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Delineating the long-term trajectories of social and occupational functioning of young people attending primary-care based, early intervention mental health services

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ABSTRACT

Objectives: Mental disorders typically emerge during adolescence and young adulthood and put young people at risk for prolonged socio-economic difficulties. This study describes the longitudinal course of social and occupational functioning of young people attending primary-care based, early intervention services.

Design: A longitudinal study of young people receiving mental healthcare.

Setting: Data were collected between January 2005 and August 2017 from a designated primary-care based mental health service.

Participants: 554 young people (54% female) aged 12 to 32 years.

Measures: A systematic medical file audit collected clinical and functional information at predetermined time intervals (i.e. 3 months to 5+ years) using a clinical proforma. Group-based trajectory modelling (GBTM) was used to identify distinct trajectories of social and occupational functioning over time (median number of observations per person = 4; median follow up time = 23 months).

Results: Between first clinical contact and time last seen, 15% of young people had reliably deteriorated, 23% improved and 62% did not demonstrate substantive change in function. Of the whole cohort, 69% had SOFAS scores less than 70 at time last seen, indicative of ongoing and substantive impairment. GBTM identified six distinct functional trajectories whereby over 60% had moderate to serious functional impairment at entry and remained chronically impaired over time; 7% entered with serious impairment and deteriorated further; one quarter were mildly impaired at entry and functionally recovered; and only a small minority (4%) presented with serious impairments and functionally improved over time. Not being in education, employment or training, previous hospitalisation and a younger age at baseline emerged as significant predictors of these functional trajectories.

Conclusion: Young people with emerging mental disorders have significant functional impairment at presentation for care, and for the majority, it persists over the course of clinical care. Despite the logic of providing clinical care earlier in the course of illness, these data suggest that more sophisticated and more intensive

individual-level and organisational strategies may be required to achieve significant and sustained functional improvements.

Key words: Mental health; longitudinal study; functional impairment; young people; health services

Strengths and limitations of this study

- This study is one of the first to report on the long-term functional outcomes for young people attending primary-care based, early intervention mental health services. It highlights that while improvement is likely to occur throughout the course of care, the rate of clinical impairment and functional deterioration remains high for a large number of people with 69% remaining below the clinical cut-off at time last seen.
- This study utilised a rich data set of 554 participants with between two and nine observations per person (median = 4; approximately 2200 data points) up to five years after initial presentation and applied a novel group-based trajectory modelling procedure to characterise the pattern of change in functional impairment over time. This procedure identified six distinct trajectories that differ in terms of the initial level of functional impairment at presentation and the course of functioning over a five year period.
- Although this study focuses on individuals who were continually engaged in clinical care and represents 18% of the total research register it provides valuable insight into the social and occupational functioning of young people over a long period of time. These results further our understanding of functional impairment in a cohort with common mental disorders and highlights the need for better health service and individual intervention strategies that monitor and target these outcomes.

INTRODUCTION

Mental disorders consistently rank among the leading causes of death and disability worldwide[1-3]. These disorders typically emerge during adolescence and young adulthood and put these young people at risk for prolonged socio-economic difficulties over their lifetime, even when their mental ill health subsides or is at sub-threshold levels[4-7]. There are major direct healthcare costs attributed to diagnosis and treatment, however it is their indirect costs linked to income loss through mortality, disability and regular absences from education or work that impact future income potential and have substantial global economic consequences[8 9]. The significant overlap between these disorders, economic inactivity and functional impairment reiterates the need to recognise and address the common health and economic vulnerabilities of these young people[10].

The long-term outcomes for most major mental disorders often include high rates of recurrence, and slow or incomplete functional recovery, even among those who may have symptomatically remitted[11-14]. Long term follow up studies among older adults indicate that functional impairment often persists with most people experiencing some degree of disability during the majority of the long term follow up period[15], while it is common for those within a primary care setting to spend up to one-third of the long term follow up period off work[16]. Similar patterns are evident among young people, since most medical and psychological treatments developed to address depression do not consistently improve functioning[17-19]. Of the few studies that report long-term functional outcomes for young people, most adolescents treated for depression experienced positive functional outcomes up to three years later, however persistent functional impairment was common for those with comorbidity and recurrence of depression[20].

Early intervention services and models of care have been designed to respond to the early phases of these disorders, their associated comorbidities and impairment, to prevent or delay the progression of illness and reduce the burden for those at-risk [21-23]. Although many young people present with sub-threshold syndromes, they frequently report significant functional impairment (i.e. reduced functioning in social, occupational or other areas of daily life) and a high rate of disengagement

from education, employment or training (NEET)[21 24-26]. Over time, functional impairment tends to be associated with symptom remission, however the overall level of impairment and rate of disengagement remains high compared to the community[27-29]. This is particularly the case for those with more severe presentations who, despite receiving more intensive initial interventions, are unlikely to functionally recover in relatively short-term care environments[30]. While the first 12 months of care are characterised by significant changes in functional impairment[31], the long-term patterns of functional impairment among young people engaged in primary mental health care remains largely unknown.

Understanding the changes in social and occupational functioning over time in real-world clinical cohorts is crucial for guiding the development mental health service provisions that meet the individual needs of young people with emerging mental disorders. This study examines the longitudinal course of social and occupational functioning for a cohort of young people after their initial presentation to a primary mental health care service. We report on the overall rate of change in social and occupational functioning, and aim to determine whether there are distinct long-term trajectories (via modeling) of functioning over the course of care.

METHODS

Participants

Study participants were drawn from a larger cohort of young people (n=3087; 59% female, mean age = 18.52 ± 3.8) presenting to youth mental health clinics in the Sydney area who were recruited to a case register for mood, psychotic, developmental and other mental disorders between January 2005 and August 2017 [26]. Individuals were included in the present study if they met the following inclusion criteria: (i) between 12 and 32 years of age at the time of initial assessment; and (ii) were seen by a clinician on at least two separate occasions. Exclusion criteria for all potential participants were: medical instability or lack of capacity to give informed consent (as determined by a psychiatrist), history of neurological disease (e.g. tumor, head trauma, epilepsy), medical illness known to impact cognitive and brain function (e.g. cancer, ECT in last 3 months), and/or clinically evident intellectual disability

and/or insufficient English to participate in the research protocol. The study was approved by the University of Sydney Human Research Ethics Committee.

Data collection process

All participants received clinician-based case management and relevant psychosocial and/or medical interventions over the duration of their time in care. Trained research psychologists and medical officers conducted a medical file audit to collect demographic, clinical and functional information at predetermined time intervals using a clinical proforma (see details below). The first available clinical assessment at the service was taken as the baseline time point for each participant and the date of this assessment was used to determine each of the follow up time points: 3 months, 6 months, 12 months, 2 years, 3 years, 4 years, and 5 years. If no clinical notes were available within +/- 1 month of the 3 and 6 month time points, or +/- 3 months of the yearly time points then this particular entry was left missing. A 'time last seen' entry was also used to capture final clinical information that did not align with one of the specified time points to ensure that every participant had data entered for the total time they were engaged with the clinical service. When data was available for a specified time point, all clinical notes from the preceding proforma entry, up to and including the current proforma entry were used to complete the proforma.

Clinical proforma

The clinical proforma captures key clinical information about the current episode and specific illness course characteristics, and an earlier version has been used in previous studies[21] [26]. The proforma collects information about; (i) basic demographics (age, gender, receipt of government benefits); (ii) mental health diagnoses (based on DSM-V criteria); (iii) clinical course information (hospitalisations, childhood diagnoses); (iv) comorbidities (physical health diagnoses and suicidal thoughts and behaviours); and (v) functioning (assessed using the Social Occupational Functional Assessment Scale (SOFAS)[32] and engagement in part-time or fulltime education, employment or training, used to determine not in education, employment or training [NEET] status).

Statistical analyses

Statistical analyses were performed using SAS Software (SAS Institute). Overall changes in functioning (i.e. 'improvement', 'no change' and 'deterioration') between baseline and time last seen were determined using a Reliable Change Index (RCI) score of 10-points, and a clinically significant cut-off of equal to or above 69 was used[29 31 33]. To characterise the pattern of change in functional impairment over time we used group-based trajectory modelling (GBTM) using a procedure called PROC TRAJ (Nagin & Odgers, 2010). This method estimates multiple trajectory groups within the population and uses a maximum-likelihood method to calculate the probability of membership within each trajectory for each participant. We first fit the null model (one group model), and progressively increased the number of groups until we reached the optimal number of trajectory groups, which was determined using the Bayesian Information Criterion (BIC). A higher number (i.e. smaller negative number) indicates a better balance between model complexity and model fit. The shape of each trajectory was examined by modelling three parameters (linear, quadratic, cubic) and then, starting with the higher order polynomials, dropping non-significant parameters from the model. If all three parameters were not significant the linear parameter was retained. Finally, to explore which baseline factors were associated with each trajectory group, we used stepwise logistic regression, which included baseline demographic and clinical characteristics; age, gender, receipt of government benefits, NEET status, mental health diagnosis, medical diagnosis, childhood mental health diagnosis, hospitalised (ever), suicide ideation (ever), suicide planning (ever), and suicide attempts (ever). An α level for entry and exclusion were set at *P=0.15* and based on the likelihood ratio statistic.

RESULTS

Sample characteristics

The sample consisted of 554 young people, 54% (297/554) were female and the mean age was 19.83 (SD = 3.77). At baseline, 20% (113/554) identified as NEET, 17% (95/554) were currently receiving government benefits and the majority (78%; 423/542) were in the clinical range of functional impairment (ie. SOFAS score < 69). The most common primary diagnosis was depression (43%; 237/548), followed by bipolar disorder (20%; 108/548), and then anxiety (18%; 99/548) with comorbid mental health problems identified in 79% (428/544) of participants. Physical health

comorbidities were reported in 26% (142/554) of participants, 23% (127/554) had previously been hospitalised due to a mental health problem, and 14% (75/554) had a mental health or behavioural diagnosis in childhood.

Changes in functional impairment between baseline and time last seen

The number of follow up time points recorded for an individual varied between 2 and 9 (median = 4)(figure1) and the number of months between baseline and time last seen was between 1 and 126 (median = 23 months)(figure 2). The occurrence of time last seen was spread with 38% (208/554) occurring within the first 12 months after baseline and 62% (346/554) occurring more than one year after baseline. Overall, between baseline and time last seen, 15% (79/538) had reliably deteriorated, 23% (122/538) reliably improved and 62% (337/538) did not reliably change, while 69% (370/538) were below the clinical cut-off (SOFAS <69) at time last seen.

Identifying functional impairment trajectories

GBTM identified that six distinct trajectories provided the best balance between model complexity and model fit for the data (table 1). The BIC continued to increase as the number of groups increased, however the BIC change from seven to nine trajectories were small and resulted in trajectory groups with very small sample sizes that did not add useful information beyond that provided by the six trajectories. Table 2 shows the model selection process for the shape of each of the six trajectories. We started with all three parameters in the model (linear, quadratic and cubic). The final model (model 4) had the highest BIC and contained quadratic parameters for trajectories 1, 3 and 5 and linear parameters for trajectories 2, 4, and 6.

Table 1. Criteria for selecting the number of trajectories

Number of groups	BIC	Null model	BIC change
1	-8773.03	0	-
2	-8372.01	1	401.022
3	-8243.31	2	128.695
4	-8215.51	3	27.802
5	-8207.80	4	7.710
6	-8166.46	5	41.339
7	-8164.58	6	1.882
8	-8162.05	7	2.528
9	-8155.80	8	6.251

Table 1 caption. BIC = Bayesian Information Criterion. BIC change presents the changes in the BIC value as the number of trajectory group's increases. Large changes in BIC from 1 to 6 groups justified moving towards the more complex model, however changes in BIC from 7 to 9 groups were rather small and compromised the balance between complexity and fit. Six trajectory groups was deemed to be the most parsimonious model that provided the best balance between complexity and fit.

Table 2. Model selection for each functional impairment trajectory group.

Trajectory Group	Parameter	Model 1	Model 2	Model 3	Model 4
1 Serious impairment – deterioration	Intercept	51.61208	51.77906	51.21822	50.92215
	Linear	**-0.84458*** **	**-0.86418*** **	**-0.50281*** **	**-0.49666*** **
	Quadratic	**0.02424****	**0.02483****	**0.00607****	**0.00599****
	Cubic	**-0.00022***	-0.00022	.	.
2 Serious impairment - chronic	Intercept	54.98897	54.95892	54.54367	54.75505
	Linear	-0.19938	-0.18538	0.02760	-0.03218
	Quadratic	0.00966	0.00901	-0.00110	.
	Cubic	**-0.00012***	-0.00012	.	.
3 Serious impairment - improvement	Intercept	41.08481	42.22558	42.03591	42.21444
	Linear	**1.76596*** **	**1.26818*** **	**1.26797*** **	**1.25871*** **
	Quadratic	**-0.03534***	**-0.01123*** **	**-0.01116*** **	**-0.01106*** **
	Cubic	0.00028	.	.	.
4 Moderate impairment - chronic	Intercept	61.20176	61.32354	61.52807	61.44346
	Linear	0.09497	0.04047	0.01924	0.02027
	Quadratic	-0.00309	-0.00039	.	.
	Cubic	0.00003	.	.	.
5 Mild impairment - improvement	Intercept	67.79146	68.08779	68.12046	68.11021
	Linear	**0.46038*** **	**0.31975*** **	**0.32482*** **	**0.32399*** **
	Quadratic	**-0.01202***	**-0.00468*** **	**-0.00478*** **	**-0.00477*** **
	Cubic	0.00009	.	.	.
6 Slight impairment - stable	Intercept	77.35888	77.40056	77.94966	77.93924
	Linear	0.19581	0.13170	0.04127	0.04153
	Quadratic	-0.00575	-0.00168	.	.
	Cubic	0.00005	.	.	.
Model fit	BIC	-8166.462	-8156.357	-8148.227	-8145.595

Table 2 caption. Parameter estimates are shown. Significant values are bolded. *P<.05, **P<.01, ***P<.001. The first model identified that the cubic parameters for trajectories 3, 4, 5 or 6 were not significant and were thus dropped for model 2. Model 2 identified that the quadratic parameters for trajectories 4 and 6 were not significant, and that the cubic parameter for trajectories 1 and 2 were not significant and were dropped for model 3. Model 3 identified that the quadratic parameter for trajectory 2 was not significant and was dropped for model 4. The final model (model 4) had the highest BIC and contained quadratic parameters for trajectories 1, 3 and 5 and linear parameters for trajectories 2, 4, and 6.

Figure 3 shows SOFAS score over a 5 year period for the six trajectories included in the final model (see supplementary figure 1 for individual-level trajectories for each group). Three trajectories start out with serious functional impairment at baseline but differ in the type of change in functioning over time. The first was the second largest group of the entire sample (29%; 158/554) and included individuals who followed a chronic course of serious functional impairment with little to no change in functioning over time ('serious impairment – chronic'). The second trajectory was quadratic and included individuals who significantly deteriorated in the first 12 months before plateauing between 12 and 60 months ('serious impairment – deterioration'), while the third trajectory was also quadratic and included the small minority who improved significantly over the first 24 months to mild levels of functional impairment before slightly tapering off with mild to no functional impairment ('serious impairment – improvement'). By contrast, the remaining three trajectories each started out with moderate to mild levels of functional impairment. The first included the largest number of people across the entire sample (33%; 185/554) who presented with moderate impairment and followed a chronic course of moderate impairment over time ('moderate impairment – chronic'). The second trajectory was quadratic and characterised by individuals who were mildly impaired at baseline, but improved/functionally recovered in the first 6 to 12 months before tapering off and remaining in the functional recovered population over time ('mild impairment – improvement'). The final trajectory group characterised the small number of individuals who were functioning well with no more than slight impairment at baseline and whose functioning was stable over time ('slight impairment – stable').

Differentiating between functional impairment trajectories

The aim of these analyses were to identify any demographic and clinical differences at baseline between the trajectory groups. The 'serious impairment – chronic' trajectory was chosen as the reference group because of the most impaired groups at entry, this group was the largest group and followed a stable/chronic trajectory over time. Of the demographic and clinical variables at baseline (table 3); NEET status, age and previous hospitalisations emerged as the factors that differentiated trajectory groups and were included in the redcued model. NEET status distinguished between

most trajectories, whereby those on the 'serious impairment – chronic' trajectory were less likely to be engaged in education, employment or training compared to 'moderate impairment – chronic' (OR = 0.47, 95% CI 0.27 – 0.83, p < 0.01), 'mild impairment – improvement' (OR = 0.08, 95% CI 0.03 – 0.23, p < 0.001) and 'slight impairment – stable' (OR = 0.09, 95% CI 0.01 – 0.70, p < 0.05). Regarding age, those on the 'serious impairment – chronic' trajectory were: older than those on the 'serious impairment – improvement' trajectory (OR = 0.83, 95% CI 0.71 – 0.98, p < 0.05), and younger than those on the 'mild impairment – improvement' trajectory (OR = 1.08, 95% CI 1.00 – 1.16, p < 0.05). For previous hospitalisation, those on the serious impairment – chronic' trajectory were more likely to have been previously hospitalised than those on the 'mild impairment – improvement' trajectory (OR = 2.72, 95% CI 1.39 – 5.33, p < 0.01).

Table 3: Baseline characteristics by functional impairment trajectory group (n=554)

	Total sample	**Serious impairment - deterioration**	**Serious impairment - chronic**	**Serious impairment - improvement**	**Moderate impairment - chronic**	**Mild impairment - improvement**	**Slight impairment - stable**
N (%)	554 (100 %)	39 (7%)	158 (29%)	19 (4%)	185 (33%)	129 (23%)	24 (4%)
Age, mean (sd)	19.83 (3.77)	20.26 (4.05)	19.68 (3.70)	18.37 (4.76)	19.75 (3.88)	20.12 (3.35)	20.29 (4.23)
Female, n (%)	297 (54%)	18 (49%)	77 (52%)	10 (56%)	103 (60%)	70 (58%)	19 (83%)
NEET, n (%)	113 (20%)	20 (51%)	47 (30%)	9 (47%)	32 (17%)	4 (3%)	1 (4%)
Receiving gov. benefits, n (%)	95 (17%)	16 (41%)	35 (22%)	4 (21%)	27 (15%)	11 (9%)	2 (8%)
SOFAS score, mean (sd)	60.45 (9.19)	50.61 (7.25)	54.90 (5.63)	43.83 (7.05)	61.39 (5.24)	68.06 (5.35)	78.13 (7.56)
Depression, n (%)	237 (43%)	14 (37%)	70 (45%)	10 (53%)	72 (39%)	59 (47%)	12 (50%)
Anxiety, n	99	6 (16%)	24 (15%)	1 (5%)	36 (20%)	27 (21%)	5 (21%)

(%)	(18%)						
Bipolar, n (%)	108 (20%)	4 (11%)	31 (20%)	3 (16%)	38 (21%)	26 (21%)	6 (25%)
Psychosis, n (%)	34 (6%)	5 (13%)	10 (6%)	1 (5%)	14 (8%)	4 (3%)	0 (0%)
Other, n (%)	70 (13%)	9 (24%)	22 (14%)	4 (21%)	23 (13%)	11 (9%)	1 (4%)
Has a medical diagnosis, n (%)	142 (26%)	10 (26%)	41 (26%)	5 (26%)	51 (28%)	28 (22%)	7 (29%)
Had a childhood diagnosis, n (%)	75 (14%)	8 (24%)	23 (17%)	4 (22%)	21 (12%)	18 (15%)	1 (4%)
Hospitalised (ever), n (%)	127 (23%)	9 (27%)	48 (35%)	7 (37%)	40 (23%)	18 (16%)	5 (24%)
Suicide ideation (ever), n (%)	258 (47%)	15 (44%)	76 (57%)	10 (59%)	89 (53%)	59 (50%)	9 (41%)
Suicide planning (ever), n (%)	94 (17%)	4 (12%)	38 (29%)	5 (29%)	29 (18%)	16 (14%)	2 (10%)
Suicide attempts (ever), n (%)	91 (16%)	7 (20%)	36 (27%)	5 (28%)	22 (13%)	17 (15%)	4 (18%)

Table 3 caption: Column percentages are shown, except for the first row which shows the sample size for each trajectory group as a percentage of the total N. NEET, Not in Education, Employment or Training; SOFAS, Social and Occupational Functional Assessment Scale.

