Supplementary Material

The economic burden of myalgic encephalomyelitis/chronic fatigue syndrome in Australia

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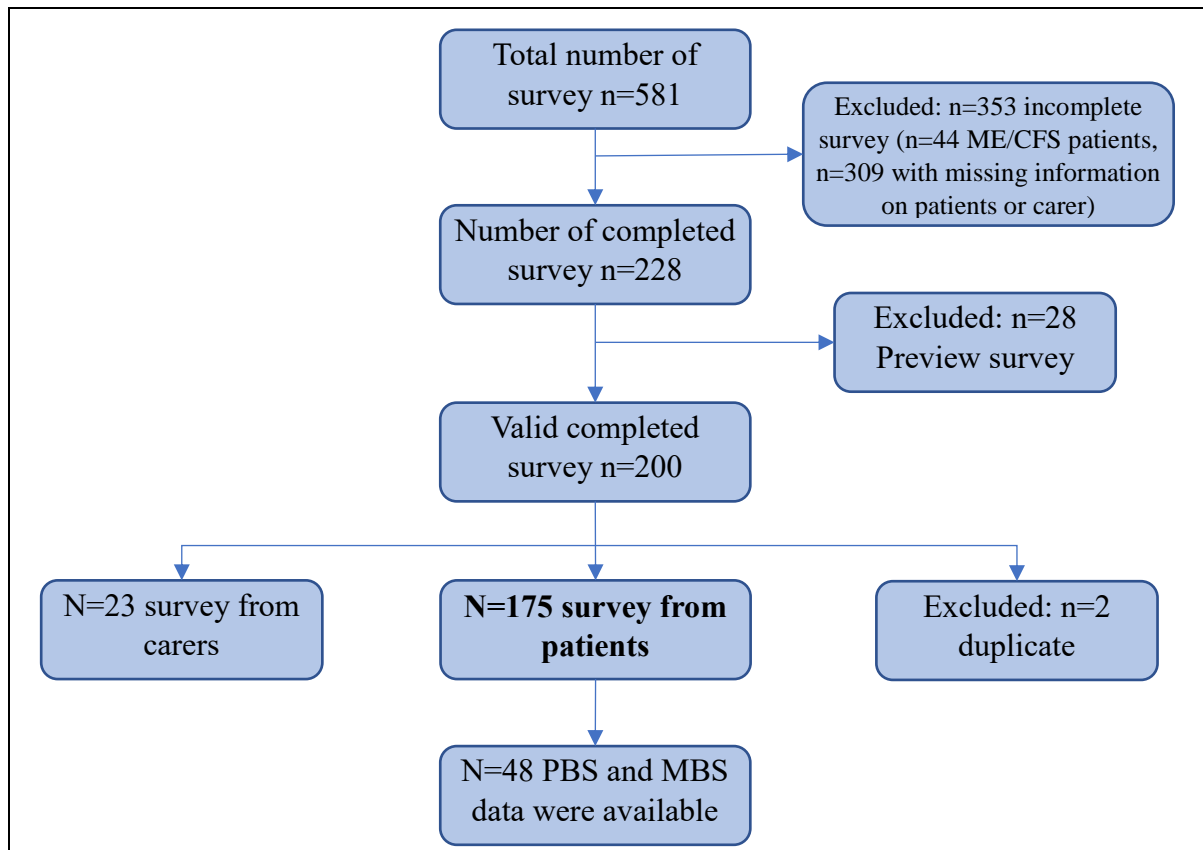**Supplement Figure 1 Participants' flow into the study**

Figure S1. A summary of participants' flow into the study

Supplement 1: The items reported by participants for direct non-medical costs

Digital equipment
Tablet, Ipad, Video doorbell, Electric toothbrush, Tens machine, heart rate graph app, google home nest, smart phone, Fitbit, Activity tracker app, Massager, Laptop computer, Apple watch, Heart rate monitor watch, Nintendo Switch plus games, All in one PC, Garmin Lily Watch, Echo dot, Wifi mesh, Calm radio meditation and calming music app, noise canceling headphones, Apps, Pedaller, Sit stand desk, Ergonomic keyboard, Ergonomic chair, Pacing app, Ipad pen, Polar watch, Wrist worn heart rate monitor, Blood pressure monitor, Mindfulness app, Todo app, Assorted home automation equipment, Screen reader, Internet, PC power supply, Smart controllers, Wireless earbuds, Detached keyboard, Computer microphone, Audiobooks, Communication App

