Epidemiology of paediatric chronic fatigue syndrome in Australia

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ABSTRACT

Objective To estimate the paediatrician-diagnosed incidence of chronic fatigue syndrome (CFS) in Australia, and describe demographic and clinical features, as well as approaches to diagnosis and management.

Methods The Australian Paediatric Surveillance Unit facilitates monthly national surveillance of uncommon conditions seen by paediatricians. Data from young people aged <18 years diagnosed with CFS were collected. Incidence was estimated based on new cases reported from April 2015 to April 2016.

Results A total of 164 cases of newly diagnosed CFS in young people aged 4–17 years were identified for inclusion. The estimated national incidence for children aged 4–9 years was 0.25 per 100 000 per annum. In children aged 10–17 years, the estimated incidence of paediatrician-diagnosed cases for Victoria (17.48 per 100 000) was substantially greater than other Australian states (range 1.31–5.51 per 100 000). Most cases were female and Caucasian, most commonly presenting after an infectious illness with symptoms gradual in onset. The majority were diagnosed at least 13 months after symptom onset. Symptoms, associations, investigations and management strategies were highly variable.

Conclusions Current findings suggest that, consistent with other countries, the Australian incidence of CFS in children aged <10 years is very low. In contrast, the national incidence of CFS in older children and adolescents (aged 10–17 years) is more unclear, with marked variability between geographical regions apparent. This may be due to variation in service accessibility and clinician understanding of CFS. Accordingly, national initiatives to improve equity of care for children with CFS may be required.

What is already known on this topic?

- Paediatric chronic fatigue syndrome (CFS) causes significant disability.
- Estimates of the incidence of paediatric CFS vary.
- We know little about how common the condition is or how it is currently managed in Australia.

What this study adds?

- CFS is uncommon in children aged <10 years.
- The Australian incidence of CFS in older children and adolescents (aged 10–17 years) is unclear, with marked variability between geographical regions apparent.

Chronic fatigue syndrome (CFS) is a condition of unknown aetiology characterised by severe, persistent, unexplained fatigue. This fatigue may be accompanied by other symptoms including postexertional malaise, pain, cognitive deficits and disrupted sleep.[1] In children and adolescents, CFS can lead to significant functional impairment, including a substantial reduction in school attendance.[2]

As the aetiology of CFS is unknown and there is no diagnostic test for CFS,[3] it is diagnosed clinically through the use of case definitions.[4] Several case definitions and terminologies for CFS have been used internationally in clinical practice and research since the first case definition was published in 1988.[5]

Epidemiological estimates of prevalence for CFS vary significantly. A meta-analysis of adult studies found estimates of prevalence varying between 0.2% and 6.41%, with a pooled prevalence of 3.48% for self-reported cases, and 0.76% for clinically assessed cases.[6] There is less literature specifically examining the epidemiology of paediatric CFS, with varying prevalence estimates ranging from 0% to 2.91%.[7–18] Four published studies, from the Netherlands, Norway and the UK, report variable incidence rates of paediatric CFS with estimates ranging from 12 (0.012%) to 500 (0.5%) per 100 000.[7 8 19 20] Some of the variation in incidence estimates may be explained by variation in diagnostic methods, case ascertainment and age range captured.

The primary aim of this study was to provide an estimate of the paediatrician-diagnosed incidence of CFS in Australian young people, based on prospective national reporting by paediatricians. Secondary aims were to describe demographics, symptomatology, diagnosis and management of CFS, based on reported cases.

PATIENTS AND METHODS

The Australian Paediatric Surveillance Unit (APSU) facilitated national surveillance of CFS in young people aged under 18 years from April 2015 to April 2016. The APSU undertakes national surveillance of rare paediatric conditions in Australia.[21] Each month clinicians on the APSU contact database are

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emailed a report card listing conditions currently being studied by the APSU. Clinicians are asked to report children newly diagnosed. In April 2015–April 2016, the total number of paediatricians reporting to the APSU was 1467 and the overall monthly report card return rate was 93%. According to the Australia Government Department of Health, there were 2059 paediatricians employed in Australia in 2015[22]; therefore, approximately 71% of Australian paediatricians reported to the APSU at the time of the study.