DISCUSSION

Young people with emerging mental disorders have significant functional impairment that is dynamic and chronic over the course of clinical care. Improvement is likely to occur throughout the course of care, however the rate of clinical impairment and functional deterioration remains high for a large number of

people. The results also indicate that while individual trajectories may be highly variable, there are distinct patterns of social and occupational functioning that are differentiated by the level of functioning at entry and rate of change over the course of clinical care. Over 60% of the sample had moderate to serious functional impairment at entry and remained chronically impaired over time, a further 7% entered with serious impairment and deteriorated further, while approximately a quarter of the sample were mildly impaired at entry and were able to improve and functionally recover. Only a small minority (4%), the youngest of the trajectory groups, presented with serious impairments and were able to functionally improve over time. This may reflect the benefits of early intervention, however this requires further investigation. These distinct trajectories highlight the need for improving mental health service and individual intervention strategies to monitor and directly target these problems over the course of care to facilitate clinical, social and occupational recovery[10].

The overall rate of reliable change in this study was comparable to studies conducted in similar cohorts that were followed for relatively short-term occasions of service. The rate of reliable improvement in this study (23%) is consistent with a similar cohort of young people followed for approximately 6 months (25%)[31] and slightly lower than an Australian national study of young people attending *headspace* followed for approximately 3 months (31%)[29]. Interestingly, the rate of reliable deterioration in this study was consistent with the national study at approximately 15%, which suggests that deterioration occurs early and often persists over longer periods. While the overall rate of change is important, this study examined the long term patterns of change, which were informed by multiple time points over a long-term period of care. This revealed that across all levels of impairment there were high rates of chronicity with many individuals remaining at similar levels of functioning over the course of care. For some who may have been on a path of deterioration prior to presentation for care, maintaining a consistent level of impairment may reflect a positive outcome whereby engagement with care stabilised their situation or prevented further deterioration or worsening. For others, however, not being able to return to work or education, or improve social functioning could be detrimental to their future health and socio-economic wellbeing and may reflect a

lack of sufficient integrated psychological and vocational interventions to directly address these outcomes[34 35]. Previous research has shown that only a small number of young people attending primary mental health services received specific vocational support in the previous year[27], despite evidence to suggest that adjunctive interventions targeting vocational activity can have a positive impact on functional outcomes[36 37]. Together, this reiterates the need for early intervention and ongoing care that does more to directly address functional impairment over longer periods.

For health services and clinicians, determining when to adopt these intervention strategies and for whom, is critical. The general trajectories observed in this study are characterised by substantial individual variation from one time point to the next (see supplementary figure 1). This individual variability highlights the challenge health professionals often face when planning effective long-term interventions in a cohort with emerging mental health disorders. Being NEET, previous hospitalisation and a younger age at entry was associated with the serious impairment trajectories compared to the moderate, mild and slight impairment trajectories, however the long-term predictive utility of these characteristics is still limited. Though, through the development and integration of new and emerging technologies within health services, there is an in increased capacity to track these outcomes in real-time through routine outcome measurement to deliver more personalised interventions that respond to an individual's needs[38 39]. Regular feedback to clinicians and individuals can provide important insights into the effectiveness of particular interventions for addressing key clinical and functional outcomes[40]. These approaches could also make use of assessments that aim to identify underlying characteristics, such as cognition, which have demonstrated some utility in predicting changes in functioning overtime[41-43].

This study has some limitations. The sample used for this study focuses on individuals who were continually engaged in clinical care, which means that the overall rate of improvement or deterioration among those who disengaged is unknown. Furthermore, the overall rate of improvement and deterioration in functioning at time last seen is imperfect given that many young people may be still engaged in care and so time last seen may not align with a complete period of care.

This is where the group-based trajectory modelling is beneficial over the overall rate of change, since it accounts for the overall trends to provide a clearer picture of change over time. While we know that this sample represents approximately 18% of the research register (554/3087), it is unclear what proportion of the whole population attending these services this sample represents. This was beyond the scope of this work but it is an important issue to be resolved in future studies, particularly given the patterns of functional impairment chronicity, to ensure current primary care service models are appropriate to address these issues. Finally, there may be other factors that account for these trajectories or differences in functional outcome, such as the type of interventions an individual received or treatment resistance. It is important for future work to determine the effectiveness of specific interventions on functional impairment trajectories and improving these outcomes.

This study provides valuable insights into the long-term functional trajectories of young people engaged in primary mental health care. The significant chronicity observed in this clinical cohort reiterates that ongoing functional impairment is prevalent among young people with emerging mental health disorders and should be a primary focus of intervention, in addition to symptomatic recovery/improvement. The substantial variability in individuals trajectories over time highlight the need for better health service and individual intervention strategies that monitor and target these outcomes so that early social and occupational impairment does not result in lifetime socio-economic burden.

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COMPETING INTERESTS

All authors have completed the ICMJE uniform disclosure at www.icmje.org/coi_disclosure.pdf and declare: Professor Ian Hickie has been a Commissioner in Australia's National Mental Health Commission since 2012. He is the Co-Director, Health and Policy at the Brain and Mind Centre (BMC) University of Sydney. The BMC operates an early-intervention youth services at Camperdown under contract to headspace. Professor Hickie has previously led community-based and pharmaceutical industry-supported (Wyeth, Eli Lily, Servier, Pfizer, AstraZeneca) projects focused on the identification and better management of anxiety and depression. He is a Board Member of Psychosis Australia Trust and a member of Veterans Mental Health Clinical Reference group. He was a member of the Medical Advisory Panel for Medibank Private until Oct 2017. He is the Chief Scientific Advisor to, and an equity shareholder in, Innowell. InnoWell has been formed by the University of Sydney and PwC to administer the $30M Australian Government Funded Project Synergy. Project Synergy is a three year program for the transformation of mental health services through the use of innovative technologies. A/Prof Elizabeth Scott is the Medical Director, Young Adult Mental Health Unit, St Vincent's Hospital Darlinghurst, Discipline Leader of Adult Mental Health, School of Medicine, University of Notre Dame, Research Affiliate, The University of Sydney and Consultant Psychiatrist. She has received honoraria for educational seminars related to the clinical management of depressive disorders supported by Servier and Eli-Lilly

pharmaceuticals. She has participated in a national advisory board for the antidepressant compound Pristiq, manufactured by Pfizer. She was the National Coordinator of an antidepressant trial sponsored by Servier. All remaining authors declare no support from any organisation for the submitted work besides the acknowledged financial support; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

CONTRIBUTORSHIP STATEMENT

FI, DFH, SC and IBH designed the study, interpreted the results and drafted the manuscript. FI and CAB conducted the statistical analyses. FI, NZ, AN, JG and ES were involved in study coordination, data collection. All authors contributed to and have approved the final manuscript.

DATA SHARING

No additional data available.

TRANSPARENCY STATEMENT

The lead authors, affirm that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained.

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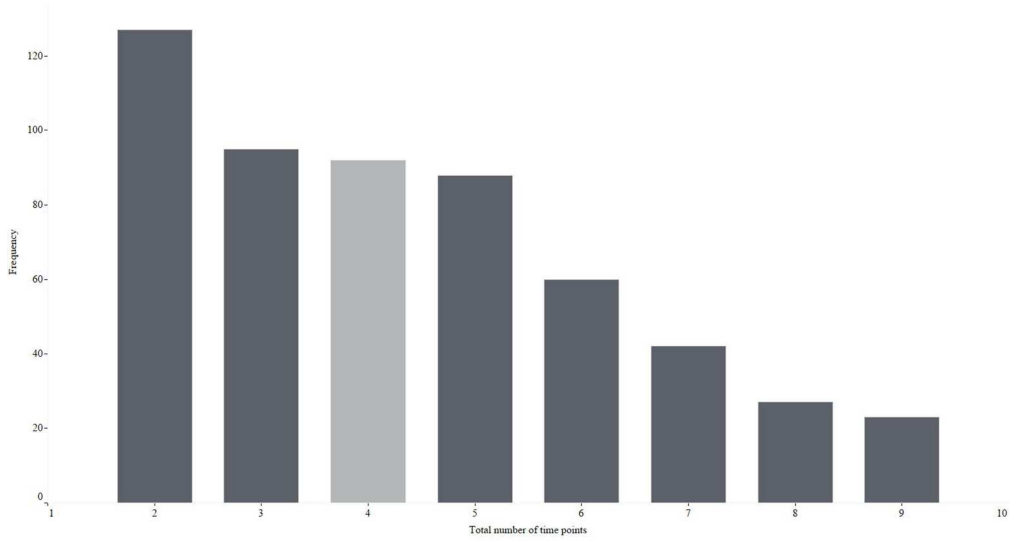

Figure 1 shows the frequency of the total number of time points recorded for each participant (median = 4; light grey bar).

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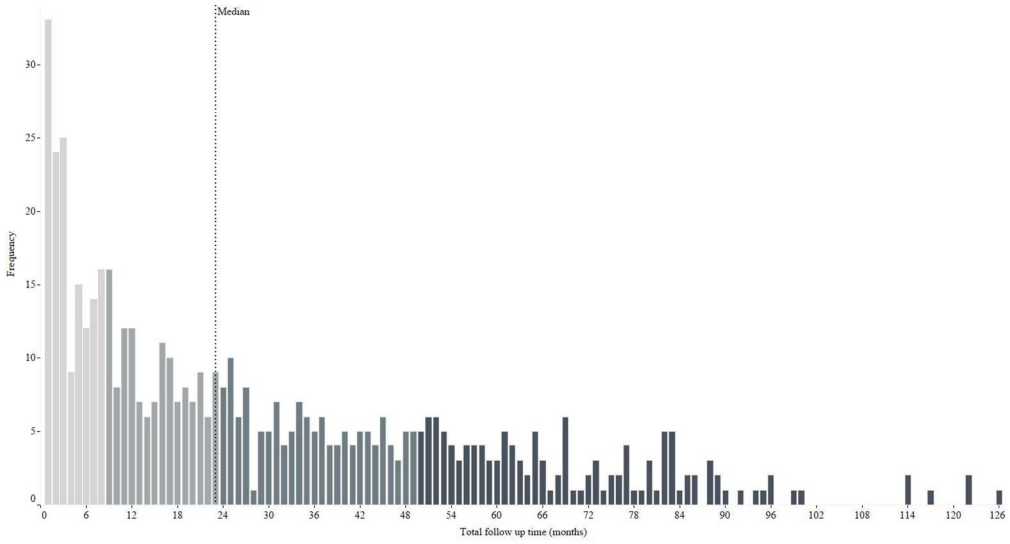

Figure 2 shows the distribution of the total follow up time for each participant in months. The bars have been shaded into quartiles (median = 23 months). The majority of participants (50%) were followed up between 9 months and 49 months (i.e. 4 years) after initial presentation, while 25% were followed up between 1 and 8 months, and the remaining 25% followed up between 50 months (i.e 4 years) and 126 months (i.e. 10 years).

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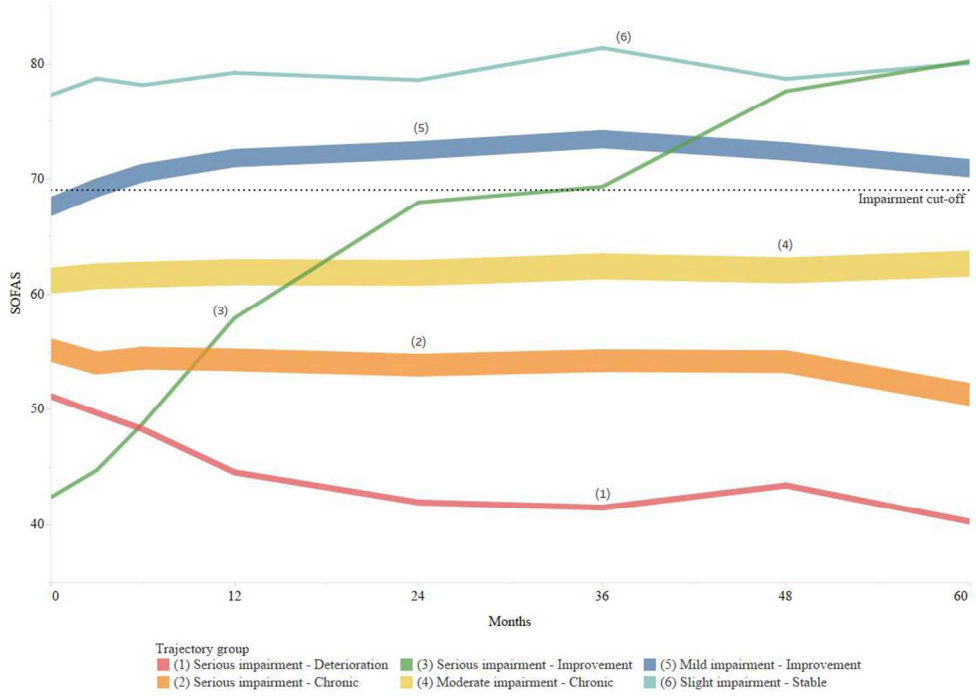

Figure 3 shows the six distinct trajectories identified for SOFAS score over a five year period. The thickness of each line represents the sample size of that particular trajectory, relative to all others. The dotted line represents the clinical impairment cut-off, which is set at a SOFAS score of 69. Slight impairment – stable (n=24, 4%), intercept equal to 78 and linear trend over time; Mild impairment – improvement (n=129, 23%), intercept equal to 68 and quadratic trend over time; Moderate impairment – chronic (n=185, 33%), intercept equal to 61 and linear trend over time; Serious impairment – chronic (n=158, 29%), intercept equal to 55 and linear trend over time; Serious impairment – improvement (n=19, 4%), intercept equal to 42 and quadratic trend over time; Serious impairment – deterioration (n=39, 7%), intercept equal to 51 and quadratic trend over time.