Travelling
car, taxi, Uber, Stateliner bus, Door to Door medical transport, car parking, Tram, Train, Sheba, CTST, Support worker, Rail, Private wheelchair taxi service, Neighbour driving me in my car, public transport, private car to medical appts, Aeroplane

Community services
Meals on wheels, home and community care, welfare organisation, housing organisation, house cleaning, gardening, mid coast assist-support workers, linc pine reiver volunteer drivers, home library service, church community, housing, library delivery, ME/CFS Australia on Facebook, ME/CFS local group, ME/CFS Zoom, ME/CFS SA, ME/CFS & Lyme WA support group, HACP-ACT Govt program, CTG

Everyday living
Household chores, gardening, Cleaning, Home meal delivery, Grocery delivery, Courier Handyman, House Maintenance, pool cleaning, mowing, car cleaning, window cleaning, Laundry, Hedges trimmed, Domestic Assistance, Cooking, meal services, Household repairs - plumbing, Kitchen repair, Gutters, Labourers, Vacuuming/mopping, Changing bed sheets, Support worker, Dog walker, End of lease clean, personal care, shopping

Special modification/renovation
Rail in bathroom, Bars in toilet and bathroom, Building a new home, Land costs, Move into my own room, ramp, Handrail by front step, shower grab rail, moved to a smaller house, Shower hand held, Moved house, Shower repairs, Bathroom, house shielding, Renovation to fix mould, Kitchen, lowered shelving, Double glazed windows, replace carpet with hard floors, moving furniture, Triple glazed windows, New flooring, Upgraded to double glazed windows, Kitchen renovation, Purchase low allergy bed linen, Install fume extraction, Automatic Garage doors, Recliner

Special diet
Premade meals, sourdough bread (no preservatives), tuna (in olive oil), zymil milk, decaf coffee, dahl, fresh ginger and lemon for tea, Organic food, Gluten free food, Dairy free foods, MSG free foods, Amine free foods, Low sugar/Low GI foods, Keto bread, Almond meal, Stevia, Low food map foods, Stevia so sugar free, Coffee for enemas, pre prepared food delivery, bread substitute, Electrolytes, Gluten free food, Ready meals from supermarket, meal delivery, Love Ya Guts box, Bone broth, Lite'nEasy, Hello Fresh, Takeaway, Developing recipes, Making shopping list, Prepared Meals, Fibre supplements, Lean Cuisine, low carb meals, All food prep by support worker, Sheep yoghurt, sheep cheese, Prepared ingredients, Gut relief meds, Restricted diet, probiotics, constipation meds, FODMAP - Frozen Meals, high protein low carb meals, Low-FODMAP food, Weekly Prepared meal delivery service, Food Replacement Drink Sustagen/Ensure

Supplement 2: Direct Cost calculation

2.1 Prescription medication

For those who did not consent to data linkage, name of drug, strength, dosage and frequency of ME/CFS-related prescriptions were collected through the cost diaries. Unit costs of prescriptions reported in cost diaries were calculated using two methods: 1) for items that can be found from the extracted PBS records, we imputed unit costs using the mean patient out-of-pocket and government costs from the extracted PBS records; and 2) for items that were not available from the extracted PBS records, we used unit costs from the online PBS cost schedule, and the average co-payment i.e. 9% for general patients and 91% for concessional patients[19].

Cost per unit paid by patient = $P_{general} * 0.09 + P_{concession} * 0.91$, where $P_{general}$ represented the unit cost for general patients, and $P_{concession}$ represented the unit costs for concessional patients.

Cost per unit paid by government = $P_{unitcost}$ − Cost per unit paid by patient, where $P_{unitcost}$ represent the unit costs of the item.

The annual total costs of the prescribed item were calculated by formula: $Cost_{presc}$ = number of units in 4 weeks* unit cost*12, where number of units were calculated by: number of units = (dose per day * days took in 4 weeks) / dose per unit.

2.2 Non-prescription medication

The information on non-prescription medications related to ME/CFS collected in cost diary included the name of medications, strength, dosage took per day and days took in 4 weeks. The unit costs of the non-prescription medications were calculated using the average price from the three largest Australian pharmacy groups[20].. The annual total costs of the non-prescription item were calculated by formula: $Cost_{nonpresc}$ = number of units in 4 weeks* unit costs*12, where number of units were calculated by: number of units = (dose per day * days took in 4 weeks) / dose per unit.