Paediatricians received a protocol which included CFS case definition (online supplement 1). Reportable cases were defined as young people aged under 18 years, who were newly diagnosed with CFS in the past month. The upper age limit was defined by the APSU. CFS was defined according to the Centers for Disease Control and Prevention Case Definition (modified for a paediatric population under the auspices of the Royal Australasian College of Physicians).[23] For every newly reported case, paediatricians completed a 20-item questionnaire which included: date of birth, sex, postcode, ethnicity, presenting symptoms including duration, type of onset, severity of and triggers for symptoms, comorbid conditions, family history, investigations undertaken and advised management.

DATA ANALYSIS

Data were analysed using Stata V.14.1 (StataCorp, 2016). Population data from the Australian Bureau of Statistics were used to calculate estimates of incidence of CFS. Values were calculated as the mathematical average of the 2015 and 2016 population estimates to coincide with the current study data collection period. Poisson regression was used to determine estimated incidences and were presented as rates per 100 000 persons per annum, with 95% CIs. National level incidence estimates for all children aged 4–9 years, all adolescents aged 10–17 years, female adolescents aged 10–17 years and male adolescents aged 10–17 years, were calculated. Age ranges were determined based on previous epidemiological studies in the paediatric CFS literature to allow for comparison of results. State-specific and gender-specific incidences were not calculated for the 4–9 years due to the low number of reports. In two cases, paediatricians failed to report the sex of the young person. In order to prevent under-reporting of male and female incidences, the female incidence assumed these two individuals were female, while the male incidence assumed they were male.

The characteristics of CFS were presented as frequencies and percentages of the total sample of reported cases. Missing data from the questionnaire were categorised in the results as being 'not specified'. Chi-square analyses were used to compare demographics and clinical characteristics of Victorian patients with those in other states and territories. Due to multiple comparison, $p<0.01$ was considered to be statistically significant.

RESULTS

Incidence estimates

Between April 2015 and April 2016, 191 cases were reported to the APSU. Questionnaires were returned for 184 (96%) cases, and 164 were confirmed as CFS cases. Of the remaining cases for which questionnaires were returned, 10 were duplicates and 10 were classified as errors (administrative errors or cases outside the case definition or age range). Ages ranged from 4 to 17 years for the 164 young people with confirmed CFS. Five confirmed cases were children aged 4–9 years, while 159 were adolescents aged 10–17 years.

The estimated national incidence of paediatrician-diagnosed cases of CFS was 0.25 per 100 000 per annum (95% CI 0.08 to 0.59) for children aged 4–9 years, and 6.38 per 100 000 per annum (95% CI 5.43 to 7.45) for adolescents aged 10–17 years. Estimated national incidence for adolescent males was 3.68 per 100 000 per annum (95% CI 2.70 to 4.89), and 9.39 per 100 000 per annum (95% CI 7.75 to 11.28) for adolescent females. There was mild variation in the estimated incidence rates of paediatrician-diagnosed cases of CFS for adolescents according to state or territory of Australia, but incidence rate of CFS in adolescents for the state of Victoria (17.48 per 100 000) was greater when compared with other Australia states (range 1.31–5.51 per 100 000) (table 1). During the study period, the rates of reporting of CFS were disproportionally higher in some states and unexpectedly low in others compared with non-CFS conditions being reported to the APSU (online supplement 2).

Demographics

Average age of included cases was 14.9 years (95% CI 14.6 to 15.2) (table 2). Females constituted 68.9% of cases (female-to-male ratio=2.3:1). Majority of cases (95.1%) were Caucasian. Patient demographics did not differ between regions; therefore, national data are reported.