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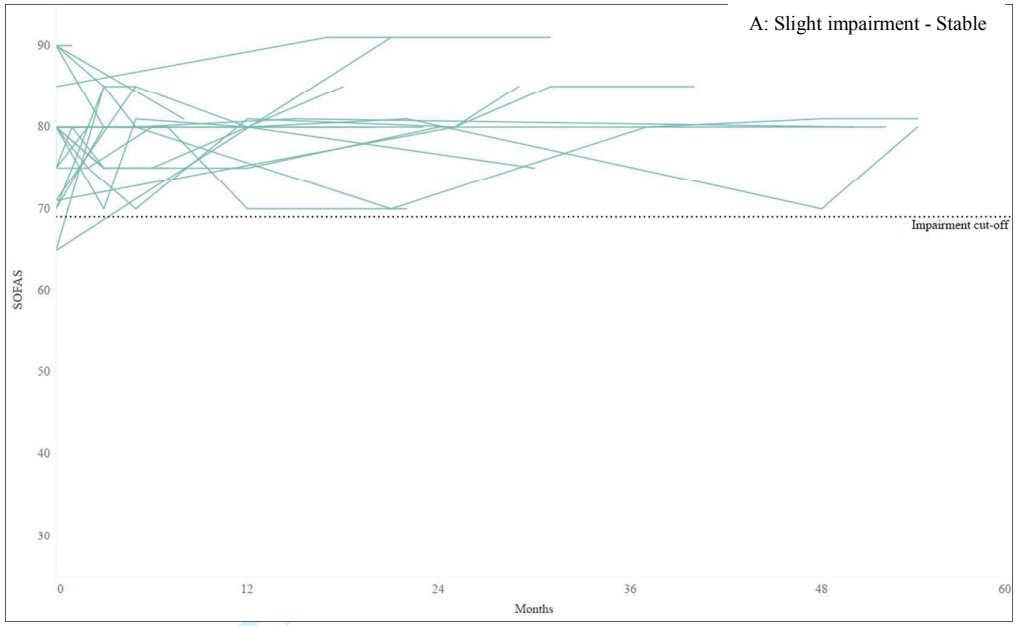
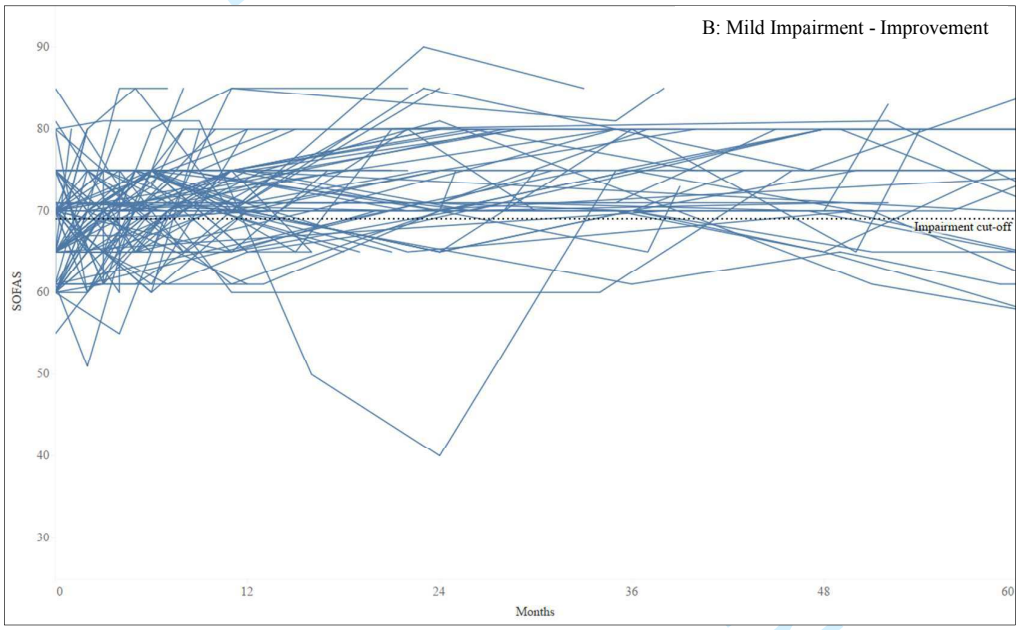
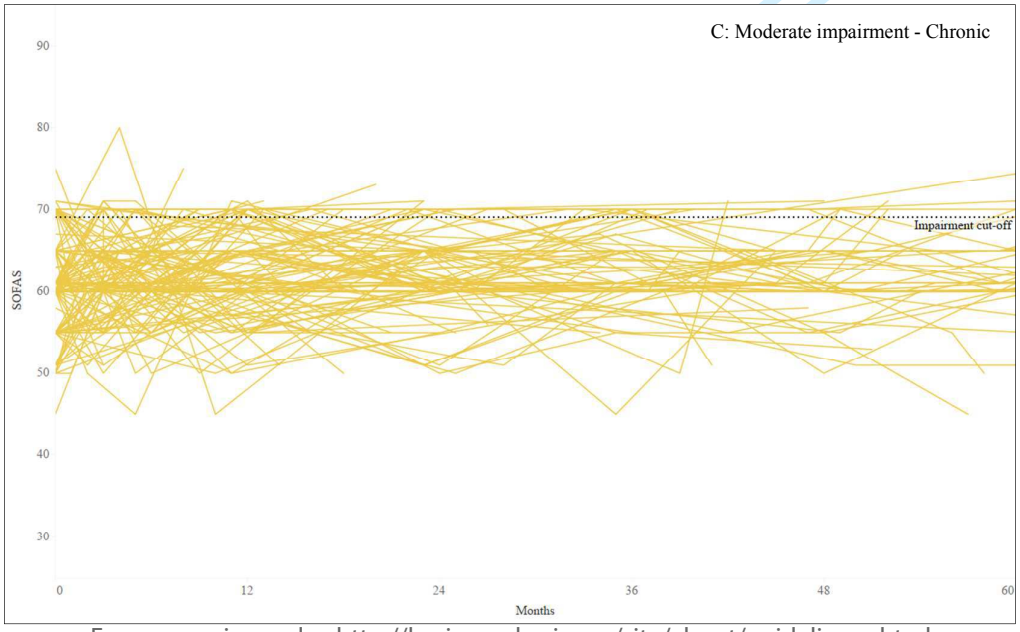
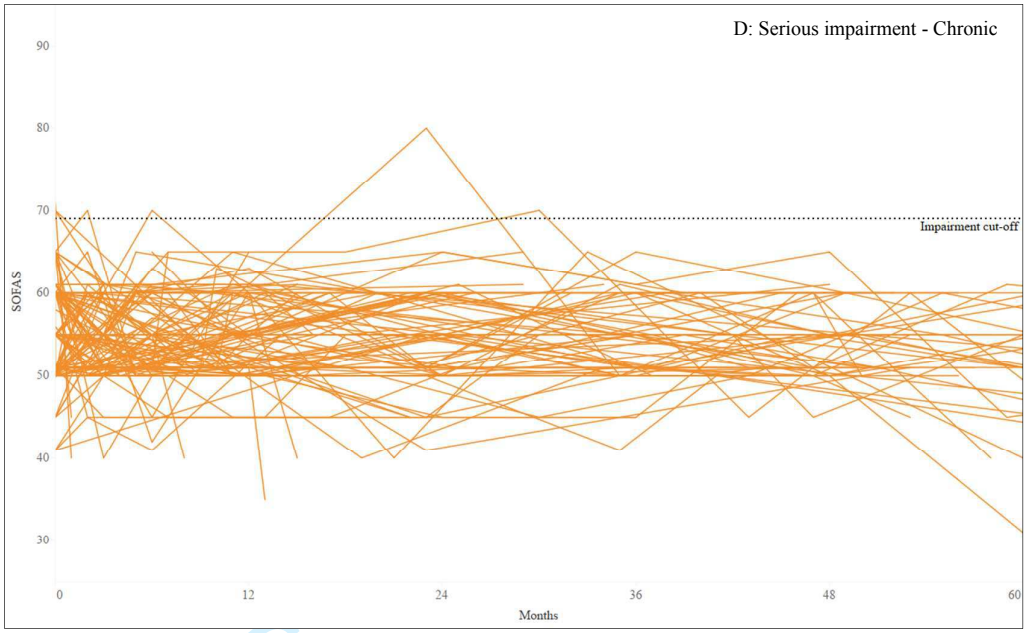
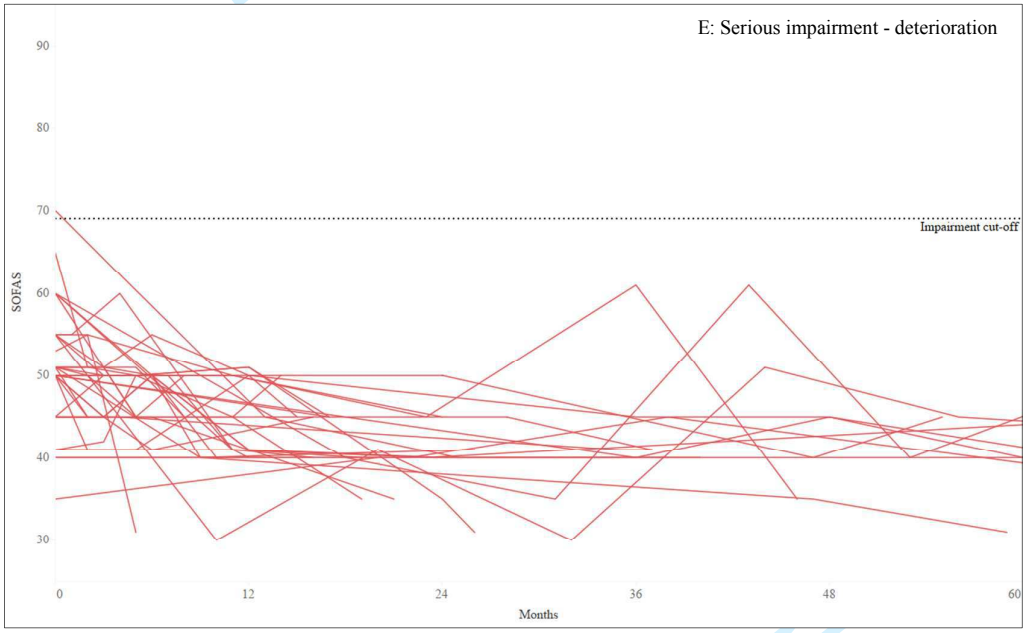
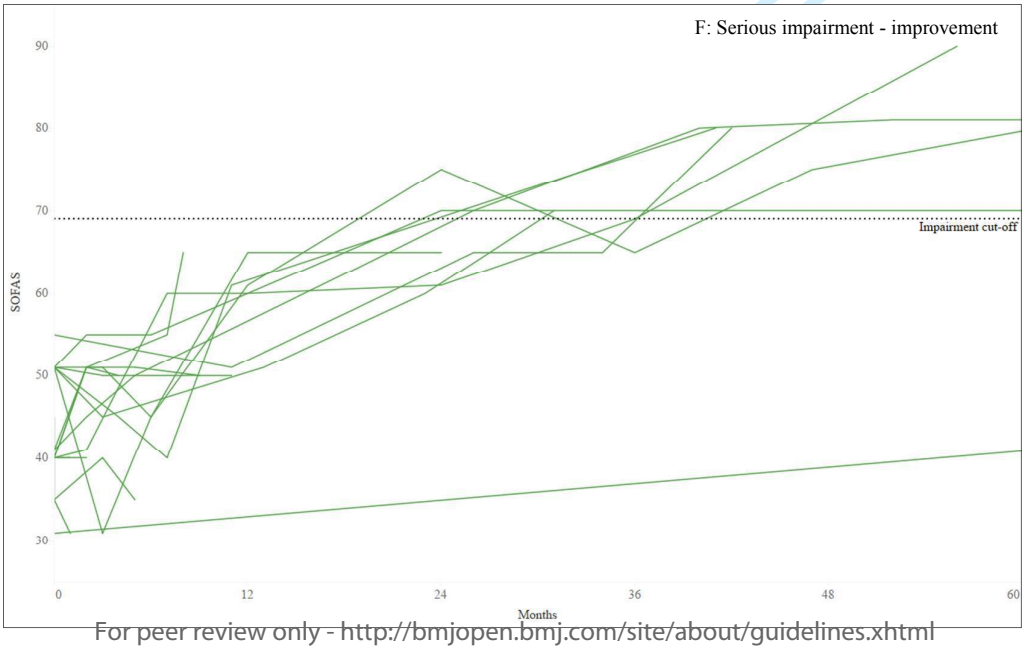

A: Slight impairment - Stable
SOFAS
90
80
70
60
50
40
30
Impairment cut-off
0
12
24
36
48
60
Months


B: Mild Impairment - Improvement
SOFAS
90
80
70
60
50
40
30
Impairment cut-off
0
12
24
36
48
60
Months


C: Moderate impairment - Chronic
SOFAS
90
80
70
60
50
40
30
Impairment cut-off
0
12
24
36
48
60
Months







Supplementary Figure 1 caption

Supplementary figure 1 shows the individual-level trajectories for each group identified and shown in figure 1. Each line represents one individual and their SOFAS score ratings over time. The dotted line represents the clinical impairment cut-off, which is set at a SOFAS score of 69. Panel A: Slight impairment – stable (n=24, 4%), intercept equal to 78 and linear trend over time; Panel B: Mild impairment – improvement (n=129, 23%), intercept equal to 68 and quadratic trend over time; Panel C: Moderate impairment – chronic (n=185, 33%), intercept equal to 61 and linear trend over time; Panel D: Serious impairment – chronic (n=158, 29%), intercept equal to 55 and linear trend over time; Panel E: Serious impairment – improvement (n=19, 4%), intercept equal to 42 and quadratic trend over time; Panel F: Serious impairment – deterioration (n=39, 7%), intercept equal to 51 and quadratic trend over time.

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation	
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	P1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	P2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	P4-5
Objectives	3	State specific objectives, including any prespecified hypotheses	P5
Methods			
Study design	4	Present key elements of study design early in the paper	P5-6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	P5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	P5
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	-
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	P5-7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	P6
Bias	9	Describe any efforts to address potential sources of bias	-
Study size	10	Explain how the study size was arrived at	-
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	P7
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	P7
		(*b*) Describe any methods used to examine subgroups and interactions	P7
		(*c*) Explain how missing data were addressed	P6-7
		(*d*) If applicable, explain how loss to follow-up was addressed	
		(*e*) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	P7
		(b) Give reasons for non-participation at each stage	P6
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	P7,8,12,13
		(b) Indicate number of participants with missing data for each variable of interest	P7-8
		(c) Summarise follow-up time (eg, average and total amount)	P8
Outcome data	15*	Report numbers of outcome events or summary measures over time	P8-13
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear	P11-12

		which confounders were adjusted for and why they were included	
		(*b*) Report category boundaries when continuous variables were categorized	-
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	-
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	P8-11
Discussion			
Key results	18	Summarise key results with reference to study objectives	P13-14
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	P15-16
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	P14-15
Generalisability	21	Discuss the generalisability (external validity) of the study results	P14-16
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	P17

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

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Delineating the trajectories of social and occupational functioning of young people attending primary-care based, early intervention mental health services: A longitudinal study

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Secondary Subject Heading:	Health services research
Keywords:	MENTAL HEALTH, Health services, Longitudinal study, Young people, Functional impairment

Delineating the trajectories of social and occupational functioning of young people attending primary-care based, early intervention mental health services: A longitudinal study

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Word count: 3572

ABSTRACT

Objectives: Mental disorders typically emerge during adolescence and young adulthood and put young people at risk for prolonged socio-economic difficulties. This study describes the longitudinal course of social and occupational functioning of young people attending primary-care based, early intervention services.

Design: A longitudinal study of young people receiving mental healthcare.

Setting: Data were collected between January 2005 and August 2017 from a designated primary-care based mental health service.

Participants: 554 young people (54% female) aged 12 to 32 years.

Measures: A systematic medical file audit collected clinical and functional information at predetermined time intervals (i.e. 3 months to 5+ years) using a clinical proforma. Group-based trajectory modelling (GBTM) was used to identify distinct trajectories of social and occupational functioning over time (median number of observations per person = 4; median follow up time = 23 months).

Results: Between first clinical contact and time last seen, 15% of young people had reliably deteriorated, 23% improved and 62% did not demonstrate substantive change in function. Of the whole cohort, 69% had SOFAS scores less than 70 at time last seen, indicative of ongoing and substantive impairment. GBTM identified six distinct functional trajectories whereby over 60% had moderate to serious functional impairment at entry and remained chronically impaired over time; 7% entered with serious impairment and deteriorated further; one quarter were mildly impaired at entry and functionally recovered; and only a small minority (4%) presented with serious impairments and functionally improved over time. Not being in education, employment or training, previous hospitalisation and a younger age at baseline emerged as significant predictors of these functional trajectories.

Conclusion: Young people with emerging mental disorders have significant functional impairment at presentation for care, and for the majority, it persists over the course of clinical care. Despite the logic of providing clinical care earlier in the course of illness, these data suggest that more sophisticated and more intensive

individual-level and organisational strategies may be required to achieve significant and sustained functional improvements.

Key words: Mental health; longitudinal study; functional impairment; young people; health services

Strengths and limitations of this study

- This study utilised a rich data set of 554 participants with between two and nine observations per person (median = 4; approximately 2200 data points) up to five years after initial presentation and applied a novel group-based trajectory modelling procedure to characterise the pattern of change in functional impairment over time. This procedure identified six distinct trajectories that differ in terms of the initial level of functional impairment at presentation and the course of functioning over a five year period.
- This study is one of the first to report on the long-term functional outcomes for young people attending primary-care based, early intervention mental health services. Its naturalistic design provides valuable insight into the extent of functional impairment over the course of these common mental disorders and identifies the specific needs of young people with these disorders. The study raises specific questions about how to improve health service and individual intervention strategies to monitor, target and improve these outcomes.
- Since this was a naturalistic cohort study, there may be some factors that account for the trajectories or differences in functional outcome that weren't collected in this study, such as socio-economic status, the type and intensity of interventions an individual received or treatment resistance. Since these factors were not uniformly collected it is difficult to make specific conclusions about the effect of specific intervention or service models on these trajectories or outcomes. This will be important for future studies to determine, however it was beyond the scope of this study.
- Since this study focuses on individuals who were continually engaged in clinical care and represents 18% of the total research register it is unclear how representative this sample is of the whole population presenting to these

services. Similarly, there is a lack of information about the differences between those who continually engage in care versus those who may have disengaged.

INTRODUCTION

Mental disorders consistently rank among the leading causes of death and disability worldwide[1-3]. These disorders typically emerge during adolescence and young adulthood and put these young people at risk for prolonged socio-economic difficulties over their lifetime, even when their mental ill health subsides or issub-threshold[4-7]. There are major direct healthcare costs attributed to diagnosis and treatment, however it is their indirect costs linked to income loss through mortality, disability and regular absences from education or work that impact future income potential and have substantial global economic consequences[8 9]. The significant overlap between these disorders, economic inactivity and functional impairment reiterates the need to recognise and address the common health and economic vulnerabilities of these young people[10].

The long-term outcomes for most major mental disorders often include high rates of recurrence, and slow or incomplete functional recovery, even among those who may have symptomatically remitted[11-14]. Long term follow up studies among older adults indicate that functional impairment often persists with most people experiencing some degree of disability during the majority of the long term follow up period[15], while it is common for those within a primary care setting to spend up to one-third of the long term follow up period off work[16]. These patterns are also evident among young people, since most medical and psychological treatments developed to address depression do not consistently improve functioning in these poulations[17-19]. Of the few studies that report long-term functional outcomes for young people, most adolescents treated for depression experienced positive functional outcomes up to three years later, however persistent functional impairment was common for those with comorbidity and recurrence of depression[20]. Similarly, young people with psychosis tend to experience significant social disability that persists over time and may be indicative of the difficulty of achieving functional recovery in these groups[21]. For many of these severe mental disorders, the onset of functional deterioration

tends to occur prior to the onset of illness and suggests there is the capacity to address these problems early[22 23].

Early intervention services and models of care have been designed to respond to the early phases of these disorders, their associated comorbidities and impairment, to prevent or delay the progression of illness and reduce the burden for those at-risk [24-26]. Although many young people present with sub-threshold syndromes, they frequently report significant functional impairment (i.e. reduced functioning in social, occupational or other areas of daily life) and a high rate of disengagement from education, employment or training (NEET)[24 27-29]. Over time, functional impairment tends to be associated with symptom remission, however the overall level of impairment and rate of disengagement remains high compared to the community[30-32]. This is particularly the case for those with more severe presentations who, despite receiving more intensive initial interventions, are unlikely to functionally recover in relatively short-term care environments[33]. While the first 12 months of care are characterised by significant changes in functional impairment[34], the long-term patterns of functional impairment among young people engaged in primary mental health care remains largely unknown.

Understanding the changes in social and occupational functioning over time in real-world clinical cohorts is crucial for guiding the development mental health service provisions that meet the individual needs of young people with emerging mental disorders. This study examines the longitudinal course of social and occupational functioning for a cohort of young people after their initial presentation to a primary mental health care service. We report on the overall rate of change in social and occupational functioning, and aim to determine whether there are distinct long-term trajectories (via modeling) of functioning over the course of care.

METHODS

Participants

Study participants were drawn from a larger cohort of young people (n=3087; 59% female, mean age = 18.52 ± 3.8) presenting to the Brain and Mind Centre's youth

mental health clinics in the Sydney suburbs of Camperdown and Campbelltown. These clinics consist of an integrated mix of primary-level services branded as *headspace*[35] as well as more specialised services including psychiatric services. These clinics primarily attract young people with a range of mental health problems, including those with sub-threshold and full threshold mental disorders, who may have been self-referred, referred via a family member or friend, or else via the community including external general practitioner, schools or university[29]. The young people in this study were recruited to a research register for mood, psychotic, developmental and other mental disorders between January 2005 and August 2017. All young people received clinician-based case management and relevant psychological, social and/or medical interventions over the duration of their time in care, which may also include referral to/from higher tier mental health services or hospitalisation for those whose needs exceed the capacity of the primary care services Individuals were included in the present study if they met the following inclusion criteria: (i) between 12 and 32 years of age at the time of initial assessment; (ii) were seen by a clinician on at least two separate occasions. Exclusion criteria for all potential participants were: medical instability or lack of capacity to give informed consent (as determined by a psychiatrist), history of neurological disease (e.g. tumor, head trauma, epilepsy), medical illness known to impact cognitive and brain function (e.g. cancer, ECT in last 3 months), and/or clinically evident intellectual disability and/or insufficient English to participate in the research protocol. The study was approved by the University of Sydney Human Research Ethics Committee.

Data collection process

Trained research psychologists and medical officers conducted a medical file audit to collect demographic, clinical and functional information at predetermined time intervals using a clinical proforma (see details below). The first available clinical assessment at the service was taken as the baseline time point for each participant and the date of this assessment was used to determine each of the follow up time points: 3 months, 6 months, 12 months, 2 years, 3 years, 4 years, and 5 years. If no clinical notes were available within +/- 1 month of the 3 and 6 month time points, or +/- 3 months of the yearly time points then this particular entry was left missing. A

'time last seen' entry was also used to capture final clinical information that did not align with one of the specified time points to ensure that every participant had data entered for the total time they were engaged with the clinical service. When data was available for a specified time point, all clinical notes from the preceding proforma entry, up to and including the current proforma entry were used to complete the proforma.

Clinical proforma

The clinical proforma captures key clinical information about the current episode and specific illness course characteristics, and an earlier version has been used in previous studies[24 29]. The proforma collects information about; (i) basic demographics (age, gender, receipt of government benefits); (ii) mental health diagnoses (based on DSM-V criteria); (iii) clinical course information (hospitalisations, childhood diagnoses); (iv) comorbidities (physical health diagnoses, such as autoimmune, endocrine, metabolic etc., and suicidal thoughts and behaviours); and (v) functioning (assessed using the Social Occupational Functional Assessment Scale (SOFAS)[36] and engagement in part-time or fulltime education, employment or training, used to determine not in education, employment or training [NEET] status). The SOFAS is a clinician-rated measure that assesses functioning on a 0–100 scale, with lower scores suggesting more severe impairment. The instructions emphasise that the rater should aim to avoid confounding the rating with clinical symptoms.