2.3 Health care professional visits and investigation costs

The information on health care professional visits and investigation tests related to ME/CFS collected in cost diary included service name, number of visits and average length of visit. The annual total costs of health care professional visits and investigation costs were calculated by the formula: $Cost_{healthcare}$ = number of visits in 6 months * unit costs * 2.

2.4 Hospital costs

Information on hospital admissions, emergency department and outpatient attendances was collected in the cost diary. This included the number and reasons of visits/admissions, length of stay, fee charged per visit/admission and cost to patients. As only three (of 15) participants who reported a hospital admission/attendance provided sufficient data to assign costs, costs were estimated based on the number of hospital and emergency department visits/admissions reported in the cost diary, combined with the national average hospital inpatient admission costs for 2020/21: $4,971 [22]. The price weights of 0.0471 and 0.1781 for non-admitted

patients and emergency department attendance were applied respectively. The price weights were sourced from the latest national efficient price 2022-23 (for which, the costing information were drawn from the national Hospital Cost Data Collection Round 2019-20)[23].

2.5 Special equipment

The cost diary collected information on the special equipment purchased for ME/CFS in last 12 months including item name, number, expected lifespan (in year) and the price. The total cost of the special equipment for last 12 months were calculated by the formula: $Cost_{sequip}$ = (number of item * price) / expected lifespan.

2.6 Digital equipment

The cost diary collected information on the digital equipment purchased for ME/CFS in last 12 months including item name and costs. The patient reported costs for 12 months were used as annual cost.

2.7 Travelling

The cost diary collected information on travel costs because of ME/CFS in last 12 months including type of transport, frequency, and price per time. The total travel costs for last 12 months were calculated by the formula: $Cost_{travel}$ = Frequency * Price per time.

2.8 Community service

The cost diary collected information on community services related to ME/CFS in last 12 months including service name, number of services, and total costs of the service. Patient reported total costs were used as 12 months costs.

2.9 Everyday living

The cost diary collected information on services for everyday living (e.g., household chore, cleaning, gardening) related to ME/CFS in last 12 months including service name, frequency, and costs per service. The total costs for everyday living in last 12 months were calculated by the formula: $Cost_{living}$ = costs per service * frequency.

2.10 Special modification/renovation

The cost diary collected information on modification/renovations done to home because of ME/CFS in last 5 years including type of modification and total costs. The expected lifespan (in year) for the modification were found from website. The annual cost of the modification was calculated by the formula: $Cost_{modif}$ = total cost of modification / expected lifespan.

2.11 Special diet

The cost diary collected information on special food and food preparation to manage ME/CFS in last 4 weeks including items of preparation and total costs. The annual costs of special diet were calculated by the formula: $Cost_{diet}$ = $Costs_{4week}$ * 12.

Manager
Professional
Technicians and trades worker
Community and personal service worker
Clerical and administrative worker
Sales worker
Machinery operators and driver
Labourer

Supplement 4: Indirect cost calculation

Indirect costs due to lost wages

The questions in the cost diary that were related to the calculation of lost wages included:

Q140: Paid Employment   Have you <u>ever</u> had a job/paid employment? please tick all that apply

☐ No, too unwell to work due to ME/CFS (1)

☐ No, other reasons not related to ME/CFS (2)

☐ Yes, full time (3)

☐ Yes, part time/casual (4)

☐ Yes, self-employed full time (5)

☐ Yes, self-employed part time (6)

☐ Student (7)

☐ Other (8)

Q142: Do you currently have a job/paid employment?

○ No, too unwell to work due to ME/CFS (1)

○ No, unemployed (2)

○ No, retired (3)

○ Yes, full time (4)

○ Yes, part time/casual (5)

○ Yes, self-employed full time (6)

○ Yes, self-employed part time (7)

○ Student (8)

○ Other (9)

Q146: We are interested to understand if ME/CFS has had an impact on the type of paid work you have been involved in. If you were working before ME/CFS, how would you classify this job? (please select one, and answer this for your main job)

○ Manager (1)

○ Professional (2)

○ Technicians and trades worker (3)

○ Community and personal service worker (4)

○ Clerical and administrative worker (5)

○ Sales worker (6)

○ Machinery operators and driver (7)

○ Labourer (8)

Q147: If your main job type has changed <u>because of the impact of ME/CFS</u>, how would you classify your current job, or the last job you had?