Morbidity

There were no differences in symptomatology between Victorian patients and those in other states; therefore, national data reported (table 3). The most common pattern for onset of symptoms was gradual (56% cases), while 37% were sudden. Fifty-two per cent of diagnoses were made at least 13 months after symptom onset, while 29% were diagnosed after 24

Table 1 Estimated total, female and male incidence rates (95% CI) of paediatrician-diagnosed cases of CFS according to region in adolescents aged 10–17 years

	Total	Female	Male
Victoria	17.48 (14.30 to 21.16)	25.95 (20.45 to 32.48)	9.75 (6.58 to 13.92)
New South Wales	3.16 (2.04 to 4.66)	4.16 (2.38 to 6.75)	2.45 (1.18 to 4.51)
Western Australia	5.51 (3.08 to 9.08)	9.74 (5.18 to 16.65)	1.44 (0.17 to 5.20)
Queensland	1.31 (0.53 to 2.71)	1.54 (0.42 to 3.95)	1.10 (0.23 to 3.21)
Northern Territory	3.47 (0.09 to 19.32)	7.18 (0.18 to 40.02)	0
Tasmania	3.61 (0.44 to 13.04)	7.48 (0.91 to 27.02)	0
Australian Capital Territory	5.22 (0.63 to 18.85)	10.65 (1.29 to 38.47)	0
South Australia	1.17 (0.14 to 4.22)	0	2.28 (0.28 to 8.24)
National	6.38 (5.43 to 7.45)	9.39 (7.75 to 11.28)	3.68 (2.70 to 4.89)

Rates are per 100 000 and are age-adjusted to the 2015–2016 Australian Bureau of Statistics Census data.
CFS, chronic fatigue syndrome.

Table 2 Demographics for included cases

	n (%)
Age, mean (95% CI)	14.9 (14.6 to 15.2)
Gender	
Female	113 (69)
Male	49 (30)
Not specified	2 (1)
State	
Victoria	108 (66)
New South Wales	25 (15)
Western Australia	17 (10)
Queensland	7 (4)
South Australia	2 (1)
Tasmania	2 (1)
Australian Capital Territory	2 (1)
Northern Territory	1 (1)
Ethnicity	
Caucasian	156 (95)
African/Middle Eastern	1 (1)
Indigenous	1 (1)
Unknown/not specified	6 (4)

months. For approximately two-thirds of patients, an infectious illness was reported as the trigger for symptom onset. On average, individuals had 9.9 symptoms (95% CI 9.2 to 10.4) over the course of their illness. The seven most common symptoms, being fatigue, postexertional malaise, sleep disturbance/unrefreshing sleep, headache, attention/concentration difficulties, light-headedness/dizziness and musculoskeletal pain, were present in more than two-thirds of patients. Symptom severity was reported as moderate for 63.4% of cases.

The most commonly associated medical condition was postural orthostatic tachycardia syndrome (POTS), observed in 26.2% of patients (table 4). Joint hypermobility, fibromyalgia/chronic widespread pain and migraines were present in over 10% of cases. No medical comorbidities were reported for 41% of patients and most patients (59.8%) did not have any reported comorbid psychiatric conditions. Paediatricians reported that anxiety and depression (26% and 13% of cases, respectively) were the most common psychiatric comorbidities. In terms of self-reported family history, patients were reported to have a first-degree relative with anxiety disorder (18%), depression (17%) or CFS (13%), respectively. There was no relevant family history for 50% of patients.

Investigations

Clinicians requested a variety of investigations (online supplement 3). As there were no major observed differences in requested investigations according to state, total results are presented. Eight tests were ordered for >50% of cases: full blood count and differential urea, electrolytes and creatinine, thyroid function tests, erythrocyte sedimentation rate, liver function tests, Epstein-Barr virus (EBV) serology, C reactive protein and coeliac screen. The investigations that had the highest proportion of abnormal results were EBV serology (34%), allergy tests (33%), cytomegalovirus serology (25%), serum vitamin D (24%) and antinuclear antibodies (ANA) (23%).