Statistical analyses

Statistical analyses were performed using SAS Software (SAS Institute). Overall changes in functioning (i.e. 'improvement', 'no change' and 'deterioration') between baseline and time last seen were determined using a Reliable Change Index (RCI) score of 10-points, and a clinically significant cut-off of equal to or above 69 was used[32 34 37]. To characterise the pattern of change in functional impairment over time we used group-based trajectory modelling (GBTM) using a procedure called PROC TRAJ (Nagin & Odgers, 2010). This method estimates multiple trajectory groups within the population and uses a maximum-likelihood method to calculate the probability of membership within each trajectory for each participant. We first fit the

null model (one group model), and progressively increased the number of groups until we reached the optimal number of trajectory groups, which was determined using the Bayesian Information Criterion (BIC). A higher number (i.e. smaller negative number) indicates a better balance between model complexity and model fit. The shape of each trajectory was examined by modelling three parameters (linear, quadratic, cubic) and then, starting with the higher order polynomials, dropping non-significant parameters from the model. If all three parameters were not significant the linear parameter was retained. Finally, to explore which baseline factors were associated with each trajectory group, we used stepwise logistic regression, which included baseline demographic and clinical characteristics; age, gender, receipt of government benefits, NEET status, mental health diagnosis, medical diagnosis, childhood mental health diagnosis, hospitalised (ever), suicide ideation (ever), suicide planning (ever), and suicide attempts (ever). An α level for entry and exclusion were set at *P=0.15* and based on the likelihood ratio statistic.

RESULTS

Sample characteristics

The sample consisted of 554 young people, 54% (297/554) were female and the mean age was 19.83 (SD = 3.77). At baseline, 20% (113/554) identified as NEET, 17% (95/554) were currently receiving government benefits and the majority (78%; 423/542) were in the clinical range of functional impairment (ie. SOFAS score < 69). The most common primary diagnosis was depression (43%; 237/548), followed by bipolar disorder (20%; 108/548), and then anxiety (18%; 99/548) with comorbid mental health problems identified in 79% (428/544) of participants. Physical health comorbidities were reported in 26% (142/554) of participants, 23% (127/554) had previously been hospitalised due to a mental health problem, and 14% (75/554) had a mental health or behavioural diagnosis in childhood.

Changes in functional impairment between baseline and time last seen

The number of follow up time points recorded for an individual varied between 2 and 9 (median = 4)(figure1) and the number of months between baseline and time last seen was between 1 and 126 (median = 23 months)(figure 2). The occurrence of time last seen was spread with 38% (208/554) occurring within the first 12 months

after baseline and 62% (346/554) occurring more than one year after baseline. Overall, between baseline and time last seen, 15% (79/538) had reliably deteriorated, 23% (122/538) reliably improved and 62% (337/538) did not reliably change, while 69% (370/538) were below the clinical cut-off (SOFAS <69) at time last seen.

Identifying functional impairment trajectories

GBTM identified that six distinct trajectories provided the best balance between model complexity and model fit for the data (table 1). The BIC continued to increase as the number of groups increased, however the BIC change from seven to nine trajectories were small and resulted in trajectory groups with very small sample sizes that did not add useful information beyond that provided by the six trajectories. Table 2 shows the model selection process for the shape of each of the six trajectories. We started with all three parameters in the model (linear, quadratic and cubic). The final model (model 4) had the highest BIC and contained quadratic parameters for trajectories 1, 3 and 5 and linear parameters for trajectories 2, 4, and 6.

Table 1. Criteria for selecting the number of trajectories

Number of groups	BIC	Null model	BIC change
1	-8773.03	0	-
2	-8372.01	1	401.022
3	-8243.31	2	128.695
4	-8215.51	3	27.802
5	-8207.80	4	7.710
6	-8166.46	5	41.339
7	-8164.58	6	1.882
8	-8162.05	7	2.528
9	-8155.80	8	6.251

Table 1 caption. BIC = Bayesian Information Criterion. BIC change presents the changes in the BIC value as the number of trajectory group's increases. Large changes in BIC from 1 to 6 groups justified moving towards the more complex model, however changes in BIC from 7 to 9 groups were rather small and compromised the balance between complexity and fit. Six trajectory groups was deemed to be the most parsimonious model that provided the best balance between complexity and fit.

Table 2. Model selection for each functional impairment trajectory group.

Trajectory Group	Parameter	Model 1	Model 2	Model 3	Model 4
1 Serious impairment – deterioration	Intercept	51.61208	51.77906	51.21822	50.92215
	Linear	**-0.84458*** **	**-0.86418*** **	**-0.50281*** **	**-0.49666*** **
	Quadratic	**0.02424****	**0.02483****	**0.00607****	**0.00599****
	Cubic	**-0.00022***	-0.00022	.	.
2 Serious impairment - chronic	Intercept	54.98897	54.95892	54.54367	54.75505
	Linear	-0.19938	-0.18538	0.02760	-0.03218
	Quadratic	0.00966	0.00901	-0.00110	.
	Cubic	**-0.00012***	-0.00012	.	.
3 Serious impairment - improvement	Intercept	41.08481	42.22558	42.03591	42.21444
	Linear	**1.76596*** **	**1.26818*** **	**1.26797*** **	**1.25871*** **
	Quadratic	**-0.03534***	**-0.01123*** **	**-0.01116*** **	**-0.01106*** **
	Cubic	0.00028	.	.	.
4 Moderate impairment - chronic	Intercept	61.20176	61.32354	61.52807	61.44346
	Linear	0.09497	0.04047	0.01924	0.02027
	Quadratic	-0.00309	-0.00039	.	.
	Cubic	0.00003	.	.	.
5 Mild impairment - improvement	Intercept	67.79146	68.08779	68.12046	68.11021
	Linear	**0.46038*** **	**0.31975*** **	**0.32482*** **	**0.32399*** **
	Quadratic	**-0.01202***	**-0.00468*** **	**-0.00478*** **	**-0.00477*** **
	Cubic	0.00009	.	.	.
6 Slight impairment - stable	Intercept	77.35888	77.40056	77.94966	77.93924
	Linear	0.19581	0.13170	0.04127	0.04153
	Quadratic	-0.00575	-0.00168	.	.
	Cubic	0.00005	.	.	.
Model fit	BIC	-8166.462	-8156.357	-8148.227	-8145.595

Table 2 caption. Parameter estimates are shown. Significant values are bolded. *P<.05, **P<.01, ***P<.001. The first model identified that the cubic parameters for trajectories 3, 4, 5 or 6 were not significant and were thus dropped for model 2. Model 2 identified that the quadratic parameters for trajectories 4 and 6 were not significant, and that the cubic parameter for trajectories 1 and 2 were not significant and were dropped for model 3. Model 3 identified that the quadratic parameter for trajectory 2 was not significant and was dropped for model 4. The final model (model 4) had the highest BIC and contained quadratic parameters for trajectories 1, 3 and 5 and linear parameters for trajectories 2, 4, and 6.

Figure 3 shows SOFAS score over a 5 year period for the six trajectories included in the final model (see supplementary figure 1 for individual-level trajectories for each group). Three trajectories start out with serious functional impairment at baseline but differ in the type of change in functioning over time. The first was the second largest group of the entire sample (29%; 158/554) and included individuals who followed a chronic course of serious functional impairment with little to no change in functioning over time ('serious impairment – chronic'). The second trajectory was quadratic and included individuals who significantly deteriorated in the first 12 months before plateauing between 12 and 60 months ('serious impairment – deterioration'), while the third trajectory was also quadratic and included the small minority who improved significantly over the first 24 months to mild levels of functional impairment before slightly tapering off with mild to no functional impairment ('serious impairment – improvement'). By contrast, the remaining three trajectories each started out with moderate to mild levels of functional impairment. The first included the largest number of people across the entire sample (33%; 185/554) who presented with moderate impairment and followed a chronic course of moderate impairment over time ('moderate impairment – chronic'). The second trajectory was quadratic and characterised by individuals who were mildly impaired at baseline, but improved/functionally recovered in the first 6 to 12 months before tapering off and remaining in the functional recovered population over time ('mild impairment – improvement'). The final trajectory group characterised the small number of individuals who were functioning well with no more than slight impairment at baseline and whose functioning was stable over time ('slight impairment – stable').

Differentiating between functional impairment trajectories

The aim of these analyses were to identify any demographic and clinical differences at baseline between the trajectory groups. The 'serious impairment – chronic' trajectory was chosen as the reference group because of the most impaired groups at entry, this group was the largest group and followed a stable/chronic trajectory over time. Of the demographic and clinical variables at baseline (table 3); NEET status, age and previous hospitalisations emerged as the factors that differentiated trajectory groups and were included in the redcued model. NEET status distinguished between

most trajectories, whereby those on the 'serious impairment – chronic' trajectory were less likely to be engaged in education, employment or training compared to 'moderate impairment – chronic' (OR = 0.47, 95% CI 0.27 – 0.83, p < 0.01), 'mild impairment – improvement' (OR = 0.08, 95% CI 0.03 – 0.23, p < 0.001) and 'slight impairment – stable' (OR = 0.09, 95% CI 0.01 – 0.70, p < 0.05). Regarding age, those on the 'serious impairment – chronic' trajectory were: older than those on the 'serious impairment – improvement' trajectory (OR = 0.83, 95% CI 0.71 – 0.98, p < 0.05), and younger than those on the 'mild impairment – improvement' trajectory (OR = 1.08, 95% CI 1.00 – 1.16, p < 0.05). For previous hospitalisation, those on the serious impairment – chronic' trajectory were more likely to have been previously hospitalised than those on the 'mild impairment – improvement' trajectory (OR = 2.72, 95% CI 1.39 – 5.33, p < 0.01).

Table 3: Baseline characteristics by functional impairment trajectory group (n=554)

	Total sample	Serious impairment - deterioration	Serious impairment - chronic	Serious impairment - improvement	Moderate impairment - chronic	Mild impairment - improvement	Slight impairment - stable
N (%)	554 (100 %)	39 (7%)	158 (29%)	19 (4%)	185 (33%)	129 (23%)	24 (4%)
Age, mean (sd)	19.83 (3.77)	20.26 (4.05)	19.68 (3.70)	18.37 (4.76)	19.75 (3.88)	20.12 (3.35)	20.29 (4.23)
Female, n (%)	297 (54%)	18 (49%)	77 (52%)	10 (56%)	103 (60%)	70 (58%)	19 (83%)
NEET, n (%)	113 (20%)	20 (51%)	47 (30%)	9 (47%)	32 (17%)	4 (3%)	1 (4%)
Receiving gov. benefits, n (%)	95 (17%)	16 (41%)	35 (22%)	4 (21%)	27 (15%)	11 (9%)	2 (8%)
SOFAS score, mean (sd)	60.45 (9.19)	50.61 (7.25)	54.90 (5.63)	43.83 (7.05)	61.39 (5.24)	68.06 (5.35)	78.13 (7.56)
Depression, n (%)	237 (43%)	14 (37%)	70 (45%)	10 (53%)	72 (39%)	59 (47%)	12 (50%)
Anxiety, n	99	6 (16%)	24 (15%)	1 (5%)	36 (20%)	27 (21%)	5 (21%)

(%)	(18%)						
Bipolar, n (%)	108 (20%)	4 (11%)	31 (20%)	3 (16%)	38 (21%)	26 (21%)	6 (25%)
Psychosis, n (%)	34 (6%)	5 (13%)	10 (6%)	1 (5%)	14 (8%)	4 (3%)	0 (0%)
Other, n (%)	70 (13%)	9 (24%)	22 (14%)	4 (21%)	23 (13%)	11 (9%)	1 (4%)
Has a medical diagnosis, n (%)	142 (26%)	10 (26%)	41 (26%)	5 (26%)	51 (28%)	28 (22%)	7 (29%)
Had a childhood diagnosis, n (%)	75 (14%)	8 (24%)	23 (17%)	4 (22%)	21 (12%)	18 (15%)	1 (4%)
Hospitalised (ever), n (%)	127 (23%)	9 (27%)	48 (35%)	7 (37%)	40 (23%)	18 (16%)	5 (24%)
Suicide ideation (ever), n (%)	258 (47%)	15 (44%)	76 (57%)	10 (59%)	89 (53%)	59 (50%)	9 (41%)
Suicide planning (ever), n (%)	94 (17%)	4 (12%)	38 (29%)	5 (29%)	29 (18%)	16 (14%)	2 (10%)
Suicide attempts (ever), n (%)	91 (16%)	7 (20%)	36 (27%)	5 (28%)	22 (13%)	17 (15%)	4 (18%)

Table 3 caption: Column percentages are shown, except for the first row which shows the sample size for each trajectory group as a percentage of the total N. NEET, Not in Education, Employment or Training; SOFAS, Social and Occupational Functional Assessment Scale.

DISCUSSION

Young people with emerging mental disorders have significant functional impairment that is dynamic and chronic over the course of clinical care. Improvement occurs throughout the course of care, however the rate of clinical impairment and functional deterioration remains high for a large number of people.

The results also indicate that while individual trajectories may be highly variable, there are distinct patterns of social and occupational functioning that are differentiated by the level of functioning at entry and rate of change over the course of clinical care. Over 60% of the sample had moderate to serious functional impairment at entry and remained chronically impaired over time, a further 7% entered with serious impairment and deteriorated further, while approximately a quarter of the sample were mildly impaired at entry and were able to improve and functionally recover. Only a small minority (4%), the youngest of the trajectory groups, presented with serious impairments and were able to functionally improve over time. This may reflect the benefits of early intervention, however this requires further investigation. These distinct trajectories highlight the need for improving mental health service and individual intervention strategies to monitor and directly target these problems over the course of care to facilitate clinical, social and occupational recovery[10].

The overall rate of reliable change in this study was comparable to studies conducted in similar cohorts that were followed for relatively short-term occasions of service. The rate of reliable improvement in this study (23%) is consistent with a similar cohort of young people followed for approximately 6 months (25%)[34] and slightly lower than an Australian national study of young people attending *headspace* followed for approximately 3 months (31%)[32]. Interestingly, the rate of reliable deterioration in this study was consistent with the national study at approximately 15%, which suggests that deterioration occurs early and often persists over longer periods. While the overall rate of change is important, this study examined the longer term patterns of change (i.e. over a 5-year period), which were informed by multiple time points. This revealed that across all levels of impairment there were high rates of chronicity with many individuals remaining at similar levels of functioning over the course of care. For some who may have been on a path of deterioration prior to presentation for care, maintaining a consistent level of impairment may reflect a positive outcome whereby engagement with care stabilised their situation or prevented further deterioration or worsening. For others, however, not being able to return to work or education, or improve social functioning could be detrimental to their future health and socio-economic wellbeing and may reflect a lack of sufficient

integrated psychological and vocational interventions to directly address these outcomes [38 39]. These results suggest that for those who present with mild functional impairment, functional improvement is likely to occur relatively quickly (i.e. evident from the quadratic trend toward improvement within the first 6 months), however for those with more serious impairment there may be the need for more intensive strategies delivered over a longer period of time to prevent or address ongoing functional impairment. Previous research has shown that only a small number of young people attending these primary mental health services received specific vocational support in the previous year[30], despite evidence to suggest that adjunctive interventions targeting vocational activity can have a positive impact on functional outcomes[40 41]. Even among those with severe, comorbid disorders, early intervention combined with focused social recovery has demonstrated clinical utility over early intervention alone for improving functional outcomes[42]. Together, this reiterates the need for early intervention and ongoing care that does more to directly address functional impairment over longer periods, particularly for those who present with substantial functional impairment.

For health services and clinicians, determining when to adopt these intervention strategies and for whom, is critical. The general trajectories observed in this study are characterised by substantial individual variation from one time point to the next (see supplementary figure 1). This individual variability highlights the challenge health professionals often face when planning effective long-term interventions in a cohort with emerging mental health disorders. Being NEET, previous hospitalisation and a younger age at entry was associated with the serious impairment trajectories compared to the moderate, mild and slight impairment trajectories, however the long-term predictive utility of these characteristics is still limited. Thus, there is a need to improve health service approaches to help clinicians identify and track individual functional outcomes and trajectories over the course of care, so that the appropriate interventions can be strategically implemented. One solution may be the development and integration of new and emerging technologies that use routine outcome measurement and feedback within health services, to deliver more personalised interventions that respond to an individual's needs[43 44]. Regular feedback to clinicians and individuals can provide important insights about

functional impairment overtime as well as the effectiveness of particular interventions for addressing key clinical and functional outcomes[45]. These approaches could also make use of assessments that aim to identify underlying characteristics, such as cognition, which have demonstrated some utility in predicting changes in functioning overtime[46-48].

This study has some limitations. The sample used for this study focuses on individuals who were continually engaged in clinical care, which means that the overall rate of improvement or deterioration among those who disengaged is unknown. Furthermore, the overall rate of improvement and deterioration in functioning at time last seen is imperfect given that many young people may be still engaged in care and so time last seen may not align with a complete period of care. This is where the group-based trajectory modelling is beneficial over the overall rate of change, since it accounts for the overall trends to provide a clearer picture of change over time. While we know that this sample represents approximately 18% of the research register (554/3087), it is unclear what proportion of the whole population attending these services this sample represents. Moreover, given that the study was conducted within the context of normal clinical service, the clinical and functional information available for particular individuals was diverse and while the option for "not enough information available" was provided to raters, it is unclear how the type of information available impacted on the completion of the clinical proforma. Finally, there may be other factors that account for these trajectories or differences in functional outcome that weren't collected, such as, but not limited to, socio-economic status, the type and intensity of interventions an individual received or pre-existing undiagnosed learning or developmental disorders. It is important for future work to determine the effectiveness of specific interventions on functional impairment trajectories and improving these outcomes to determine the reliability and validity of the medical file audit process used in this study.

This study provides valuable insights into the long-term functional trajectories of young people engaged in primary mental health care. The significant chronicity observed in this clinical cohort reiterates that ongoing functional impairment is

prevalent among young people with emerging mental health disorders and should be a primary focus of intervention, in addition to symptomaticimprovement. The substantial variability in individuals trajectories over time highlight the need for better health service and individual intervention strategies that monitor and target these outcomes so that early social and occupational impairment does not result in lifetime socio-economic burden.

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COMPETING INTERESTS

All authors have completed the ICMJE uniform disclosure at www.icmje.org/coi_disclosure.pdf and declare: Professor Ian Hickie has been a Commissioner in Australia's National Mental Health Commission since 2012. He is the Co-Director, Health and Policy at the Brain and Mind Centre (BMC) University of Sydney. The BMC operates an early-intervention youth services at Camperdown under contract to headspace. Professor Hickie has previously led community-based and pharmaceutical industry-supported (Wyeth, Eli Lily, Servier, Pfizer, AstraZeneca) projects focused on the identification and better management of anxiety and depression. He is a Board Member of Psychosis Australia Trust and a member of Veterans Mental Health Clinical Reference group. He was a member of the Medical Advisory Panel for Medibank Private until Oct 2017. He is the Chief Scientific Advisor to, and an equity shareholder in, Innowell. InnoWell has been formed by the University of Sydney and PwC to administer the $30M Australian Government Funded Project Synergy. Project Synergy is a three year program for the transformation of mental health services through the use of innovative technologies. A/Prof Elizabeth Scott is the Medical Director, Young Adult Mental Health Unit, St Vincent's Hospital Darlinghurst, Discipline Leader of Adult Mental Health, School of Medicine, University of Notre Dame, Research Affiliate, The University of Sydney and Consultant Psychiatrist. She has received honoraria for educational seminars related to the clinical management of depressive disorders supported by Servier and Eli-Lilly

pharmaceuticals. She has participated in a national advisory board for the antidepressant compound Pristiq, manufactured by Pfizer. She was the National Coordinator of an antidepressant trial sponsored by Servier. All remaining authors declare no support from any organisation for the submitted work besides the acknowledged financial support; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

CONTRIBUTORSHIP STATEMENT

FI, DFH, SC and IBH designed the study, interpreted the results and drafted the manuscript. FI and CAB conducted the statistical analyses. FI, NZ, AN, JG and ES were involved in study coordination, data collection. All authors contributed to and have approved the final manuscript.

DATA SHARING

No additional data available.

TRANSPARENCY STATEMENT

The lead authors, affirm that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained.

