BMJ Paediatrics Open

Disease control and psychiatric comorbidity among adolescents with chronic physical conditions - an observational cross-sectional study

Journal:	*BMJ Paediatrics Open*
Manuscript ID	bmjpo-2022-001605
Article Type:	Original research
Date Submitted by the Author:	08-Jul-2022
Complete List of Authors:	Kallio, Mira; University of Helsinki Faculty of Medicine, Department of Pediatrics Tornivuori, Anna; Turun yliopisto Miettinen, Päivi; University of Helsinki Faculty of Medicine, Department of Pediatrics Kolho, kaija-Leena; University of Helsinki Faculty of Medicine, Department of Pediatrics Culnane, Evelyn; The Royal Children's Hospital Melbourne Sawyer, Susan; The Royal Children's Hospital Melbourne Kosola, Silja; University of Helsinki Faculty of Medicine
Keywords:	Adolescent Health, Gastroenterology, Neurology, Rheumatology, Endocrinology

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

Disease control and psychiatric comorbidity among adolescents with chronic physical conditions - an observational cross-sectional study

Kallio Mira [a,c], Tornivuori Anna [a,b], Miettinen Päivi J. [a,c], Kolho Kaija-Leena [a,c,d], Culnane Evelyn [e], Sawyer Susan M [f,g,h] Kosola Silja [a,c]

Affiliations: [a] Department of Pediatrics, Helsinki University Hospital and University of Helsinki, Helsinki, Finland; [b] Nursing Science of University of Turku, Turku, Finland; [c] Pediatric Research Center, Helsinki University Hospital and University of Helsinki, Helsinki, Finland; [d] Faculty of Medicine and Health Technology, Tampere University, Tampere, Finland; [e] Transition Support Service, The Royal Children's Hospital, Melbourne, Australia; [f] Centre for Adolescent Health, Royal Children's Hospital, Melbourne, Australia; [g] Murdoch Children's Research Institute, Melbourne, Australia; [h] Department of Paediatrics, University of Melbourne, Australia.

Address correspondence to: Mira Kallio, Department of Pediatrics, University of Helsinki, Biomedicum 6, Haartmaninkatu 8, 00290 Helsinki, [mira.kallio@hus.fi], +35840 778 5221.

Clinical Trial registration: Trial registration name The Bridge and registration number NCT04631965 (https://clinicaltrials.gov/ct2/show/NCT04631965). Data Sharing Statement: Deidentified individual participant data will not be made available.

Word count: 3218 words

Abstract

Background

To investigate disease control, psychiatric comorbidity, substance use and their possible associations in adolescents with chronic health conditions before transfer to adult health care.

Methods

We collected clinical data from the year preceding transfer of care and psychiatric data from the records of our tertiary care Children´s Hospital, Helsinki, Finland (population base 1.7 million). Participants were grouped into three disease and/or adherence control categories (good, some evidence of concern, poor). Participants completed the Adolescent`s Substance Use Measurement questionnaire before transfer of care and were divided into four risk subgroups accordingly.

Results

In total, 253 adolescents (mean age 17.3 years, SD 1.2) from six pediatric subspecialties participated in this study. Disease control and/or adherence was good in 28% (n=70), moderate in 42% (n=105) and poor in 30% (n=76) of participants during the last year before the transfer of care to adult health services. A quarter of participants had at least one adolescence psychiatric diagnosis. Adolescents with concomitant psychiatric diagnoses more often had poor disease control of their chronic physical condition than adolescents with only a physical condition (44% vs 26%). In total 10% (n=26) of the adolescents reported hazardous substance use, and this was more frequent among adolescents with than without a psychiatric comorbidity (19% vs. 8%).

Conclusions

Psychiatric comorbidity in transition-aged adolescents with chronic physical conditions is common and its negative association with disease control and substance use should be considered in the transition process to adult health care services.

What is already known on this topic

Adolescents with chronic physical disorders have a higher prevalence of mental health disorders, but it is not known what impact this has on disease control prior to transfer to adult health care.

What this study adds

Adolescents with chronic physical disorders and comorbid psychiatric diagnoses more frequently have poor control of their physical disorder than those without psychiatric comorbidities, which will reduce the likelihood of a successful transition to adult health services.

How this study might affect research, practice or policy

In transition-aged adolescents with chronic physical disorders, psychiatric comorbidity is associated with worse disease control and hazardous substance use. This highlights the importance of physical health care providers preventing, identifying, and organizing treatment of mental health disorders also as a part of transitional care.