Table 3 Medical characteristics of included cases

	n (%)
Symptom onset	
Gradual	92 (56)
Sudden	60 (37)
Unknown/not specified	12 (7)
Symptom duration prior to diagnosis	
3–6 months	10 (18)
7–12 months	45 (27)
13–24 months	38 (23)
>24 months	47 (29)
Not specified	3 (2)
Trigger for onset	
Infectious illness	109 (67)
Psychological stress	129 (7)
Non-infectious illness	11 (7)
Injury	4 (2)
Human papillomavirus vaccination	3 (2)
Menarche	2 (1)
Physical exertion	2 (1)
Unknown/not specified	42 (26)
Presenting symptoms	
Fatigue	163 (99)
Postexertional malaise	138 (84)
Sleep disturbance/unrefreshing sleep	134 (82)
Headache	126 (77)
Attention/concentration difficulties	122 (74)
Light-headedness/dizziness	118 (72)
Musculoskeletal pain	110 (67)
Difficulty processing information	89 (54)
Gastrointestinal symptoms	87 (53)
Flu-like symptoms	79 (48)
Cardiovascular symptoms	62 (38)
Abdominal pain	48 (29)
Loss of thermostatic ability	46 (28)
Joint pain	45 (27)
Susceptibility to viral infections	43 (26)
Hypersensitivity to noise or light	42 (26)
Short-term memory loss	29 (18)
Marked weight change	23 (14)
Chest pain	22 (13)
Motor symptoms	19 (12)
New sensitivities to food or medications	16 (10)
Perceptual/sensory disturbance	15 (9)
Respiratory symptoms	14 (9)
Genitourinary symptoms	9 (6)
Pain (unspecified)	6 (4)
Syncope	2 (1)
Other	7 (4)
Symptoms not specified	1 (1)
Number of symptoms, mean (95% CI)	9.9 (9.2 to 10.4)
Symptom severity	
Mild	18 (11)
Moderate	104 (63)
Severe	37 (23)
Very severe	1 (1)
Not specified	4 (2)

Management

Most commonly used services were teacher and school-based services (42%) and specialised CFS services (40%) (online supplemen 4). Psychology (27%) and physiotherapy services (20%) were generally included. Paediatricians reported

Table 4 Comorbidities and family history of included cases

	n (%)
Comorbid medical conditions	
Postural orthostatic tachycardia syndrome	43 (26.2)
Joint hypermobility	21 (12.8)
Fibromyalgia/chronic widespread pain	17 (10.4)
Migraine	17 (10.4)
Inflammatory bowel disease/functional bowel disorder	14 (8.5)
Dysmenorrhoea	12 (7.3)
Multiple food or chemical sensitivities/food intolerance	9 (5.5)
Diabetes and other endocrine disorders	4 (2.4)
Inflammatory bowel disease/coeliac disease	3 (1.8)
Atopic syndrome	2 (1.2)
Other	8 (4.9)
No medical conditions specified	67 (40.9)
Comorbid psychiatric conditions	
Anxiety	43 (26.2)
Depression	22 (13.4)
Somatisation	5 (3.0)
Autism spectrum/attention deficit hyperactivity disorder	4 (2.4)
School phobia	3 (1.8)
Eating disorder	2 (1.2)
Other	10 (6.1)
No psychiatric conditions specified	98 (59.8)
Family history in first-degree relatives	
Anxiety disorder	29 (17.7)
Depression	27 (16.5)
Chronic fatigue/chronic fatigue syndrome	22 (13.4)
Arthritis/connective tissue disorder	13 (7.9)
Fibromyalgia	13 (7.9)
Chronic pain	10 (6.1)
Psychosocial stressors	7 (4.3)
Diabetes and other endocrine disorders	6 (3.7)
Hypothyroidism/Hashimoto's thyroiditis	4 (2.4)
Joint hypermobility	4 (2.4)
Autism spectrum/attention deficit hyperactivity disorder	4 (2.4)
Inflammatory bowel disease/coeliac disease	3 (1.8)
Migraine	3 (1.8)
No relevant family history specified	82 (50.0)