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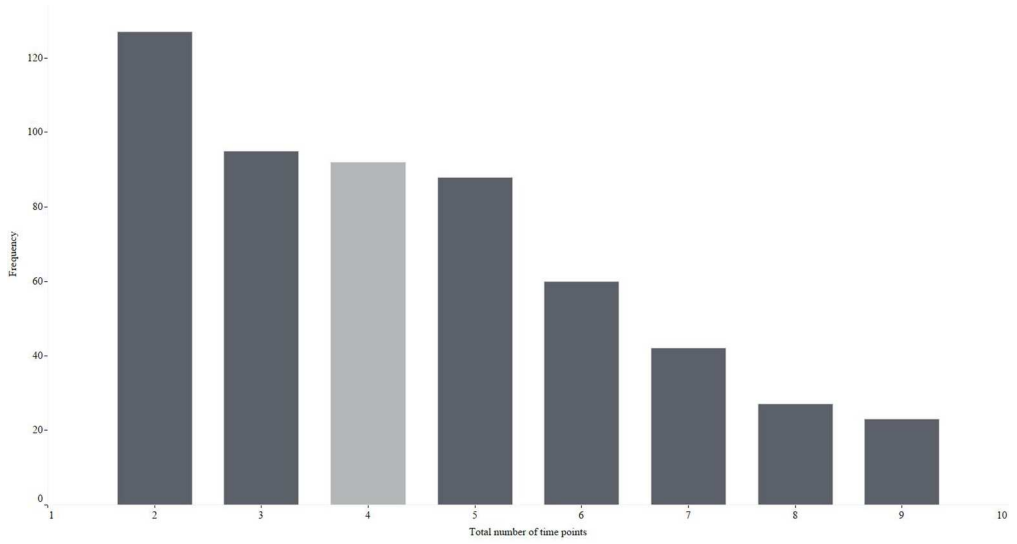
Figure 1 shows the frequency of the total number of time points recorded for each participant (median = 4; light grey bar).

Figure 2 shows the distribution of the total follow up time for each participant in months. The bars have been shaded into quartiles (median = 23 months). The majority of participants (50%) were followed up between 9 months and 49 months (i.e. 4 years) after initial presentation, while 25% were followed up between 1 and 8 months, and the remaining 25% followed up between 50 months (i.e 4 years) and 126 months (i.e. 10 years).

Figure 3 shows the six distinct trajectories identified for SOFAS score over a five year period. The thickness of each line represents the sample size of that particular trajectory, relative to all others. The dotted line represents the clinical impairment cut-off, which is set at a SOFAS score of 69. Slight impairment – stable (n=24, 4%), intercept equal to 78 and linear trend over time; Mild impairment – improvement (n=129, 23%), intercept equal to 68 and quadratic trend over time; Moderate impairment – chronic (n=185, 33%), intercept equal to 61 and linear trend over time; Serious impairment – chronic (n=158, 29%), intercept equal to 55 and linear trend over time; Serious impairment – improvement (n=19, 4%), intercept equal to 42 and quadratic trend over time; Serious impairment – deterioration (n=39, 7%), intercept equal to 51 and quadratic trend over time.



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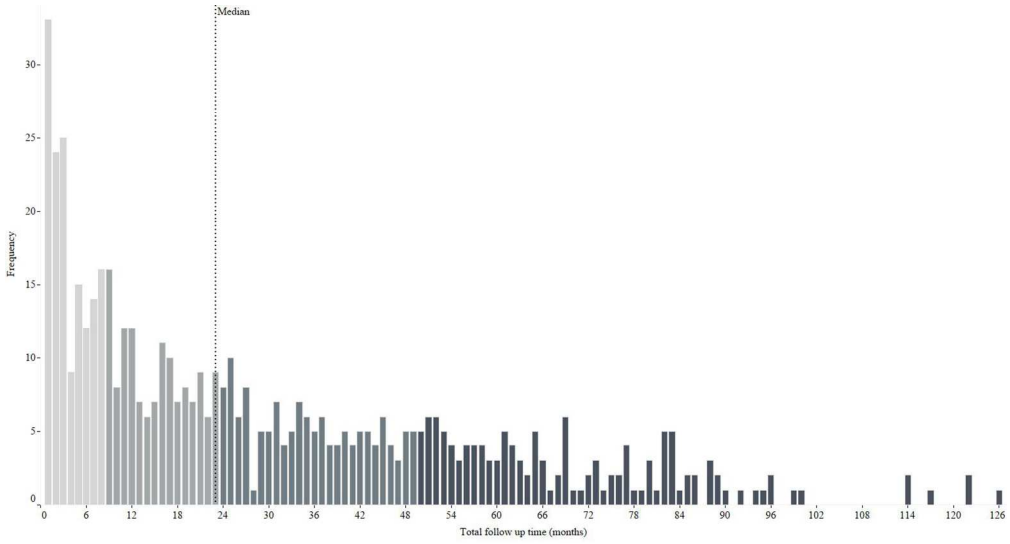

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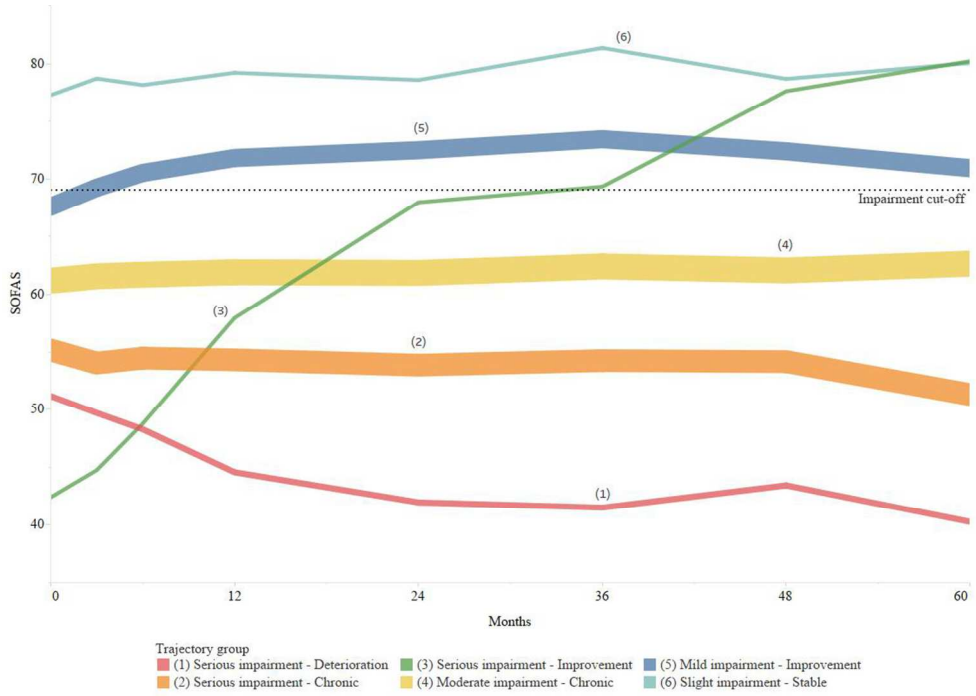

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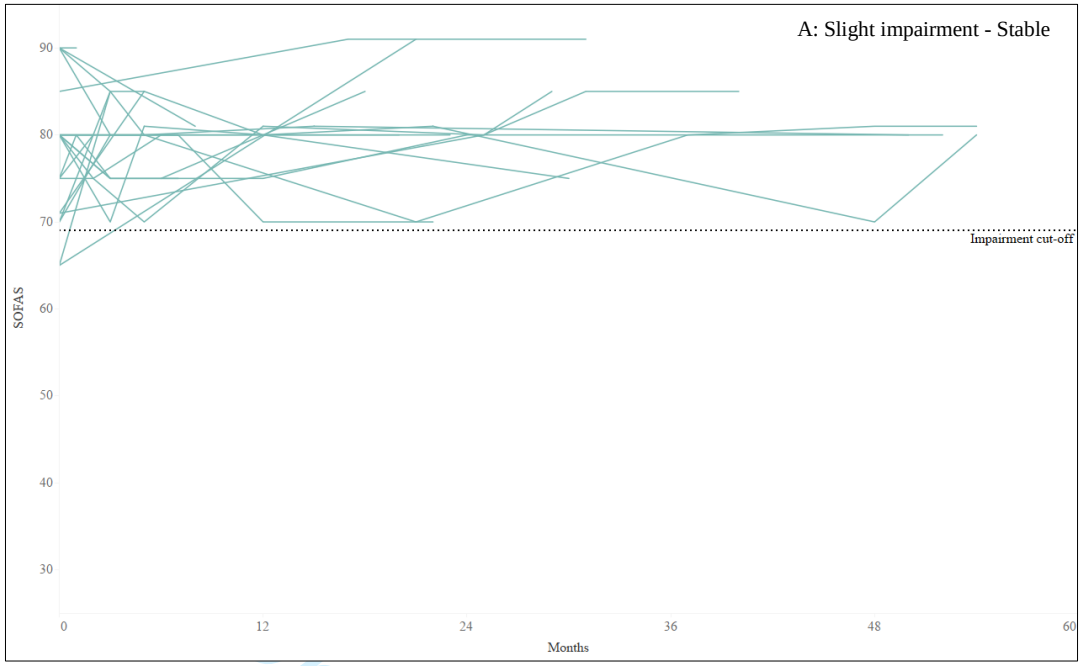
A: Slight impairment - Stable
SOFAS
90
80
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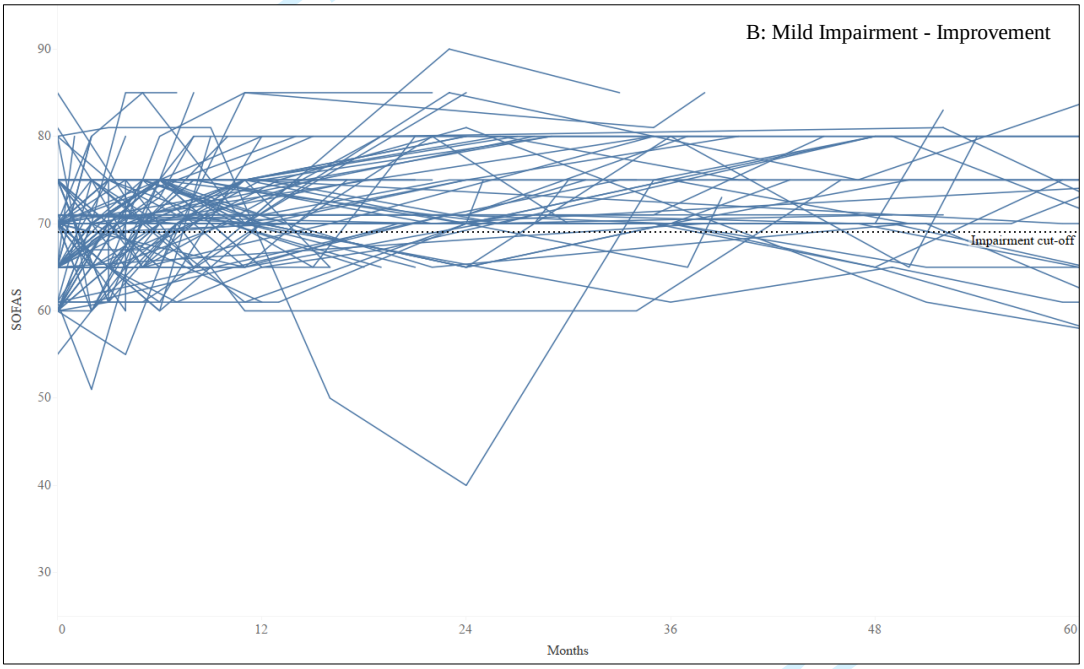
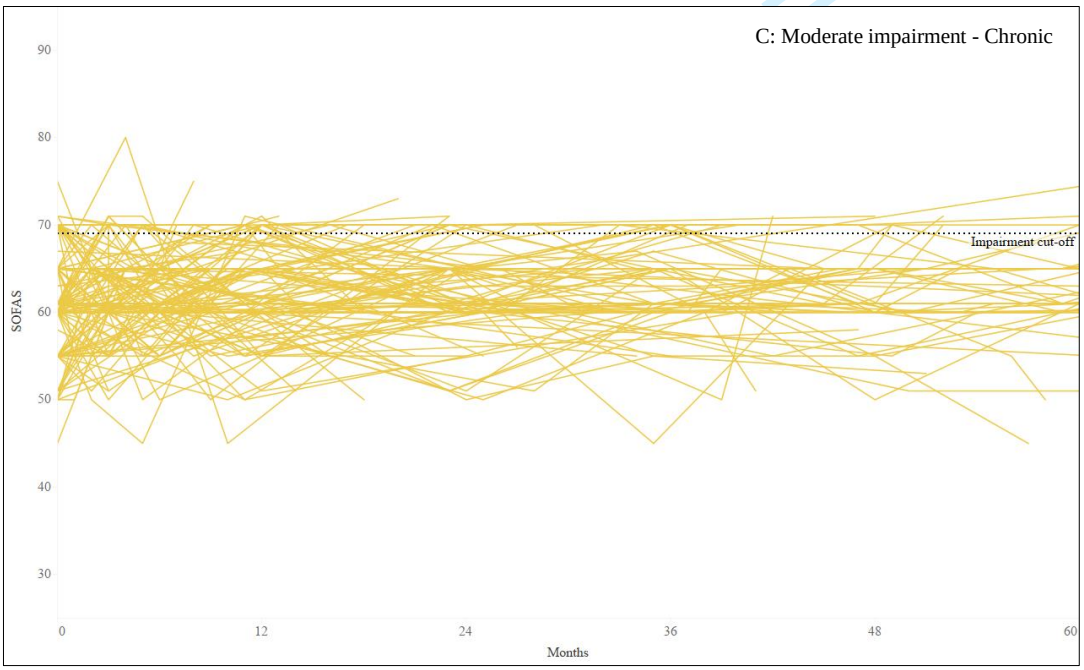
50
40
30
Impairment cut-off
0
12
24
36
48
60
Months


B: Mild Impairment - Improvement
SOFAS
90
80
70
60
50
40
30
Impairment cut-off
0
12
24
36
48
60
Months


C: Moderate impairment - Chronic
SOFAS
90
80
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40
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Impairment cut-off
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36
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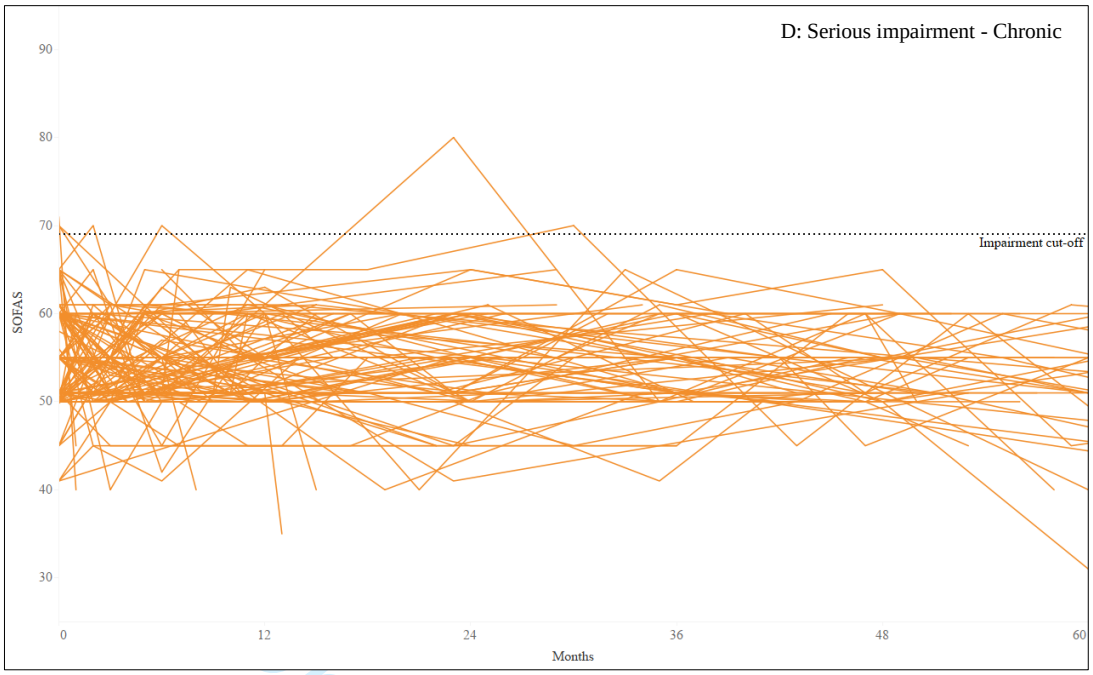
60
Months


D: Serious impairment - Chronic
SOFAS
Impairment cut-off
Months
90
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48
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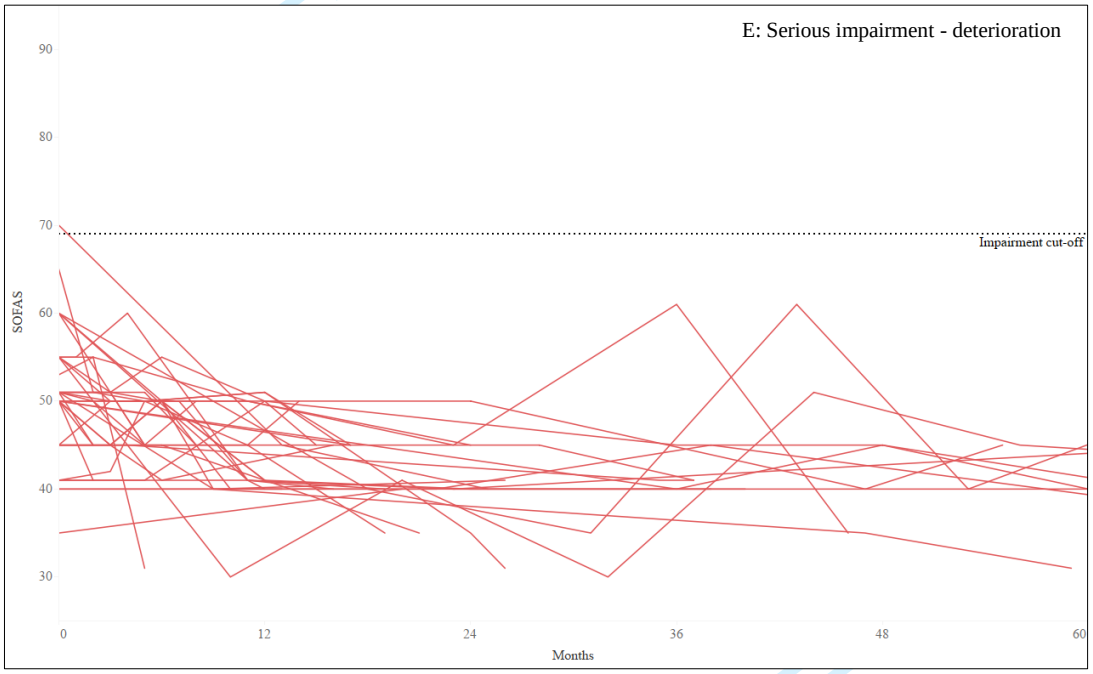
E: Serious impairment - deterioration
SOFAS
Impairment cut-off
Months
90
80
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60
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40
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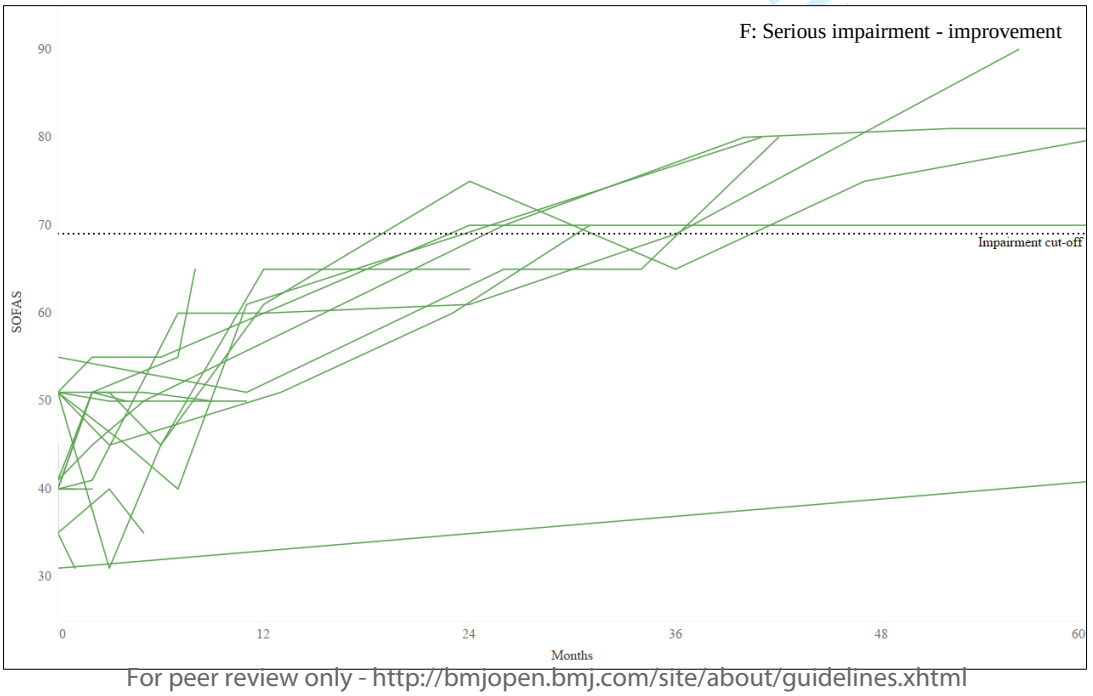
48
60


F: Serious impairment - improvement
SOFAS
Impairment cut-off
Months
90
80
70
60
50
40
30
0
12
24
36
48
60

Supplementary Figure 1 caption

Supplementary figure 1 shows the individual-level trajectories for each group identified and shown in figure 1. Each line represents one individual and their SOFAS score ratings over time. The dotted line represents the clinical impairment cut-off, which is set at a SOFAS score of 69. Panel A: Slight impairment – stable (n=24, 4%), intercept equal to 78 and linear trend over time; Panel B: Mild impairment – improvement (n=129, 23%), intercept equal to 68 and quadratic trend over time; Panel C: Moderate impairment – chronic (n=185, 33%), intercept equal to 61 and linear trend over time; Panel D: Serious impairment – chronic (n=158, 29%), intercept equal to 55 and linear trend over time; Panel E: Serious impairment – improvement (n=19, 4%), intercept equal to 42 and quadratic trend over time; Panel F: Serious impairment – deterioration (n=39, 7%), intercept equal to 51 and quadratic trend over time.