○ Not applicable (1)

○ Manager (2)

○ Professional (3)

○ Technicians and trades worker (4)

○ Community and personal service worker (5)

○ Clerical and administrative worker (6)

○ Sales worker (7)

○ Machinery operators and driver (8)

○ Labourer (9)

To calculate the lost wages, we assume that the answer to Q140 is the employment history before ME/CFS, for those who gave multiple choice, select their highest employment level. For example, those who selected multiple answers, when the answer included "Yes, full time (3)", those patients were thought to have full time work before ME/CFS. The lost wages occurred when participants clearly stated the impact was due to ME/CFS, which included participants who selected "No, too unwell to work due to ME/CFS" to Q140 or Q142.

For those who selected both "No, too unwell to work due to ME/CFS" for Q140 and Q142, their annual lost wages were calculated using the 2021 national mean income ($1394.10 per week) multiplying with 52 weeks, which equal to $72,493.2.

For those who ever had a paid employment (which selected 3/4/5/6 for Q140), and current too unwell to work due to ME/CFS (which selected 1 for Q142), their lost wages were calculated by considering of occupation classification answered to Q146. Their lost wages were calculated by multiplying the 2021 national average wage for each occupation classification with 52 weeks for those who worked full-time (selected 3/5 for Q140), or by

multiplying the 2021 national average wage for part-time with 52 weeks for those who worked part-time or casual (selected 4/6 for Q140).

For those who currently have a job/paid employment (selected 4/5/6/7 for Q142), the lost wages due to the job type change because of the impact of ME/CFS were calculated based on the answer to Q146 and Q147. 2021 national average wage by job type were attributed to participants pre- and post-ME/CFS, the lost wages were calculated by multiplying the difference on wages with 52 weeks. If participants' wage increased because of job type changing, then the lost wages were assumed to be 0.

Productivity loss due to absenteeism and presenteeism

Productivity loss due to absenteeism and presenteeism is only applicable for those who are currently have a job (selected 4/5/6/7/8/9 for Q142, N=64)

The questions in the cost diary that were related to the calculation of productivity loss included:

Q144: Please mark the usual total (before tax) weekly income you receive. This includes any payments from government such as the Disability Support Pension.

○ Negative income (1)

○ Nil income (2)

○ $1-$199 ($1-$10,399) (3)

○ $200-$299 ($10,400-$15,599) (4)

○ $300-$399 ($15,600-$20,799) (5)

○ $400-$599 ($20,800-$31,199) (6)

○ $600-$799 ($31,200-$41,599) (7)

○ $800-$999 ($41,600-$51,999) (8)

○ $1,000-$1,249 ($52,000-$64,999) (9)

○ $1,250-$1,499 ($65,000-$77,999) (10)

○ $1,500-$1,999 ($78,000-$103,999) (11)

○ $2,000 or more ($104,000 or more) (12)

Q167: How many days in the last 4 weeks have you stayed away from your work for more than half the day because of ME/CFS-related problems?

Q168: How many days in the last 4 weeks did you go to work while suffering from problems related to ME/CFS?

Q169: On these days when you went to work suffering from problems related to ME/CFS, what percentage of your time were you as productive as usual? For example, if you were exactly as productive as usual, please mark '100 %'.

We assume within 4 weeks, working days will no more than 20 days. Lost productive days due to absenteeism were captured by Q167. Lost productive days due to presenteeism were calculated by multiplying the answer to Q168 by how much ME/CFS affected productivity while working [100%-(Q169)]. The total lost productive days in 4 weeks was the sum of lost productive days due to absenteeism and lost productive days due to presenteeism (Q167 + Q168*(100%-Q169)). Annual total work productivity loss was the costs from absenteeism and presenteeism which was calculated by multiplying the total lost productive percentage (total lost productive days in 4 weeks/20) by their annual personal income. The annual personal income was calculated using the midpoint of each annual income category.