that alternative and complementary medicine services were not often used by patients. Victorian patients were significantly more likely to be seen in a specialist CFS service compared with other states (Victoria: 53%, other states/territories: 16%, $\chi^2=20.67$, $p<0.001$), while patients in other states and territories were significantly more likely to be seen in adolescent medicine (Victoria: 5%, other states/territories: 36%, $\chi^2=25.14$, $p<0.001$), use physiotherapy (Victoria: 8%, other states/territories: 43%, $\chi^2=27.35$, $p<0.001$), occupational therapy (Victoria: 6%, other states/territories: 38%, $\chi^2=27.36$, $p<0.001$) or rheumatology (Victoria: 7%, other states/territories: 32%, $\chi^2=16.9$, $p<0.001$). There were no other significant state-based differences in services used by patients.

Sleep hygiene was a treatment strategy recommended to almost all patients (95%), with graded exercise therapy, a modified school programme/home tutoring, pacing/balancing activities or symptom management with medication/supplementation frequently recommended. There were no significant differences in treatment strategies used for Victorian patients compared with those in other states, with the exception of cognitive behavioural therapy, which was reported to be less likely to be recommended in Victoria than in other states (Victoria: 19%, other states: 71%, $\chi^2=44.50$, $p<0.001$).

DISCUSSION

This study is the first to provide estimates of paediatrician-reported incidence of CFS in the Australian paediatric population, and the second worldwide to collect prospective incidence data.[8] The estimated incidence in children aged 4–9 years was 0.25 per 100 000 per annum (95% CI 0.08 to 0.59), while the estimated incidence in adolescents aged 10–17 years was 6.38 per 100 000 per annum (95% CI 5.43 to 7.45). The reported incidence for the state of Victoria (17.48 per 100 000) was substantially higher compared with other Australian states and territories (1.31–5.51 per 100 000).

There has been very little data available to quantify the clinical impression that CFS is rarely diagnosed in children aged under 10 years. Our results support this by demonstrating that CFS is uncommonly diagnosed in Australian children aged under 10 years. The only other study to document the incidence of CFS in younger children also reported this age range to have the lowest incidence.[20]

Australian estimates of incidence of CFS in the current study is lower than estimates from other countries in the current literature. The estimated Victorian incidence is similar to that in other countries,[8 20] suggesting incidence rates in Victoria could be more reflective of the true incidence of CFS. The underlying reasons for the geographic variation of diagnostic rates in Australia are unclear, but likely multiple. While the contribution of true geographical or biological factors in the observed incidence rates between regions cannot be ruled out based on the results of the current study, we believe that the differences between Victoria and the other states is most likely attributable to local phenomena affecting case ascertainment. The geographical reporting pattern of CFS in this study is not consistent with the overall pattern of APSU reporting rates across states, suggesting that results cannot be explained by the current study methodology. Contextual factors causing variation in diagnosis could relate to differences in access to specialists and/or diagnostic practices/culture (eg, lack of recognition or misconceptions about CFS). Further research is required to understand the influence of service provision on the epidemiology of this condition. For example, from the current study we cannot determine whether the incidence is greater in Victoria due to increased access to CFS specialist services or whether there is greater access to services due to increased need. Furthermore, it is unclear whether Victorian paediatricians are more likely to make a diagnosis of CFS as there is a dedicated service to refer to where access requires a formal diagnosis of CFS or whether greater access to specialist services in certain areas influences physician awareness and education of CFS, resulting in increased diagnostic rates.

Our results regarding gender ratio, ethnicity and symptom frequency are comparable to that in the international literature.[8 15 24–30] Every study that reports ethnicity data, including our own, occurred in high-income countries with Caucasian majority populations. It is possible that the high proportion of Caucasian cases of CFS found in the literature reflects this ethnic group's majority in the population, rather than an increased susceptibility compared with other ethnicities.

