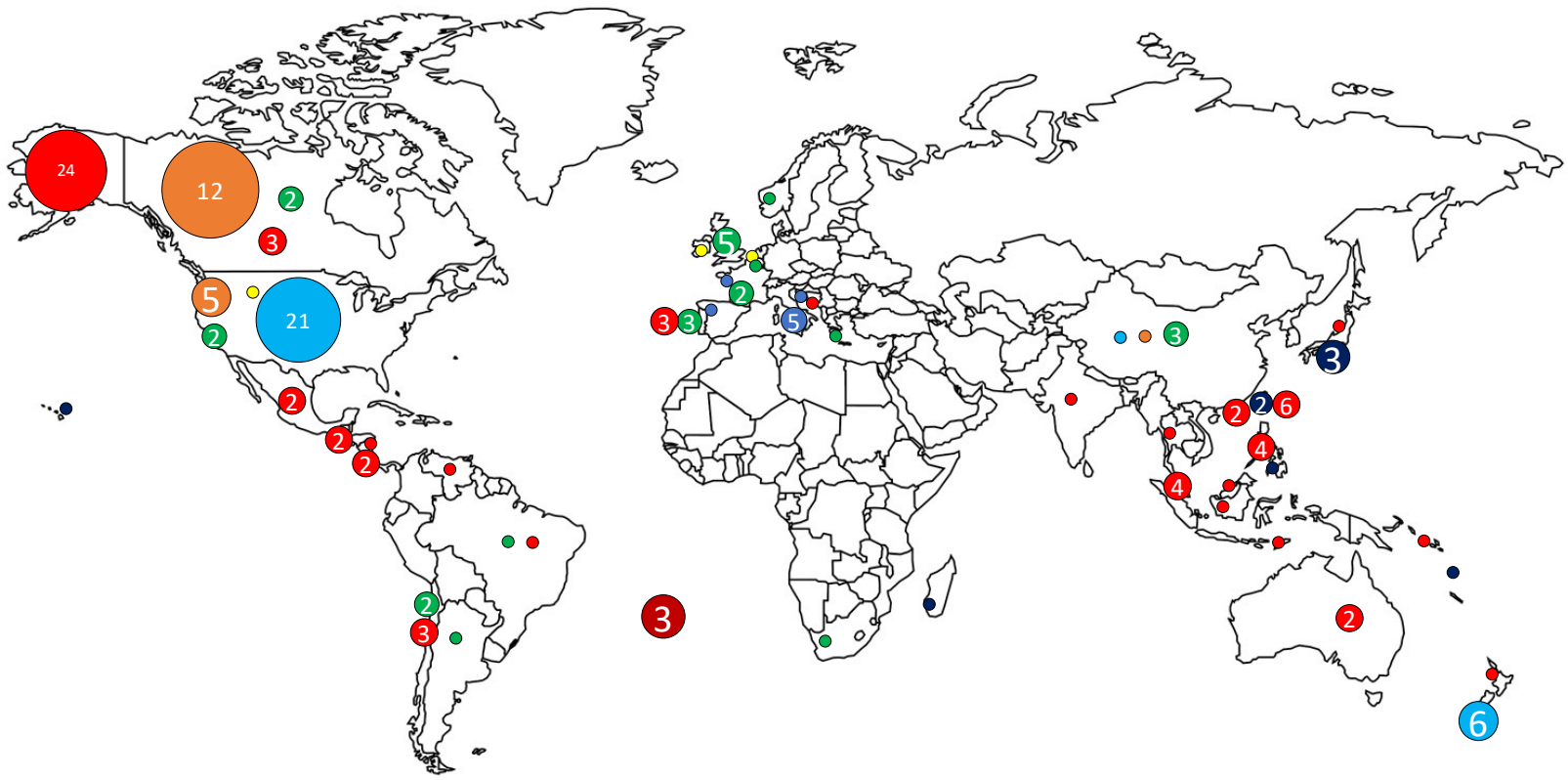
Acute *vs* Chronic

Study characteristic (number of studies)		Count* (%)
Exposure	Acute	340 (89.5)
	Chronic	4 (1.1)
	Not-specified	36 (9.5)
Health Outcome	Acute	233 (61.3)
	Both acute and chronic	69 (18.2)
	Chronic	18 (4.7)
	Not-specified	60 (15.8)

Author; year	Syndrome	Country	Exposure	Outcome
Grattan, 2016	ASP	USA	Razor clam consumption	Memory
Grattan, 2018	ASP	USA	Domoic acid exposure [as razor clam consumption]	Memory
Cordier, 2000	DSP	France	Mussel harvesting closures	Digestive cancer mortality rates
Lopez-Rodas, 2006	DSP	Spain	Mollusc consumption	Colonrectal cancer

Chronic exposure studies

Outcome by geography (excluding CFP)