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation	
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	P1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	P2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	P4-5
Objectives	3	State specific objectives, including any prespecified hypotheses	P5
Methods			
Study design	4	Present key elements of study design early in the paper	P5-6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	P5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	P5
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	-
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	P5-7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	P6
Bias	9	Describe any efforts to address potential sources of bias	-
Study size	10	Explain how the study size was arrived at	-
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	P7
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	P7
		(*b*) Describe any methods used to examine subgroups and interactions	P7
		(*c*) Explain how missing data were addressed	P6-7
		(*d*) If applicable, explain how loss to follow-up was addressed	
		(*e*) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	P7
		(b) Give reasons for non-participation at each stage	P6
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	P7,8,12,13
		(b) Indicate number of participants with missing data for each variable of interest	P7-8
		(c) Summarise follow-up time (eg, average and total amount)	P8
Outcome data	15*	Report numbers of outcome events or summary measures over time	P8-13
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear	P11-12

		which confounders were adjusted for and why they were included	
		(*b*) Report category boundaries when continuous variables were categorized	-
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	-
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	P8-11
Discussion			
Key results	18	Summarise key results with reference to study objectives	P13-14
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	P15-16
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	P14-15
Generalisability	21	Discuss the generalisability (external validity) of the study results	P14-16
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	P17

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

BMJ Open

Delineating the trajectories of social and occupational functioning of young people attending primary-care based, early intervention mental health services in Australia: A longitudinal study

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Secondary Subject Heading:	Health services research
Keywords:	MENTAL HEALTH, Health services, Longitudinal study, Young people, Functional impairment

Delineating the trajectories of social and occupational functioning of young people attending primary-care based, early intervention mental health services in Australia: A longitudinal study

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Word count: 3572

ABSTRACT

Objectives: Mental disorders typically emerge during adolescence and young adulthood and put young people at risk for prolonged socio-economic difficulties. This study describes the longitudinal course of social and occupational functioning of young people attending primary-care based, early intervention services.

Design: A longitudinal study of young people receiving mental healthcare.

Setting: Data were collected between January 2005 and August 2017 from a designated primary-care based mental health service.

Participants: 554 young people (54% female) aged 12 to 32 years.

Measures: A systematic medical file audit collected clinical and functional information at predetermined time intervals (i.e. 3 months to 5+ years) using a clinical proforma. Group-based trajectory modelling (GBTM) was used to identify distinct trajectories of social and occupational functioning over time (median number of observations per person = 4; median follow up time = 23 months).

Results: Between first clinical contact and time last seen, 15% of young people had reliably deteriorated, 23% improved and 62% did not demonstrate substantive change in function. Of the whole cohort, 69% had SOFAS scores less than 70 at time last seen, indicative of ongoing and substantive impairment. GBTM identified six distinct functional trajectories whereby over 60% had moderate to serious functional impairment at entry and remained chronically impaired over time; 7% entered with serious impairment and deteriorated further; one quarter were mildly impaired at entry and functionally recovered; and only a small minority (4%) presented with serious impairments and functionally improved over time. Not being in education, employment or training, previous hospitalisation and a younger age at baseline emerged as significant predictors of these functional trajectories.

Conclusion: Young people with emerging mental disorders have significant functional impairment at presentation for care, and for the majority, it persists over the course of clinical care. Despite the logic of providing clinical care earlier in the course of illness, these data suggest that more sophisticated and more intensive

individual-level and organisational strategies may be required to achieve significant and sustained functional improvements.

Key words: Mental health; longitudinal study; functional impairment; young people; health services

Strengths and limitations of this study

- This study utilised a rich data set of 554 participants with between two and nine observations per person (median = 4; approximately 2200 data points) up to five years after initial presentation and applied a novel group-based trajectory modelling procedure to characterise the pattern of change in functional impairment over time.
- This study is one of the first to report on the long-term functional outcomes for young people attending primary-care based, early intervention mental health services. Its naturalistic design provides valuable insight into the extent of functional impairment over the course of these common mental disorders and identifies the specific needs of young people with these disorders. The study raises specific questions about how to improve health service and individual intervention strategies to monitor, target and improve these outcomes.
- Since this was a naturalistic cohort study, there may be some factors that account for the trajectories or differences in functional outcome that weren't collected in this study, such as socio-economic status, the type and intensity of interventions an individual received or treatment resistance. Since these factors were not uniformly collected it is difficult to make specific conclusions about the effect of specific intervention or service models on these trajectories or outcomes. This will be important for future studies to determine, however it was beyond the scope of this study.
- Since this study focuses on individuals who were continually engaged in clinical care and represents 18% of the total research register it is unclear how representative this sample is of the whole population presenting to these services. Similarly, there is a lack of information about the differences between those who continually engage in care versus those who may have disengaged.

INTRODUCTION

Mental disorders consistently rank among the leading causes of death and disability worldwide[1-3]. These disorders typically emerge during adolescence and young adulthood and put these young people at risk for prolonged socio-economic difficulties over their lifetime, even when their mental ill health subsides or is sub-threshold[4-7]. There are major direct healthcare costs attributed to diagnosis and treatment, however it is their indirect costs linked to income loss through mortality, disability and regular absences from education or work that impact future income potential and have substantial global economic consequences[8 9]. The significant overlap between these disorders, economic inactivity and functional impairment reiterates the need to recognise and address the common health and economic vulnerabilities of these young people[10].

The long-term outcomes for most major mental disorders often include high rates of recurrence, and slow or incomplete functional recovery, even among those who may have symptomatically remitted[11-14]. Long term follow up studies among older adults indicate that functional impairment often persists with most people experiencing some degree of disability during the majority of the long term follow up period[15], while it is common for those within a primary care setting to spend up to one-third of the long term follow up period off work[16]. These patterns are also evident among young people, since most medical and psychological treatments developed to address depression do not consistently improve functioning in these poulations[17-19]. Of the few studies that report long-term functional outcomes for young people, most adolescents treated for depression experienced positive functional outcomes up to three years later, however persistent functional impairment was common for those with comorbidity and recurrence of depression[20]. Similarly, young people with psychosis tend to experience significant social disability that persists over time and may be indicative of the difficulty of achieving functional recovery in these groups[21]. For many of these severe mental disorders, the onset of functional deterioration tends to occur prior to the onset of illness and suggests there is the capacity to address these problems early[22 23].

Early intervention services and models of care have been designed to respond to the early phases of these disorders, their associated comorbidities and impairment, to prevent or delay the progression of illness and reduce the burden for those at-risk [24-26]. Although many young people present with sub-threshold syndromes, they frequently report significant functional impairment (i.e. reduced functioning in social, occupational or other areas of daily life) and a high rate of disengagement from education, employment or training (NEET)[24 27-29]. Over time, functional impairment tends to be associated with symptom remission, however the overall level of impairment and rate of disengagement remains high compared to the community[30-32]. This is particularly the case for those with more severe presentations who, despite receiving more intensive initial interventions, are unlikely to functionally recover in relatively short-term care environments[33]. While the first 12 months of care are characterised by significant changes in functional impairment[34], the long-term patterns of functional impairment among young people engaged in primary mental health care remains largely unknown.

Understanding the changes in social and occupational functioning over time in real-world clinical cohorts is crucial for guiding the development mental health service provisions that meet the individual needs of young people with emerging mental disorders. This study examines the longitudinal course of social and occupational functioning for a cohort of young people after their initial presentation to a primary mental health care service. We report on the overall rate of change in social and occupational functioning, and aim to determine whether there are distinct long-term trajectories (via modeling) of functioning over the course of care.

METHODS

Participants

Study participants were drawn from a larger cohort of young people (n=3087; 59% female, mean age = 18.52 ± 3.8) presenting to the Brain and Mind Centre's youth mental health clinics in the Sydney suburbs of Camperdown and Campbelltown. These clinics consist of an integrated mix of primary-level services branded as

headspace[35] as well as more specialised services including psychiatric services. These clinics primarily attract young people with a range of mental health problems, including those with sub-threshold and full threshold mental disorders, who may have been self-referred, referred via a family member or friend, or else via the community including external general practitioner, schools or university[29]. The young people in this study were recruited to a research register for mood, psychotic, developmental and other mental disorders between January 2005 and August 2017. All young people received clinician-based case management and relevant psychological, social and/or medical interventions over the duration of their time in care, which may also include referral to/from higher tier mental health services or hospitalisation for those whose needs exceed the capacity of the primary care services. Individuals were included in the present study if they met the following inclusion criteria: (i) between 12 and 32 years of age at the time of initial assessment; (ii) were seen by a clinician on at least two separate occasions. Exclusion criteria for all potential participants were: medical instability or lack of capacity to give informed consent (as determined by a psychiatrist), history of neurological disease (e.g. tumor, head trauma, epilepsy), medical illness known to impact cognitive and brain function (e.g. cancer, ECT in last 3 months), and/or clinically evident intellectual disability and/or insufficient English to participate in the research protocol. The study was approved by the University of Sydney Human Research Ethics Committee.

Data collection process

Trained research psychologists and medical officers conducted a medical file audit to collect demographic, clinical and functional information at predetermined time intervals using a clinical proforma (see details below). The first available clinical assessment at the service was taken as the baseline time point for each participant and the date of this assessment was used to determine each of the follow up time points: 3 months, 6 months, 12 months, 2 years, 3 years, 4 years, and 5 years. If no clinical notes were available within +/- 1 month of the 3 and 6 month time points, or +/- 3 months of the yearly time points then this particular entry was left missing. A 'time last seen' entry was also used to capture final clinical information that did not align with one of the specified time points to ensure that every participant had data

entered for the total time they were engaged with the clinical service. When data was available for a specified time point, all clinical notes from the preceding proforma entry, up to and including the current proforma entry were used to complete the proforma.

Clinical proforma

The clinical proforma captures key clinical information about the current episode and specific illness course characteristics, and an earlier version has been used in previous studies[24 29]. The proforma collects information about; (i) basic demographics (age, gender, receipt of government benefits); (ii) mental health diagnoses (based on DSM-V criteria); (iii) clinical course information (hospitalisations, childhood diagnoses); (iv) comorbidities (physical health diagnoses, such as autoimmune, endocrine, metabolic etc., and suicidal thoughts and behaviours); and (v) functioning (assessed using the Social Occupational Functional Assessment Scale (SOFAS)[36] and engagement in part-time or fulltime education, employment or training, used to determine not in education, employment or training [NEET] status). The SOFAS is a clinician-rated measure that assesses functioning on a 0–100 scale, with lower scores suggesting more severe impairment. The instructions emphasise that the rater should aim to avoid confounding the rating with clinical symptoms.

Statistical analyses

Statistical analyses were performed using SAS Software (SAS Institute). Overall changes in functioning (i.e. 'improvement', 'no change' and 'deterioration') between baseline and time last seen were determined using a Reliable Change Index (RCI) score of 10-points, and a clinically significant cut-off of equal to or above 69 was used[32 34 37]. To characterise the pattern of change in functional impairment over time we used group-based trajectory modelling (GBTM) using a procedure called PROC TRAJ (Nagin & Odgers, 2010). This method estimates multiple trajectory groups within the population and uses a maximum-likelihood method to calculate the probability of membership within each trajectory for each participant. We first fit the null model (one group model), and progressively increased the number of groups until we reached the optimal number of trajectory groups, which was determined

using the Bayesian Information Criterion (BIC). A higher number (i.e. smaller negative number) indicates a better balance between model complexity and model fit. The shape of each trajectory was examined by modelling three parameters (linear, quadratic, cubic) and then, starting with the higher order polynomials, dropping non-significant parameters from the model. If all three parameters were not significant the linear parameter was retained. Finally, to explore which baseline factors were associated with each trajectory group, we used stepwise logistic regression, which included baseline demographic and clinical characteristics; age, gender, receipt of government benefits, NEET status, mental health diagnosis, medical diagnosis, childhood mental health diagnosis, hospitalised (ever), suicide ideation (ever), suicide planning (ever), and suicide attempts (ever). An α level for entry and exclusion were set at *P=0.15* and based on the likelihood ratio statistic.

RESULTS

Sample characteristics

The sample consisted of 554 young people, 54% (297/554) were female and the mean age was 19.83 (SD = 3.77). At baseline, 20% (113/554) identified as NEET, 17% (95/554) were currently receiving government benefits and the majority (78%; 423/542) were in the clinical range of functional impairment (ie. SOFAS score < 69). The most common primary diagnosis was depression (43%; 237/548), followed by bipolar disorder (20%; 108/548), and then anxiety (18%; 99/548) with comorbid mental health problems identified in 79% (428/544) of participants. Physical health comorbidities were reported in 26% (142/554) of participants, 23% (127/554) had previously been hospitalised due to a mental health problem, and 14% (75/554) had a mental health or behavioural diagnosis in childhood.

Changes in functional impairment between baseline and time last seen

The number of follow up time points recorded for an individual varied between 2 and 9 (median = 4)(figure1) and the number of months between baseline and time last seen was between 1 and 126 (median = 23 months)(figure 2). The occurrence of time last seen was spread with 38% (208/554) occurring within the first 12 months after baseline and 62% (346/554) occurring more than one year after baseline. Overall, between baseline and time last seen, 15% (79/538) had reliably

deteriorated, 23% (122/538) reliably improved and 62% (337/538) did not reliably change, while 69% (370/538) were below the clinical cut-off (SOFAS <69) at time last seen.

Identifying functional impairment trajectories

GBTM identified that six distinct trajectories provided the best balance between model complexity and model fit for the data (table 1). The BIC continued to increase as the number of groups increased, however the BIC change from seven to nine trajectories were small and resulted in trajectory groups with very small sample sizes that did not add useful information beyond that provided by the six trajectories. Table 2 shows the model selection process for the shape of each of the six trajectories. We started with all three parameters in the model (linear, quadratic and cubic). The final model (model 4) had the highest BIC and contained quadratic parameters for trajectories 1, 3 and 5 and linear parameters for trajectories 2, 4, and 6.

Table 1. Criteria for selecting the number of trajectories

Number of groups	BIC	Null model	BIC change
1	-8773.03	0	-
2	-8372.01	1	401.022
3	-8243.31	2	128.695
4	-8215.51	3	27.802
5	-8207.80	4	7.710
6	-8166.46	5	41.339
7	-8164.58	6	1.882
8	-8162.05	7	2.528
9	-8155.80	8	6.251

Table 1 caption. BIC = Bayesian Information Criterion. BIC change presents the changes in the BIC value as the number of trajectory group's increases. Large changes in BIC from 1 to 6 groups justified moving towards the more complex model, however changes in BIC from 7 to 9 groups were rather small and compromised the balance between complexity and fit. Six trajectory groups was deemed to be the most parsimonious model that provided the best balance between complexity and fit.

Table 2. Model selection for each functional impairment trajectory group.

Trajectory Group	Parameter	Model 1	Model 2	Model 3	Model 4
1 Serious impairment – deterioration	Intercept	51.61208	51.77906	51.21822	50.92215
	Linear	**-0.84458*** **	**-0.86418*** **	**-0.50281*** **	**-0.49666*** **
	Quadratic	**0.02424****	**0.02483****	**0.00607****	**0.00599****
	Cubic	**-0.00022***	-0.00022	.	.
2 Serious impairment - chronic	Intercept	54.98897	54.95892	54.54367	54.75505
	Linear	-0.19938	-0.18538	0.02760	-0.03218
	Quadratic	0.00966	0.00901	-0.00110	.
	Cubic	**-0.00012***	-0.00012	.	.
3 Serious impairment - improvement	Intercept	41.08481	42.22558	42.03591	42.21444
	Linear	**1.76596*** **	**1.26818*** **	**1.26797*** **	**1.25871*** **
	Quadratic	**-0.03534***	**-0.01123*** **	**-0.01116*** **	**-0.01106*** **
	Cubic	0.00028	.	.	.
4 Moderate impairment - chronic	Intercept	61.20176	61.32354	61.52807	61.44346
	Linear	0.09497	0.04047	0.01924	0.02027
	Quadratic	-0.00309	-0.00039	.	.
	Cubic	0.00003	.	.	.
5 Mild impairment - improvement	Intercept	67.79146	68.08779	68.12046	68.11021
	Linear	**0.46038*** **	**0.31975*** **	**0.32482*** **	**0.32399*** **
	Quadratic	**-0.01202***	**-0.00468*** **	**-0.00478*** **	**-0.00477*** **
	Cubic	0.00009	.	.	.
6 Slight impairment - stable	Intercept	77.35888	77.40056	77.94966	77.93924
	Linear	0.19581	0.13170	0.04127	0.04153
	Quadratic	-0.00575	-0.00168	.	.
	Cubic	0.00005	.	.	.
Model fit	BIC	-8166.462	-8156.357	-8148.227	-8145.595

Table 2 caption. Parameter estimates are shown. Significant values are bolded. *P<.05, **P<.01, ***P<.001. The first model identified that the cubic parameters for trajectories 3, 4, 5 or 6 were not significant and were thus dropped for model 2. Model 2 identified that the quadratic parameters for trajectories 4 and 6 were not significant, and that the cubic parameter for trajectories 1 and 2 were not significant and were dropped for model 3. Model 3 identified that the quadratic parameter for trajectory 2 was not significant and was dropped for model 4. The final model (model 4) had the highest BIC and contained quadratic parameters for trajectories 1, 3 and 5 and linear parameters for trajectories 2, 4, and 6.