Consistent with current results, patients most commonly have gradual onset of symptoms, onset linked to infectious illness and moderate to high severity.[2 8 9 29 30] As in this study, existing

literature has demonstrated associations between CFS and POTS, joint hypermobility, fibromyalgia, anxiety and depression.[31–35] Although the rates of a family history of depression, anxiety and CFS in the current study need to be interpreted cautiously as they are based on self-report from the family or young person to the paediatrician, other research has suggested a likely association with depression, anxiety and CFS in first-degree relatives.[36 37]

The protracted time between symptom onset and diagnosis observed in our study has also been observed in two Australian studies.[30 38] This delay is substantial, with 54% of patients not receiving a diagnosis, and therefore likely not having access to appropriate treatment, for over a year. Investigations recommended by the Australian clinical practice guidelines[23] yielded very few abnormal results. This is consistent with the current practice of using diagnostic tests to rule out other medical conditions prior to diagnosis of CFS. Tests that most commonly yielded abnormal results, such as EBV serology and the ANA test, are not recommended by the guidelines, yet were requested for many patients. It is possible that because the existing CFS guidelines are based largely on adult care, these tests were not included as they are more relevant to a paediatric population.

Overall, the demographic and clinical characteristics, and approaches to diagnosis and management, do not vary greatly between Victoria and other states. Victorian patients were more likely to be referred to a specialist CFS service, while patients elsewhere were more likely to be seen in adolescent medicine and referred to individual allied health professionals and rheumatology. This difference likely reflects regional differences in service models and approaches to CFS management.

Strengths and limitations

This study used for case ascertainment, an established national surveillance system, which is independent of the research team. This reduces the potential for observer bias. All diagnoses were made by medical practitioners following a consultation and physical examination, which is likely to improve the validity of each diagnosis.

Although this is the most complete national dataset currently available for paediatric CFS in Australia, the study relies on self-reporting by paediatricians and some paediatricians may not report cases to the APSU. Paediatricians who are not confident in diagnosing CFS, do not believe in the existence of CFS, or the importance a diagnosis and providing management, may not report cases even though the child or adolescent meets the criteria. Accordingly, our results may underestimate the true incidence of paediatric CFS in Australia. It was not possible to include general practitioners in the data collection which may also result in an underestimate of incidence. It is possible that milder cases of CFS are not referred to paediatricians, and so were not identified in our study. The low proportion of severe and very severe cases may be influenced by selection bias, as these young people may be too sick to attend a consultation for diagnosis and so not captured by our study.

The age ranges used in the current study were informed by previous epidemiological research in paediatric CFS and were confined by the surveillance methodology used. Future research studies should consider using narrower age bands to further understand the incidence of CFS throughout childhood, particularly during the adolescent period.

CONCLUSION

This study suggests that there is substantial variation in diagnostic rates of CFS between Victoria and other states, by Australian paediatricians. The variation in diagnostic rates of CFS by paediatricians, plus protracted time to diagnosis, highlights the need for a national, coordinated approach to improving healthcare for children and adolescents with CFS. This should include prospective evaluation of health outcomes for adolescents with CFS and supporting an evidence-informed approach to management. Review and update of the national clinical practice guideline for CFS, with a systematic implementation strategy, will be crucial to ensuring children and adolescents with CFS receive access to more consistent care at national level.

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Contributors SK and AS conceptualised and designed the study, coordinated and supervised data collection and analysis, drafted the initial manuscript and reviewed and revised the manuscript. KR, CR, ST, KK, DNP, LL and SH designed the data collection instrument and reviewed and revised the manuscript. SE and JR carried out the initial analyses, drafted the initial manuscript and reviewed and revised the manuscript. AH conceptualised and designed the study, and critically reviewed the manuscript for important intellectual content. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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REFERENCES