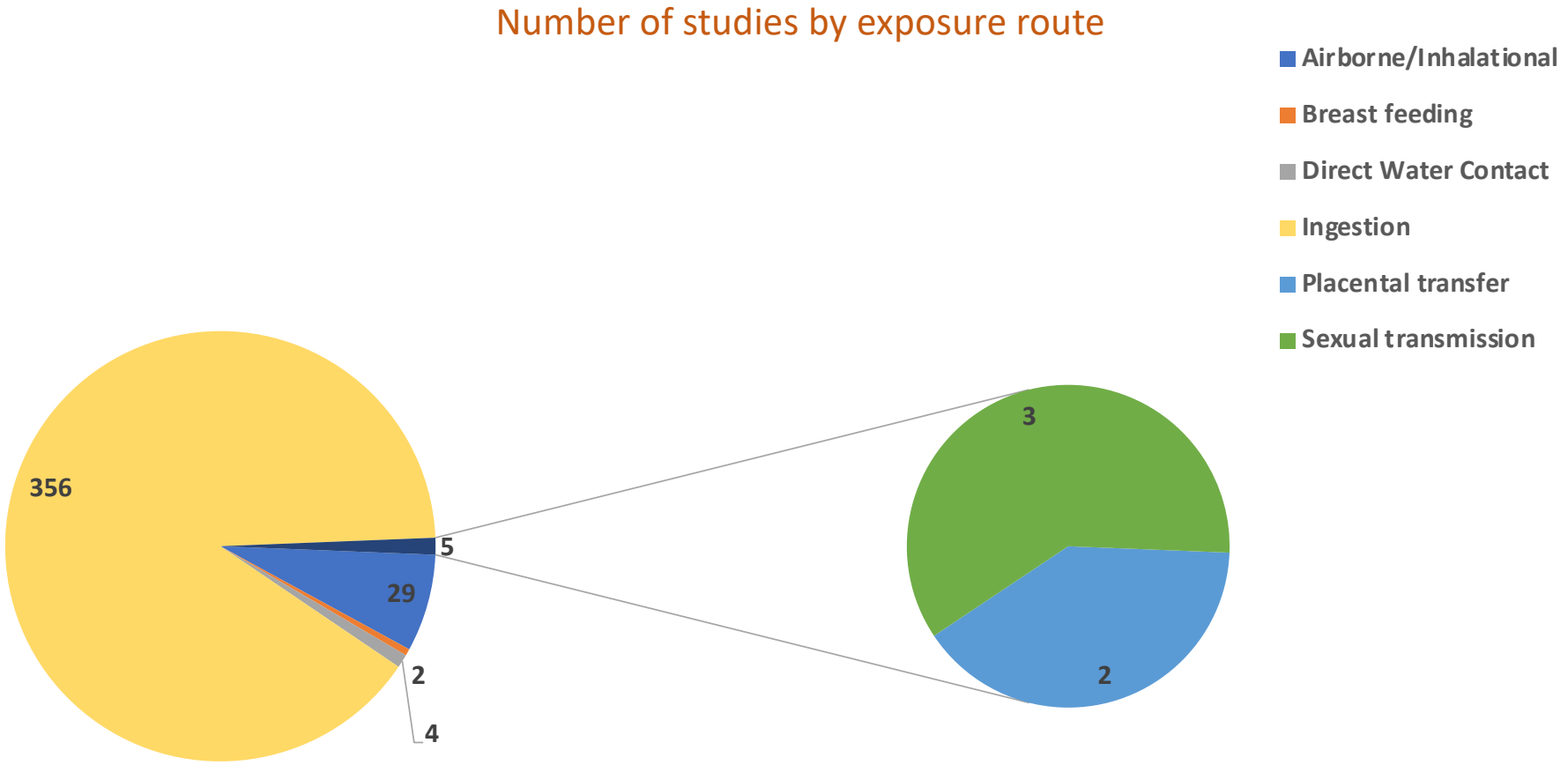


Number of studies

- Amnesic Shellfish Poisoning (ASP)
- Azaspiracid Shellfish Poisoning (AZP)
- Diarrhetic (Diarrheic) Shellfish Poisoning (DSP)
- Neurotoxic Shellfish Poisoning (NSP) and respiratory irritation:
- Palytoxicosis
- Effects of Palytoxin-like toxins
- Paralytic Shellfish Poisoning (PSP)

CFP NOT INCLUDED

Data presented are provisional and for illustrative purposes only


Number of studies by exposure route
Airborne/Inhalational
Breast feeding
Direct Water Contact
Ingestion
Placental transfer
Sexual transmission
356
5
29
2
4
3
2

Confirmation

Study characteristic (number of studies)		Count* (%)
Confirmation**	Toxin detected in food consumed	97 (25.5)
	Toxin detected in same batch	13 (3.4)
	Toxin detected same area within ± one week	68 (17.9)
	HAB species detected same area within ± one week	50 (13.2)
	Toxin detected same area > one week	7 (1.8)
	HAB species detected same area > one week	5 (1.3)
	Direct measure of exposure	7 (1.8)
	Clinical signs/symptoms only	120 (31.6)
	Toxin/metabolites in human specimens	27 (7.1)
	Human samples negative for Toxin/metabolites	5 (1.3)
	Not reported	73 (19.2)

5. Conclusions

lack of formal surveillance and epidemiological studies

Inadequate methods of exposure assessment and diagnosis

Lack of studies of chronic exposure

An interdisciplinary focus on determining the true burden disease, following acute and chronic exposures, is required to provide a baseline to facilitate the measurement and the understanding of variations in response to current and predicted climate and other environmental change. [to amend]

Limitations

- No hand searching of key journals and newsletters
- Marine cyanobacteria not included
- No searches for surveillance reports from public health agencies
- Full-texts not always obtained

Reflections

- Terminology – “outbreak”
- Lack of case definitions
- Lack of detail in case reporting

7. Acknowledgements

Review Team & Supervisors

Professor Lora Fleming – ECEHH

Dr Richard Sharpe – ECEHH/Cornwall Council

Professor Rosa Barciela - Met Office/ECEHH/University of Exeter

Professor Keith Davidson - Scottish Association of Marine Sciences

Prof Gordon Nichols – UKHSA/University of Exeter

Dr Elisa Berdalet - Institute of Marine Sciences (ICM-CSIC)

Alison Bethel - Information Specialist – University of Exeter