Figure 3 shows SOFAS score over a 5 year period for the six trajectories included in the final model (see supplementary figure 1 for individual-level trajectories for each group). Three trajectories start out with serious functional impairment at baseline but differ in the type of change in functioning over time. The first was the second largest group of the entire sample (29%; 158/554) and included individuals who followed a chronic course of serious functional impairment with little to no change in functioning over time ('serious impairment – chronic'). The second trajectory was quadratic and included individuals who significantly deteriorated in the first 12 months before plateauing between 12 and 60 months ('serious impairment – deterioration'), while the third trajectory was also quadratic and included the small minority who improved significantly over the first 24 months to mild levels of functional impairment before slightly tapering off with mild to no functional impairment ('serious impairment – improvement'). By contrast, the remaining three trajectories each started out with moderate to mild levels of functional impairment. The first included the largest number of people across the entire sample (33%; 185/554) who presented with moderate impairment and followed a chronic course of moderate impairment over time ('moderate impairment – chronic'). The second trajectory was quadratic and characterised by individuals who were mildly impaired at baseline, but improved/functionally recovered in the first 6 to 12 months before tapering off and remaining in the functional recovered population over time ('mild impairment – improvement'). The final trajectory group characterised the small number of individuals who were functioning well with no more than slight impairment at baseline and whose functioning was stable over time ('slight impairment – stable').

Differentiating between functional impairment trajectories

The aim of these analyses were to identify any demographic and clinical differences at baseline between the trajectory groups. The 'serious impairment – chronic' trajectory was chosen as the reference group because of the most impaired groups at entry, this group was the largest group and followed a stable/chronic trajectory over time. Of the demographic and clinical variables at baseline (table 3); NEET status, age and previous hospitalisations emerged as the factors that differentiated trajectory groups and were included in the redcued model. NEET status distinguished between

most trajectories, whereby those on the 'serious impairment – chronic' trajectory were less likely to be engaged in education, employment or training compared to 'moderate impairment – chronic' (OR = 0.47, 95% CI 0.27 – 0.83, p < 0.01), 'mild impairment – improvement' (OR = 0.08, 95% CI 0.03 – 0.23, p < 0.001) and 'slight impairment – stable' (OR = 0.09, 95% CI 0.01 – 0.70, p < 0.05). Regarding age, those on the 'serious impairment – chronic' trajectory were: older than those on the 'serious impairment – improvement' trajectory (OR = 0.83, 95% CI 0.71 – 0.98, p < 0.05), and younger than those on the 'mild impairment – improvement' trajectory (OR = 1.08, 95% CI 1.00 – 1.16, p < 0.05). For previous hospitalisation, those on the serious impairment – chronic' trajectory were more likely to have been previously hospitalised than those on the 'mild impairment – improvement' trajectory (OR = 2.72, 95% CI 1.39 – 5.33, p < 0.01).

Table 3: Baseline characteristics by functional impairment trajectory group (n=554)

	Total sample	Serious impairment - deterioration	Serious impairment - chronic	Serious impairment - improvement	Moderate impairment - chronic	Mild impairment - improvement	Slight impairment - stable
N (%)	554 (100 %)	39 (7%)	158 (29%)	19 (4%)	185 (33%)	129 (23%)	24 (4%)
Age, mean (sd)	19.83 (3.77)	20.26 (4.05)	19.68 (3.70)	18.37 (4.76)	19.75 (3.88)	20.12 (3.35)	20.29 (4.23)
Female, n (%)	297 (54%)	18 (49%)	77 (52%)	10 (56%)	103 (60%)	70 (58%)	19 (83%)
NEET, n (%)	113 (20%)	20 (51%)	47 (30%)	9 (47%)	32 (17%)	4 (3%)	1 (4%)
Receiving gov. benefits, n (%)	95 (17%)	16 (41%)	35 (22%)	4 (21%)	27 (15%)	11 (9%)	2 (8%)
SOFAS score, mean (sd)	60.45 (9.19)	50.61 (7.25)	54.90 (5.63)	43.83 (7.05)	61.39 (5.24)	68.06 (5.35)	78.13 (7.56)
Depression, n (%)	237 (43%)	14 (37%)	70 (45%)	10 (53%)	72 (39%)	59 (47%)	12 (50%)
Anxiety, n	99	6 (16%)	24 (15%)	1 (5%)	36 (20%)	27 (21%)	5 (21%)

(%)	(18%)						
Bipolar, n (%)	108 (20%)	4 (11%)	31 (20%)	3 (16%)	38 (21%)	26 (21%)	6 (25%)
Psychosis, n (%)	34 (6%)	5 (13%)	10 (6%)	1 (5%)	14 (8%)	4 (3%)	0 (0%)
Other, n (%)	70 (13%)	9 (24%)	22 (14%)	4 (21%)	23 (13%)	11 (9%)	1 (4%)
Has a medical diagnosis, n (%)	142 (26%)	10 (26%)	41 (26%)	5 (26%)	51 (28%)	28 (22%)	7 (29%)
Had a childhood diagnosis, n (%)	75 (14%)	8 (24%)	23 (17%)	4 (22%)	21 (12%)	18 (15%)	1 (4%)
Hospitalised (ever), n (%)	127 (23%)	9 (27%)	48 (35%)	7 (37%)	40 (23%)	18 (16%)	5 (24%)
Suicide ideation (ever), n (%)	258 (47%)	15 (44%)	76 (57%)	10 (59%)	89 (53%)	59 (50%)	9 (41%)
Suicide planning (ever), n (%)	94 (17%)	4 (12%)	38 (29%)	5 (29%)	29 (18%)	16 (14%)	2 (10%)
Suicide attempts (ever), n (%)	91 (16%)	7 (20%)	36 (27%)	5 (28%)	22 (13%)	17 (15%)	4 (18%)

Table 3 caption: Column percentages are shown, except for the first row which shows the sample size for each trajectory group as a percentage of the total N. NEET, Not in Education, Employment or Training; SOFAS, Social and Occupational Functional Assessment Scale.

DISCUSSION

Young people with emerging mental disorders have significant functional impairment that is dynamic and chronic over the course of clinical care. Improvement occurs throughout the course of care, however the rate of clinical impairment and functional deterioration remains high for a large number of people.

The results also indicate that while individual trajectories may be highly variable, there are distinct patterns of social and occupational functioning that are differentiated by the level of functioning at entry and rate of change over the course of clinical care. Over 60% of the sample had moderate to serious functional impairment at entry and remained chronically impaired over time, a further 7% entered with serious impairment and deteriorated further, while approximately a quarter of the sample were mildly impaired at entry and were able to improve and functionally recover. Only a small minority (4%), the youngest of the trajectory groups, presented with serious impairments and were able to functionally improve over time. This may reflect the benefits of early intervention, however this requires further investigation. These distinct trajectories highlight the need for improving mental health service and individual intervention strategies to monitor and directly target these problems over the course of care to facilitate clinical, social and occupational recovery[10].

The overall rate of reliable change in this study was comparable to studies conducted in similar cohorts that were followed for relatively short-term occasions of service. The rate of reliable improvement in this study (23%) is consistent with a similar cohort of young people followed for approximately 6 months (25%)[34] and slightly lower than an Australian national study of young people attending *headspace* followed for approximately 3 months (31%)[32]. Interestingly, the rate of reliable deterioration in this study was consistent with the national study at approximately 15%, which suggests that deterioration occurs early and often persists over longer periods. While the overall rate of change is important, this study examined the longer term patterns of change (i.e. over a 5-year period), which were informed by multiple time points. This revealed that across all levels of impairment there were high rates of chronicity with many individuals remaining at similar levels of functioning over the course of care. For some who may have been on a path of deterioration prior to presentation for care, maintaining a consistent level of impairment may reflect a positive outcome whereby engagement with care stabilised their situation or prevented further deterioration or worsening. For others, however, not being able to return to work or education, or improve social functioning could be detrimental to their future health and socio-economic wellbeing and may reflect a lack of sufficient

integrated psychological and vocational interventions to directly address these outcomes [38 39]. These results suggest that for those who present with mild functional impairment, functional improvement is likely to occur relatively quickly (i.e. evident from the quadratic trend toward improvement within the first 6 months), however for those with more serious impairment there may be the need for more intensive strategies delivered over a longer period of time to prevent or address ongoing functional impairment. Previous research has shown that only a small number of young people attending these primary mental health services received specific vocational support in the previous year[30], despite evidence to suggest that adjunctive interventions targeting vocational activity can have a positive impact on functional outcomes[40 41]. Even among those with severe, comorbid disorders, early intervention combined with focused social recovery has demonstrated clinical utility over early intervention alone for improving functional outcomes[42]. Together, this reiterates the need for early intervention and ongoing care that does more to directly address functional impairment over longer periods, particularly for those who present with substantial functional impairment.

For health services and clinicians, determining when to adopt these intervention strategies and for whom, is critical. The general trajectories observed in this study are characterised by substantial individual variation from one time point to the next (see supplementary figure 1). This individual variability highlights the challenge health professionals often face when planning effective long-term interventions in a cohort with emerging mental health disorders. Being NEET, previous hospitalisation and a younger age at entry was associated with the serious impairment trajectories compared to the moderate, mild and slight impairment trajectories, however the long-term predictive utility of these characteristics is still limited. Thus, there is a need to improve health service approaches to help clinicians identify and track individual functional outcomes and trajectories over the course of care, so that the appropriate interventions can be strategically implemented. One solution may be the development and integration of new and emerging technologies that use routine outcome measurement and feedback within health services, to deliver more personalised interventions that respond to an individual's needs[43 44]. Regular feedback to clinicians and individuals can provide important insights about

functional impairment overtime as well as the effectiveness of particular interventions for addressing key clinical and functional outcomes[45]. These approaches could also make use of assessments that aim to identify underlying characteristics, such as cognition, which have demonstrated some utility in predicting changes in functioning overtime[46-48].

This study has some limitations. The sample used for this study focuses on individuals who were continually engaged in clinical care, which means that the overall rate of improvement or deterioration among those who disengaged is unknown. Furthermore, the overall rate of improvement and deterioration in functioning at time last seen is imperfect given that many young people may be still engaged in care and so time last seen may not align with a complete period of care. This is where the group-based trajectory modelling is beneficial over the overall rate of change, since it accounts for the overall trends to provide a clearer picture of change over time. While we know that this sample represents approximately 18% of the research register (554/3087), it is unclear what proportion of the whole population attending these services this sample represents. Moreover, given that the study was conducted within the context of normal clinical service, the clinical and functional information available for particular individuals was diverse and while the option for "not enough information available" was provided to raters, it is unclear how the type of information available impacted on the completion of the clinical proforma. Finally, there may be other factors that account for these trajectories or differences in functional outcome that weren't collected, such as, but not limited to, socio-economic status, the type and intensity of interventions an individual received or pre-existing undiagnosed learning or developmental disorders. It is important for future work to determine the effectiveness of specific interventions on functional impairment trajectories and improving these outcomes to determine the reliability and validity of the medical file audit process used in this study.

This study provides valuable insights into the long-term functional trajectories of young people engaged in primary mental health care. The significant chronicity observed in this clinical cohort reiterates that ongoing functional impairment is

prevalent among young people with emerging mental health disorders and should be a primary focus of intervention, in addition to symptomatic improvement. The substantial variability in individuals trajectories over time highlight the need for better health service and individual intervention strategies that monitor and target these outcomes so that early social and occupational impairment does not result in lifetime socio-economic burden.

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COMPETING INTERESTS

All authors have completed the ICMJE uniform disclosure at www.icmje.org/coi_disclosure.pdf and declare: Professor Ian Hickie has been a Commissioner in Australia's National Mental Health Commission since 2012. He is the Co-Director, Health and Policy at the Brain and Mind Centre (BMC) University of Sydney. The BMC operates an early-intervention youth services at Camperdown under contract to headspace. Professor Hickie has previously led community-based and pharmaceutical industry-supported (Wyeth, Eli Lily, Servier, Pfizer, AstraZeneca) projects focused on the identification and better management of anxiety and depression. He is a Board Member of Psychosis Australia Trust and a member of Veterans Mental Health Clinical Reference group. He was a member of the Medical Advisory Panel for Medibank Private until Oct 2017. He is the Chief Scientific Advisor to, and an equity shareholder in, Innowell. InnoWell has been formed by the University of Sydney and PwC to administer the $30M Australian Government Funded Project Synergy. Project Synergy is a three year program for the transformation of mental health services through the use of innovative technologies. A/Prof Elizabeth Scott is the Medical Director, Young Adult Mental Health Unit, St Vincent's Hospital Darlinghurst, Discipline Leader of Adult Mental Health, School of Medicine, University of Notre Dame, Research Affiliate, The University of Sydney and Consultant Psychiatrist. She has received honoraria for educational seminars related to the clinical management of depressive disorders supported by Servier and Eli-Lilly

pharmaceuticals. She has participated in a national advisory board for the antidepressant compound Pristiq, manufactured by Pfizer. She was the National Coordinator of an antidepressant trial sponsored by Servier. All remaining authors declare no support from any organisation for the submitted work besides the acknowledged financial support; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

CONTRIBUTORSHIP STATEMENT

FI, DFH, SC and IBH designed the study, interpreted the results and drafted the manuscript. FI and CAB conducted the statistical analyses. FI, NZ, AN, JG and ES were involved in study coordination, data collection. All authors contributed to and have approved the final manuscript.

DATA SHARING

No additional data available.

TRANSPARENCY STATEMENT

The lead authors, affirm that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained.

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Figure 1 shows the frequency of the total number of time points recorded for each participant (median = 4; light grey bar).

Figure 2 shows the distribution of the total follow up time for each participant in months. The bars have been shaded into quartiles (median = 23 months). The majority of participants (50%) were followed up between 9 months and 49 months (i.e. 4 years) after initial presentation, while 25% were followed up between 1 and 8 months, and the remaining 25% followed up between 50 months (i.e 4 years) and 126 months (i.e. 10 years).

Figure 3 shows the six distinct trajectories identified for SOFAS score over a five year period. The thickness of each line represents the sample size of that particular trajectory, relative to all others. The dotted line represents the clinical impairment cut-off, which is set at a SOFAS score of 69. Slight impairment – stable (n=24, 4%), intercept equal to 78 and linear trend over time; Mild impairment – improvement (n=129, 23%), intercept equal to 68 and quadratic trend over time; Moderate impairment – chronic (n=185, 33%), intercept equal to 61 and linear trend over time; Serious impairment – chronic (n=158, 29%), intercept equal to 55 and linear trend over time; Serious impairment – improvement (n=19, 4%), intercept equal to 42 and quadratic trend over time; Serious impairment – deterioration (n=39, 7%), intercept equal to 51 and quadratic trend over time.

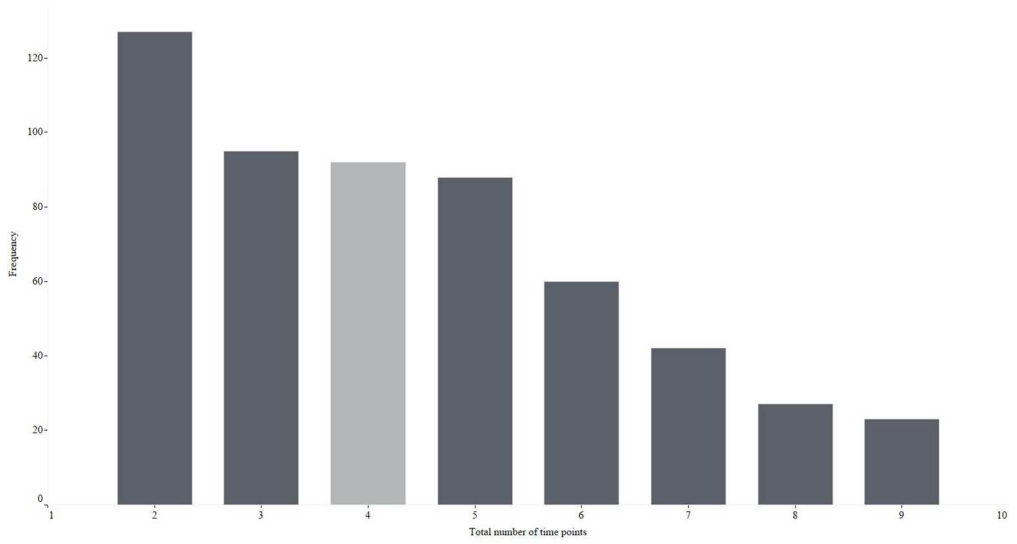


Figure 1 shows the frequency of the total number of time points recorded for each participant (median = 4; light grey bar).

129x69mm (300 x 300 DPI)

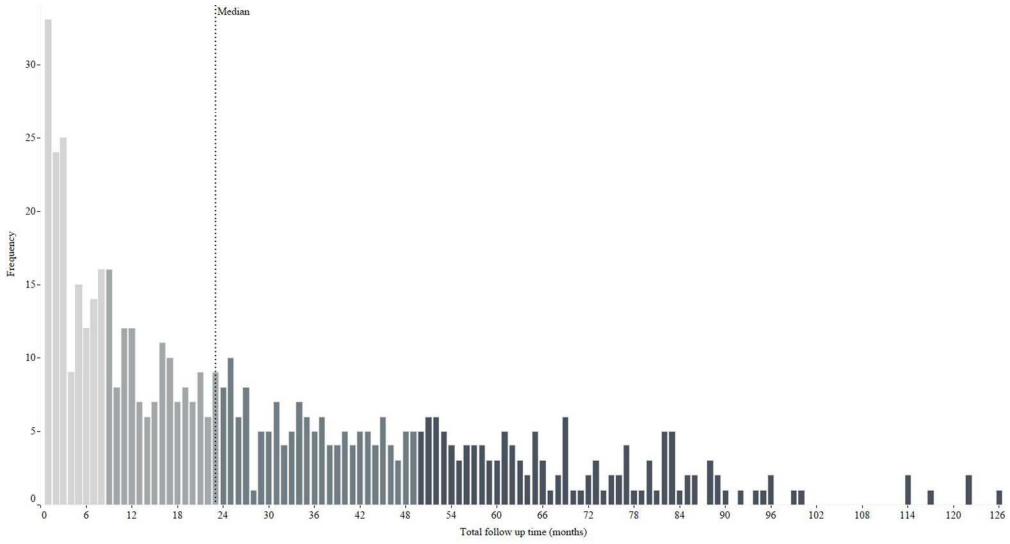


Figure 2 shows the distribution of the total follow up time for each participant in months. The bars have been shaded into quartiles (median = 23 months). The majority of participants (50%) were followed up between 9 months and 49 months (i.e. 4 years) after initial presentation, while 25% were followed up between 1 and 8 months, and the remaining 25% followed up between 50 months (i.e 4 years) and 126 months (i.e. 10 years).