1 Fukuda K, Straus SE, Hickie I, *et al*. The chronic fatigue syndrome: a comprehensive approach to its definition and study. International Chronic Fatigue Syndrome Study Group. *Ann Intern Med* 1994;121:953–9.
2 Crawley E, Sterne JA. Association between school absence and physical function in paediatric chronic fatigue syndrome/myalgic encephalopathy. *Arch Dis Child* 2009;94:752–6.
3 Rowe PC, Underhill RA, Friedman KJ, *et al*. Myalgic Encephalomyelitis/Chronic Fatigue Syndrome Diagnosis and Management in Young People: A Primer. *Front Pediatr* 2017;5:121.
4 Werker CL, Nijhof SL, van de Putte EM. Clinical Practice: Chronic fatigue syndrome. *Eur J Pediatr* 2013;172:1293–8.
5 Nacul L, Kingdon CC, Bowman EW, *et al*. Differing case definitions point to the need for an accurate diagnosis of myalgic encephalomyelitis/chronic fatigue syndrome. *Fatigue* 2017;5:1–4.
6 Johnston S, Brenu EW, Staines D, *et al*. The prevalence of chronic fatigue syndrome/myalgic encephalomyelitis: a meta-analysis. *Clin Epidemiol* 2013;5:105–10.

7 Donegan K, Beau-Lejdstrom R, King B, *et al*. Bivalent human papillomavirus vaccine and the risk of fatigue syndromes in girls in the UK. *Vaccine* 2013;31:4961–7.
8 Nijhof SL, Maijer K, Bleijenberg G, *et al*. Adolescent chronic fatigue syndrome: prevalence, incidence, and morbidity. *Pediatrics* 2011;127:e1169–e1175.
9 Jones JF, Nisenbaum R, Solomon L, *et al*. Chronic fatigue syndrome and other fatiguing illnesses in adolescents: a population-based study. *J Adolesc Health* 2004;35:34–40.
10 Chalder T, Goodman R, Wessely S, *et al*. Epidemiology of chronic fatigue syndrome and self reported myalgic encephalomyelitis in 5-15 year olds: cross sectional study. *BMJ* 2003;327:654–5.
11 Minowa M, Jiamo M. Descriptive epidemiology of chronic fatigue syndrome based on a nationwide survey in Japan. *J Epidemiol* 1996;6:75–80.
12 Lloyd AR, Hickie I, Boughton CR, *et al*. Prevalence of chronic fatigue syndrome in an Australian population. *Med J Aust* 1990;153:522–8.
13 Dobbins JG, Randall B, Reyes M, *et al*. The prevalence of chronic fatiguing illnesses among adolescents in the United States. *Journal of Chronic Fatigue Syndrome* 1997;3:15–27.
14 Jordan KM, Huang C-F, Jason LA, *et al*. Prevalence of pediatric chronic fatigue syndrome in a community-based sample. *Journal of Chronic Fatigue Syndrome* 2006;13(2-3):75–8.
15 Farmer A, Fowler T, Scourfield J, *et al*. Prevalence of chronic disabling fatigue in children and adolescents. *Br J Psychiatry* 2004;184:477–81.
16 Crawley EM, Emond AM, Sterne JA. Unidentified Chronic Fatigue Syndrome/myalgic encephalomyelitis (CFS/ME) is a major cause of school absence: surveillance outcomes from school-based clinics. *BMJ Open* 2011;1:e000252.
17 Dowsett EG, Colby J. Long-term sickness absence due to ME/CFS in UK schools: An epidemiological study with medical and educational implications. *Journal of Chronic Fatigue Syndrome* 1997;3:29–42.
18 Jordan KM, Ayers PM, Jahn SC, *et al*. Prevalence of fatigue and chronic fatigue syndrome-like illness in children and adolescents. *Journal of Chronic Fatigue Syndrome* 2000;6:3–21.
19 Rimes KA, Goodman R, Hotopf M, *et al*. Incidence, prognosis, and risk factors for fatigue and chronic fatigue syndrome in adolescents: a prospective community study. *Pediatrics* 2007;119:e603–e609.