Supplement 5: Disability assessment

Disability severity was calculated using the DePaul Symptom Questionnaire (Short Form) (DSQ-SF). The DSQ-SF includes 28 questions on the frequency and severity of symptoms, each with five response levels (1, 2, 3, 4 and 5). We adopted a validated methodology used in our previous work on another complex and chronic disease – MS – to map from the Patient Determined Disease Steps (9 questions regarding gait) to the Expanded Disability Severity Scale[27]. Following the logic of this disability severity classification, we calculated disability severity for each individual by assigning values of no disability (0), mild (1), moderate (2) and severe (3) to the 5-level responses of DSQ-SF with 0 = DSQ-SF level 1; 1 = level 2; 2 = level 3; and 3 = levels 4 and 5 for each question and then calculating the average across the 28 questions. Patients were classified into four disability severity categories based on the average score: no disability (0-0.5), mild (0.6-1.5), moderate disability (1.6-2.5) and severe disability (>2.5). In addition, as fatigue is a central impact of ME/CFS, we assessed this using a subset of questions from the DSQ-SF asking about the severity of fatigue. The responses were categorised as (1) no fatigue (2) moderate fatigue, and (3) severe fatigue.

Supplement 6: the correlation matrix of independent variables

	Age group	Gender	Highest education	Marital status	Comorbidity group	Condition categories	Disability severity	Years since first experienced symptoms	Years since first diagnosed
Age group	1.000								
Gender	-0.155	1.000							
Highest education	0.030	-0.020	1.000						
Marital status	**0.420**	0.027	0.096	1.000					
Comorbidity group	0.182	0.080	0.033	0.184	1.000				
Condition categories	0.084	0.051	0.012	0.112	0.023	1.000			
Disability severity	-0.191	0.055	-0.108	-0.138	0.097	-0.158	1.000		
Fatigue severity	-0.252	0.011	-0.172	-0.225	-0.080	-0.310	**0.496**	1.000	
Years since first experienced symptoms	**0.418**	-0.109	-0.066	0.211	0.084	0.038	0.037	0.061	1.000
Years since first diagnosed	**0.335**	-0.126	-0.171	0.121	-0.039	0.113	0.014	0.010	0.635

*The absolute correlation coefficient of 0.30 is considered a moderate correlation

Supplement 7: Annual societal costs of ME/CFS by disability and fatigue severity per person in Australia ($2021)

	Mean annual costs per person (AUD)	SE	95% CI
Disability severity			
No/mild disability	42,949	7,111	29,011–56,886
Moderate disability	67,854	3,519	60,956–74,752
Severe disability	95,895	13,610	69,219–122,570
Fatigue severity			
No fatigue	65,525	–	–
Moderate fatigue	50,367	4,313	41,913–58,821
Severe fatigue	77,663	5,340	67,197–88,129

Supplement 8: The comparisons on the costs of prescription and healthcare professional visits and investigation between PBS/MBS consenters (n=48) and non-consenters (n=127)

	PBS/MBS consenter (Mean, SD)	PBS/MBS non-consenter (Mean, SD)
Prescription costs		
Paid by government	2,143 (9,108)	357 (861)
Paid by patients	254 (327)	703 (1,021)
Total	2,397 (9200)	1,060 (1,505)
Healthcare professional visits and investigation		
Paid by government	2,552 (2,309)	1,597 (2,217)
Paid by patients	888 (1,317)	1354 (2,435)
Total	3,439 (3,433)	2,952 (3,828)

SD=standard deviation.

Supplement 9: Comparing the annual per person costs of ME/CFS and other diseases in Australia

Disease	Cost categories	Estimated costs (2021 AUD)
ME/CFS	Direct (healthcare + non-healthcare) and Indirect	63,400
Multiple Sclerosis	Direct (healthcare + non-healthcare) and Indirect	73,169
Motor Neuron Disease	Direct (healthcare + non-healthcare) and Indirect	162,547
Dementia	Direct (healthcare + non-healthcare)	96,022
Parkinson's disease	Direct (healthcare + non-healthcare) and Indirect	84,644
Stroke first year	Direct (healthcare + non-healthcare) and Indirect	59,141
Type 2 Diabetes	Direct (healthcare + non-healthcare) and government subsidies	23,420
Diabetes no symptoms	Direct (healthcare + non-healthcare) and government subsidies	12,993
Hemochromatosis (severe)	Direct (healthcare + non-healthcare) and Indirect	11,165
Obesity (BMI 30−34.9 kg/m2)	Direct (healthcare + non-healthcare) and indirect (government subsidies)	9,824
Overweight	Direct (healthcare + non-healthcare) and indirect (government subsidies)	6,793
Depression/anxiety	Direct (healthcare + non-healthcare) and Indirect	5,325
Diabetic renal failure subsequent years	Direct healthcare costs	58,639
Diabetic renal failure first year	Direct healthcare costs	36,650
Diabetes-related chronic leg ulcer first year	Direct healthcare costs	19,709