129x69mm (300 x 300 DPI)

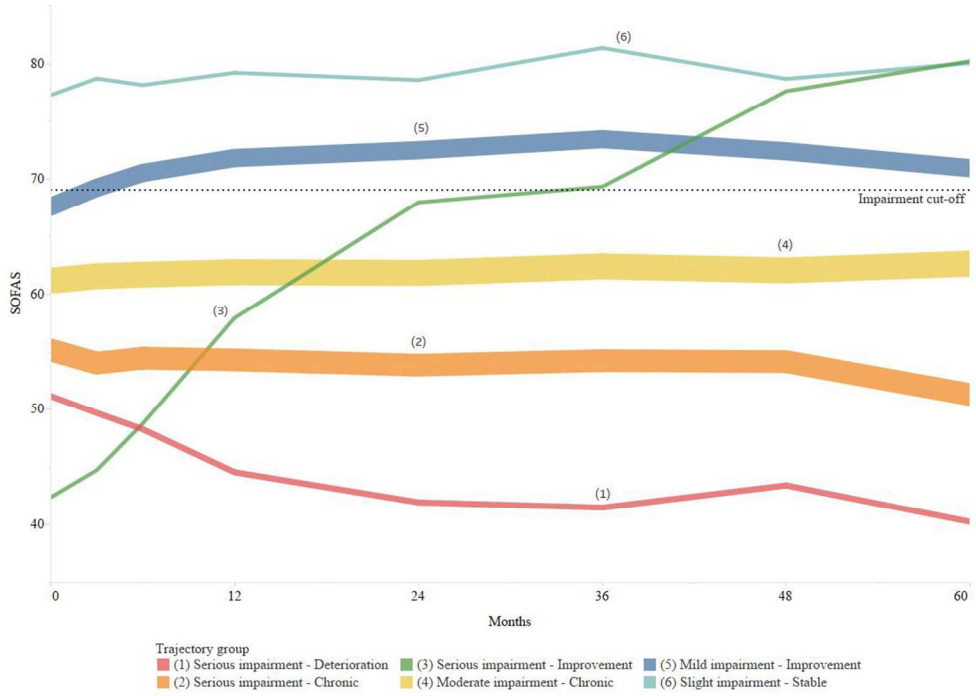
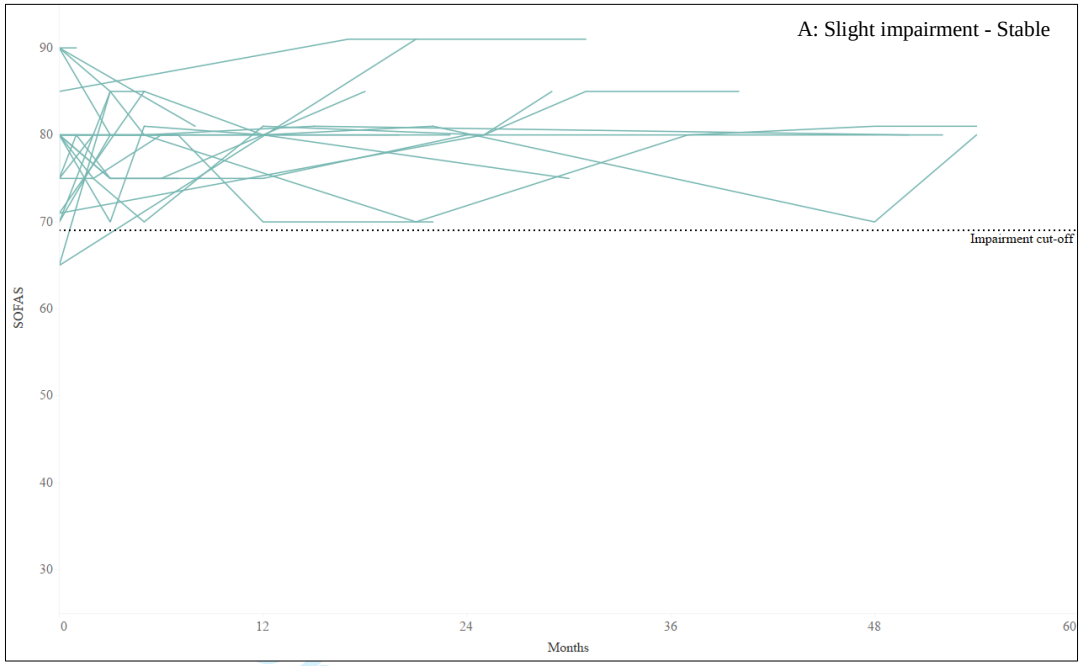
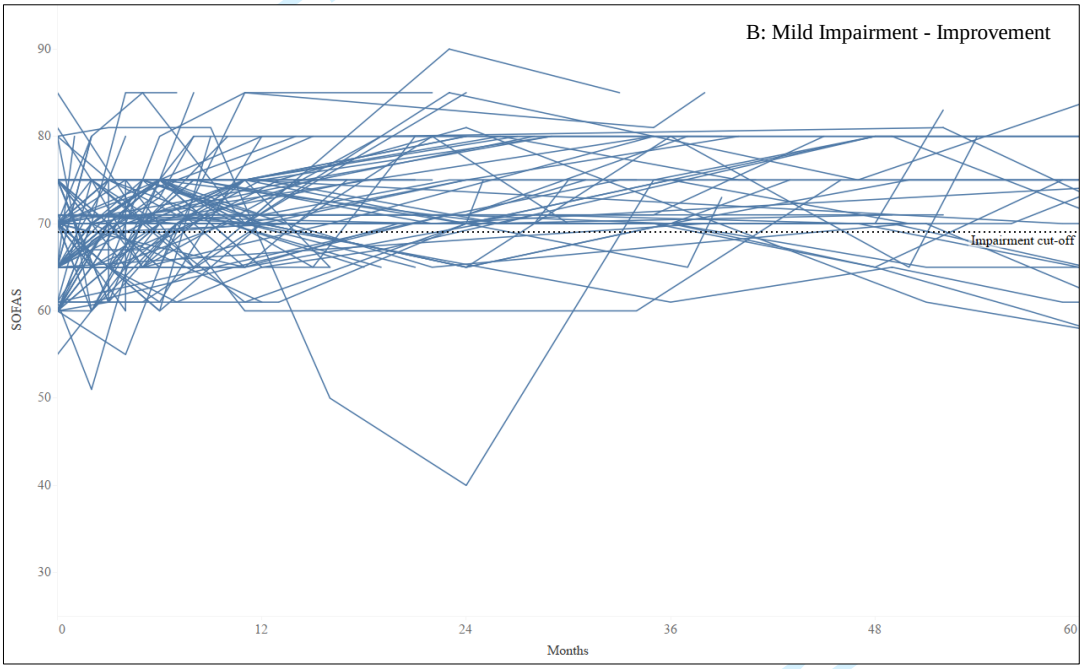
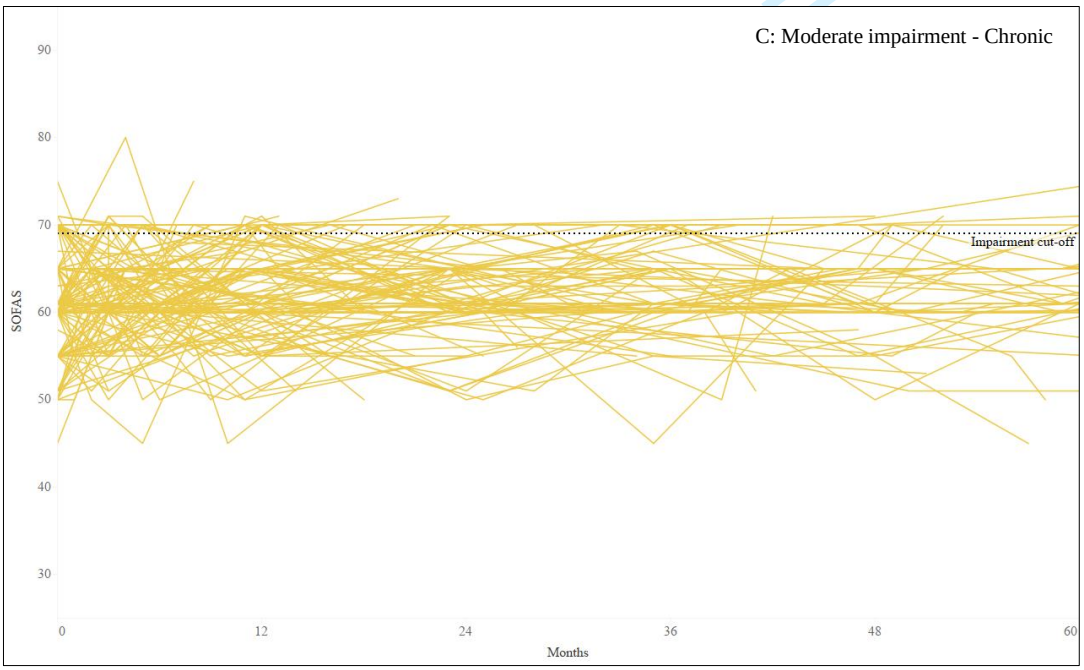


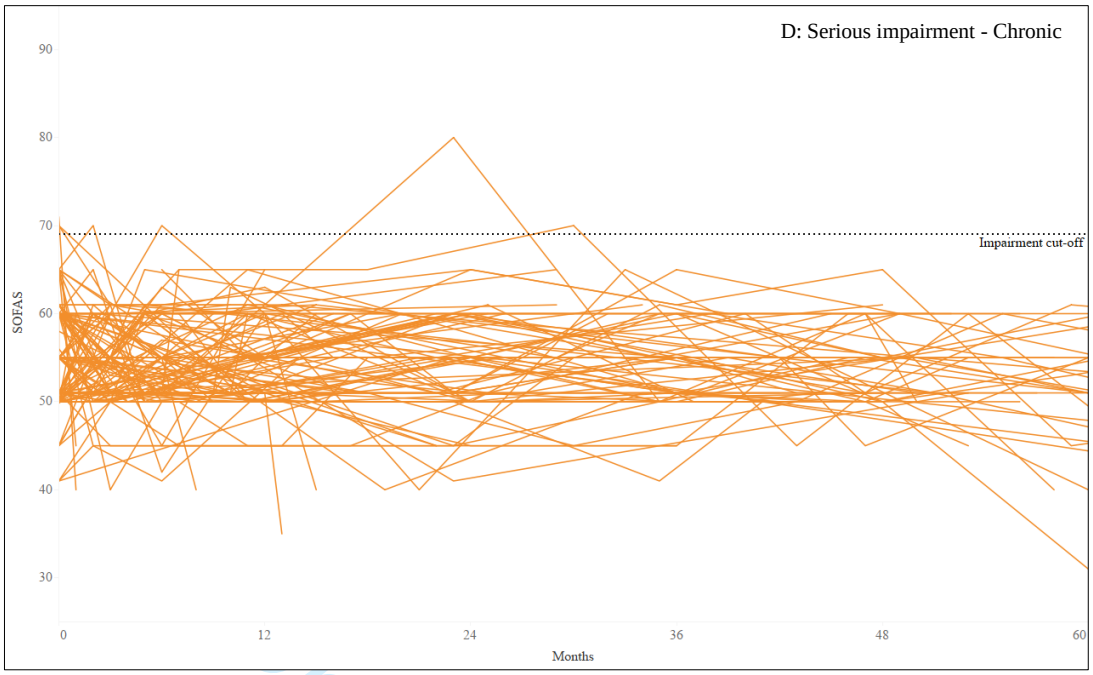
Figure 3 shows the six distinct trajectories identified for SOFAS score over a five year period. The thickness of each line represents the sample size of that particular trajectory, relative to all others. The dotted line represents the clinical impairment cut-off, which is set at a SOFAS score of 69. Slight impairment – stable (n=24, 4%), intercept equal to 78 and linear trend over time; Mild impairment – improvement (n=129, 23%), intercept equal to 68 and quadratic trend over time; Moderate impairment – chronic (n=185, 33%), intercept equal to 61 and linear trend over time; Serious impairment – chronic (n=158, 29%), intercept equal to 55 and linear trend over time; Serious impairment – improvement (n=19, 4%), intercept equal to 42 and quadratic trend over time; Serious impairment – deterioration (n=39, 7%), intercept equal to 51 and quadratic trend over time.

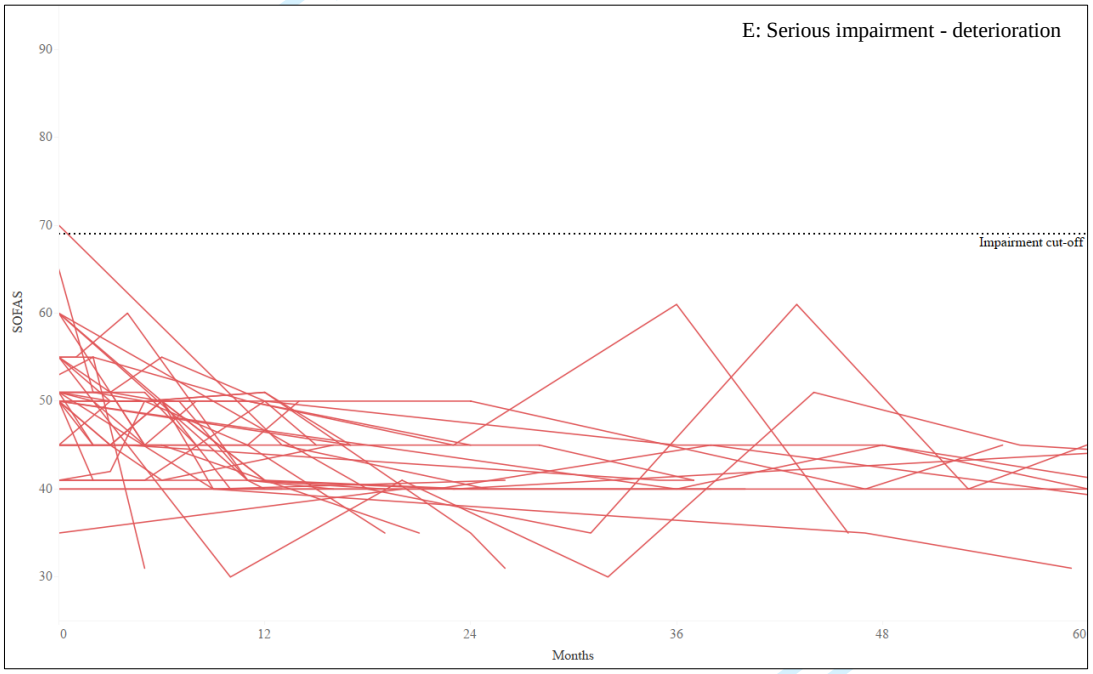
97x68mm (300 x 300 DPI)

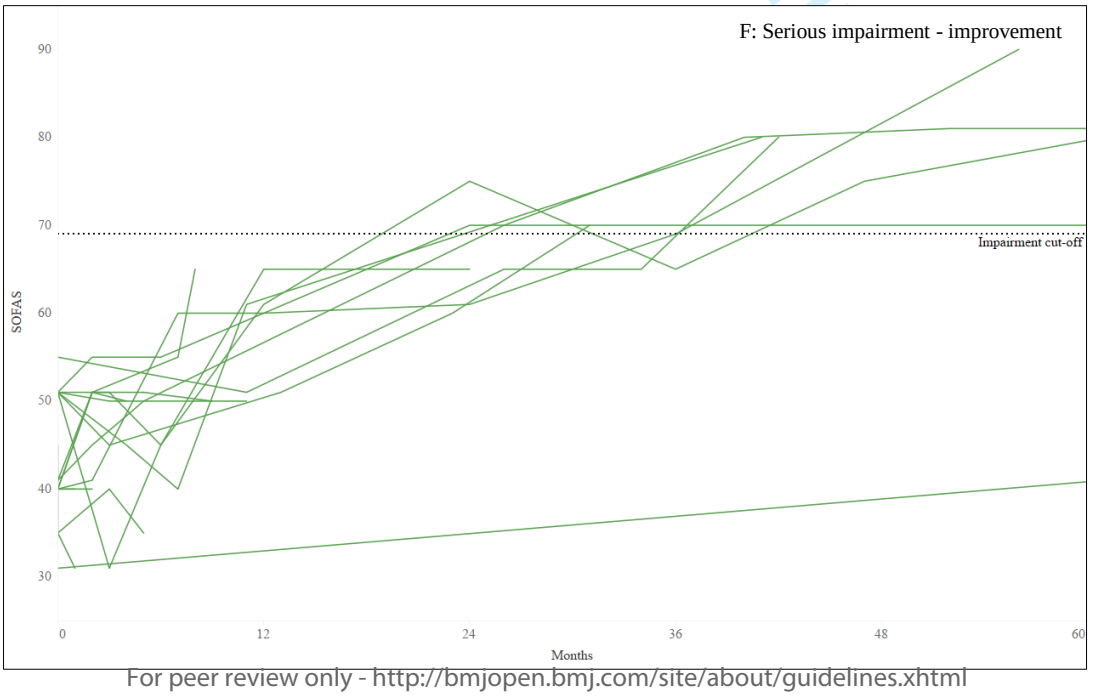

A: Slight impairment - Stable
SOFAS
90
80
70
60
50
40
30
Impairment cut-off
0
12
24
36
48
60
Months


B: Mild Impairment - Improvement
SOFAS
90
80
70
60
50
40
30
Impairment cut-off
0
12
24
36
48
60
Months


C: Moderate impairment - Chronic
SOFAS
90
80
70
60
50
40
30
Impairment cut-off
0
12
24
36
48
60
Months


D: Serious impairment - Chronic
SOFAS
Impairment cut-off
Months
90
80
70
60
50
40
30
0
12
24
36
48
60


E: Serious impairment - deterioration
SOFAS
Impairment cut-off
Months
90
80
70
60
50
40
30
0
12
24
36
48
60


F: Serious impairment - improvement
SOFAS
Impairment cut-off
Months
90
80
70
60
50
40
30
0
12
24
36
48
60

Supplementary Figure 1 caption

Supplementary figure 1 shows the individual-level trajectories for each group identified and shown in figure 1. Each line represents one individual and their SOFAS score ratings over time. The dotted line represents the clinical impairment cut-off, which is set at a SOFAS score of 69. Panel A: Slight impairment – stable (n=24, 4%), intercept equal to 78 and linear trend over time; Panel B: Mild impairment – improvement (n=129, 23%), intercept equal to 68 and quadratic trend over time; Panel C: Moderate impairment – chronic (n=185, 33%), intercept equal to 61 and linear trend over time; Panel D: Serious impairment – chronic (n=158, 29%), intercept equal to 55 and linear trend over time; Panel E: Serious impairment – improvement (n=19, 4%), intercept equal to 42 and quadratic trend over time; Panel F: Serious impairment – deterioration (n=39, 7%), intercept equal to 51 and quadratic trend over time.

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation	
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	P1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	P2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	P4-5
Objectives	3	State specific objectives, including any prespecified hypotheses	P5
Methods			
Study design	4	Present key elements of study design early in the paper	P5-6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	P5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	P5
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	-
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	P5-7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	P6
Bias	9	Describe any efforts to address potential sources of bias	-
Study size	10	Explain how the study size was arrived at	-
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	P7
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	P7
		(*b*) Describe any methods used to examine subgroups and interactions	P7
		(*c*) Explain how missing data were addressed	P6-7
		(*d*) If applicable, explain how loss to follow-up was addressed	
		(*e*) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	P7
		(b) Give reasons for non-participation at each stage	P6
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	P7,8,12,13
		(b) Indicate number of participants with missing data for each variable of interest	P7-8
		(c) Summarise follow-up time (eg, average and total amount)	P8
Outcome data	15*	Report numbers of outcome events or summary measures over time	P8-13
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear	P11-12

		which confounders were adjusted for and why they were included	
		(*b*) Report category boundaries when continuous variables were categorized	-
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	-
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	P8-11
Discussion			
Key results	18	Summarise key results with reference to study objectives	P13-14
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	P15-16
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	P14-15
Generalisability	21	Discuss the generalisability (external validity) of the study results	P14-16
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	P17

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.