20 Bakken IJ, Tveito K, Gunnes N, *et al*. Two age peaks in the incidence of chronic fatigue syndrome/myalgic encephalomyelitis: a population-based registry study from Norway 2008-2012. *BMC Med* 2014;12:167.
21 The Australian Paediatric Surveillance Unit. 2018: http://www.apsu.org.au/ (Accessed 3 Jul 2018).
22 AGDoH. Paediatrics & child health: 2016 Factsheet. 2017. 2018 http://hwd.health.gov.au/webapi/customer/documents/factsheets/2016/Paediatrics%20&%20child%20health%20data.pdf (Accessed 28 Aug 2018).
23 Toulkidis V, Loblay R, Stewart G, *et al*. Chronic fatigue syndrome. Clinical practice guidelines–2002. *Med J Aust* 2002;176 Suppl:S17–S55.
24 Saidi G, Haines L. The management of children with chronic fatigue syndrome-like illness in primary care: a cross-sectional study. *Br J Gen Pract* 2006;56:43–7.
25 Bell DS. Illness onset characteristics in children with chronic fatigue syndrome and idiopathic chronic fatigue. *Journal of Chronic Fatigue Syndrome* 1997;3:43–51.
26 Rangel L, Garralda ME, Levin M, *et al*. The course of severe chronic fatigue syndrome in childhood. *J R Soc Med* 2000;93:129–34.
27 Vereker MI. Chronic fatigue syndrome: a joint paediatric-psychiatric approach. *Arch Dis Child* 1992;67:550–5.
28 Rowe KS, Rowe KJ. Symptom patterns of children and adolescents with chronic fatigue syndrome. *International perspectives on child and adolescent mental health* 2002;2:395–421.
29 Garralda ME, Rangel L. Impairment and coping in children and adolescents with chronic fatigue syndrome: a comparative study with other paediatric disorders. *J Child Psychol Psychiatry* 2004;45:543–52.
30 Knight S, Harvey A, Lubitz L, *et al*. Paediatric chronic fatigue syndrome: complex presentations and protracted time to diagnosis. *J Paediatr Child Health* 2013;49:919–24.
31 Barron DF, Cohen BA, Geraghty MT, *et al*. Joint hypermobility is more common in children with chronic fatigue syndrome than in healthy controls. *J Pediatr* 2002;141:421–5.
32 Stewart JM, Gewitz MH, Weldon A, *et al*. Patterns of orthostatic intolerance: the orthostatic tachycardia syndrome and adolescent chronic fatigue. *J Pediatr* 1999;135:218–25.
33 Bell DS, Bell KM, Cheney PR. Primary juvenile fibromyalgia syndrome and chronic fatigue syndrome in adolescents. *Clin Infect Dis* 1994;18 Suppl 1(Suppl 1):S21–S23.
34 Bould H, Collin SM, Lewis G, *et al*. Depression in paediatric chronic fatigue syndrome. *Arch Dis Child* 2013;98:425–8.
35 Crawley E, Hunt L, Stallard P. Anxiety in children with CFS/ME. *Eur Child Adolesc Psychiatry* 2009;18:683–9.
36 Collin SM, Tilling K, Joinson C, *et al*. Maternal and childhood psychological factors predict chronic disabling fatigue at age 13 years. *J Adolesc Health* 2015;56:181–7.
37 Rangel L, Garralda ME, Jeffs J, *et al*. Family health and characteristics in chronic fatigue syndrome, juvenile rheumatoid arthritis, and emotional disorders of childhood. *J Am Acad Child Adolesc Psychiatry* 2005;44:150–8.
38 Knight S, Harvey A, Towns S, *et al*. How is paediatric chronic fatigue syndrome/myalgic encephalomyelitis diagnosed and managed by paediatricians? An Australian Paediatric Research Network Study. *J Paediatr Child Health* 2014;50:n/a–1007.
39 Toulkidis V, Loblay R, Stewart G, *et al*. Chronic fatigue syndrome: clinical practice guidelines 2002. Produced by a working group convened under the auspices of the Royal Australasian College of Physicians. *Med J Aust* 2002;176.