Introduction

Increasing numbers of adolescents with chronic physical disorders require regular follow-up in adult health care services due to advances in treatment and improved survival from previously lethal conditions, as well as an increased incidence of certain disorders in children and adolescents. [1–3] Living with a chronic physical disorder can pose many challenges during adolescence, not least due to the requirement for regular medication and other treatments, the frequency of medical appointments, and the uncertainty of future treatment such as surgical procedures. These demands for health monitoring can reduce participation in normative activities, which can be a burden for adolescents due to the impact on peer relationships, extracurricular participation and school attendance. [4]

Studies documenting the association of chronic physical disorders and mental health in adolescents indicates that chronic physical disorders are associated with increased rates of mental health problems. [5,6] In the US, 25% of children with epilepsy have anxiety and/or depression, which is more common than in the general population and comparable to children with other chronic conditions. [7,8] Children and adolescents with diabetes and inflammatory bowel disease (IBD) also have a higher prevalence of psychiatric problems than their healthy peers, and this also includes suicide attempts. [6,8–10]

Mental health problems such as depression and anxiety can affect disease control, adherence behaviors and health-related quality of life in children and adolescents with chronic health conditions, [11–12] but which particular young people are most at risk is incompletely understood. Depression is also associated with higher health care costs and emergency department visits in children and adolescents with IBD [13] although it is not known to what extent this reflects more severe disease or poor disease control.

Adolescents living with chronic conditions also often engage in risk behaviors. [14] Substance use in adolescence is associated with other mental health disorders,[15,16] and adolescent mental health disorders often continue into adulthood. [17,18] This pattern of accumulation of risk behaviors and mental health disorders among adolescents with chronic physical disorders suggests it is important to identify adolescents at greatest risk so that they can be appropriately supported.

In this cross-sectional study of adolescents with different chronic physical disorders, we aimed to investigate disease control, rates of psychiatric comorbidity and risky substance use and their associations before transfer of care to adult health care services. Our hypothesis was that psychiatric comorbidity is common and there is a connection between disease control and psychiatric disorders.

Methods

Ethics

This study was approved by the Ethics Committee for Women's and Children's Health and Psychiatry at the Helsinki University Hospital (HUS/1547/2017). Participants gave informed consent to link their routine clinical data with individual questionnaire responses. The Bridge trial has been registered with ClinicalTrials.gov (ID number NCT04631965).

Study design

This study is part of an international observational prospective cohort study named the Bridge, for which the study protocol is available online. [19] In this cross-sectional analysis, we combined retrospective data with questionnaire responses from one study site.

Participants

Participants were recruited from the Children's Hospital, Helsinki, Finland (hospital catchment area 1.7 million inhabitants) between September 2017, and August 2019. In Finland, practically all adolescents with chronic health conditions are managed by public health services with few cared for by private doctors or hospitals. Clinicians from six different pediatric subspecialty clinics (endocrinology, gastroenterology, rheumatology, nephrology and organ transplants, neurology, and cardiology) identified adolescents who were expected to transfer to adult clinics within the coming six to twelve months. Inclusion criteria were that participants were aged 15-24 years, had a chronic physical condition that had been diagnosed at least six months earlier and that would also require regular follow-up in adult health services. Eligible participants also needed to have sufficient cognitive and linguistic ability to communicate in Finnish, English or Swedish. Adolescents received a movie ticket (value 10 EUR) after completing the survey.

A research nurse, uninvolved in patient care, personally met 306 consecutive adolescents during their routine hospital visits and provided oral and written information about the Bridge study. In total, 279 (91.2%) adolescents consented to participate, and 253 (82.7%) adolescents responded to the baseline survey, either online or on paper, after a maximum of two reminders.

Patients were not involved in the design, or conduct, or reporting, or dissemination plans of our research.

Demographics

Background information was obtained from the baseline survey, and it included gender, residential area, home language and family composition (living with two parents or any other family type).

Clinical data

To determine disease control, we gathered data and laboratory test results from the electronic medical records for the year preceding the final visit at the Children's Hospital. The final visit was specified as the out-patient appointment where the clinician made a formal referral to the respective adult health service. We divided participants into one of three categories according to their health condition for which they were recruited: 1) good disease control and/or adherence; 2) some evidence of concern; and 3) poor disease control and/or adherence or more severe condition (see study protocol for further details). [19] Where appropriate, we used published cut-offs for disease control (e.g., mean glycosylated hemoglobin for adolescents with diabetes and 10-joint Juvenile Arthritis Disease Activity Score (JADAS10) for adolescents with rheumatic diseases). [19–21] For rare conditions without standard criteria of disease control and/or adherence, we subjectively categorized participants according to their symptoms, clinical and laboratory findings, need for inpatient care, and changes in medication. MK first reviewed medical records of every participant, of whom 28 (11%) were somewhat ambiguous to categorize. To evaluate the disease control group for these 28 adolescents, SK made an independent assessment. Six adolescents were categorized differently, but the final grading was based on consensus. For some analyses we combined the three smallest subspecialties (neurology, cardiology, and nephrology/organ transplant) into "others".

Psychiatric diagnoses and treatment details were collected from the electronic medical records of the Helsinki University Hospital from the age of 13 years until the first appointment in adult health care for the chronic health condition. The upper age limit for psychiatric data collection was 18 years which is the upper age limit of adolescent psychiatry in Finland. Psychiatric diagnoses were then divided into four categories: 1) mood disorders; 2) anxiety disorders; 3) others; and 4) multiple diagnoses (i.e., diagnosis from at least two different diagnostic categories). The New Children's Hospital has no general guideline regarding

psychiatric assessment and adolescents may also receive referrals to adolescent psychiatry from health-care centers or school and student health care. Outpatient appointments with mental health professionals were divided into three categories: 1) no appointments; 2) one to three appointments; and 3) more than three appointments. We also recorded the age at the first psychiatric diagnosis, possible admissions to psychiatric in-patient care and the number of days adolescents spent in psychiatric inpatient care.

Questionnaires

Participants completed the Adolescent Substance Use Measurement (ADSUME), a brief measure that was developed and validated in Finland to evaluate adolescent substance use and its possible harmful consequences during the previous year. ADSUME is reliable when compared to adult questionnaires (AUDIT, CRAFFT) and may even be superior in detecting hazardous substance use among adolescents. [22] We included the first nine questions of the questionnaire that yield a numeric score, calculated a total score (0-31 points) and divided participants into subgroups according to the guidelines of the Finnish Institute for Health and Welfare: 1) abstinence or experimental use, 0-3 points; 2) recurring use, 4-6 points; 3) risky use, 7-9 points; and 4) hazardous substance use, 10 points or more. [23]

Data analysis

Categorical data are presented as frequencies (with percentages). For continuous variables, means and standard deviations (SDs) or medians (with interquartile range) are used. The associations between disease control, psychiatric diagnoses, substance use and family composition were compared using Fisher's exact test (two-sided). To evaluate the associations between categorical data and continuous variables we used non-parametric tests (Mann-Whitney U and Kruskal-Wallis). Data analyses were executed using IBM SPSS Statistics 25 (IBM, Somers, NY). P value < 0.05 was considered significant.

Results

The demographic and clinical data of the 253 study participants are summarized in Tables 1 and 2. The mean age at diagnosis of physical condition was 9.0 years (SD 5.3) and the mean age at first psychiatric diagnosis was 13.7 years (SD 2.7). In total 215 (85.0%) adolescents completed the ADSUME before or at the same time as the defined day of the transfer of care. Age at transfer differed greatly between subspecialties: rheumatology patients were the youngest to transfer (mean age 16.2 years) and gastroenterology were the oldest (mean age 19.0 years; $p<0.001$ for difference between groups).

Table 1. Demographic and clinical data (n=253).

Sex	**N**	**%**
Male	118	46.6
Female	132	52.2
Other	3	1.2
Pediatric subspecialty care	**N**	**%**
Diabetes	92	36.4
Rheumatology	66	26.1
Gastroenterology	45	17.8
Cardiology	19	7.5
Neurology	18	7.1
Kidney or liver disease with or without organ transplant	13	5.1
Lives with	**N**	**%**
Mother and father	158	62.5
Other than with mother and father	95	37.5
Disease control *	**N**	**%**
Good control and/or adherence	70	27.7
Some evidence of concern	105	41.5
Poor control and/or adherence or more severe condition	76	30.0
Psychiatric diagnoses	**59**	**23.3**
Many diagnoses	22	8.7
Anxiety disorders	21	8.3

Other	13	5.1
Mood disorders	3	1.2
Outpatient visits in adolescent psychiatry	**N**	**%**
No visits	159	62.8
1-3 visits	36	14.2
More than 3 visits	58	22.9
Median ADSUME total scores (with IQR)**	3	(0-6)
Female	2	(0-6)
Males	3	(0-6)
ADSUME risk category**	**N**	**%**
Abstinence or experimental use (0-3 points)	142	56.1
Recurring use (4-6 p)	57	22.5
Risky use (7-9 p)	27	10.7
Hazardous use (≥10 p)	26	10.3

*Data available for 251 adolescents; transfer of two adolescents has been delayed.
** One response missing.
ADSUME = Adolescent`s Substance Use Measurement; IQR = interquartile range

Table 2. Demographic and clinical data (n=253).

	Mean, years (median)	**SD**
Age at first physical diagnosis	**9.0 (10.1)**	**5.3**
Age at first psychiatric diagnosis	**13.7 (14.3)**	**2.7**
Age when completing the ADSUME	**17.2 (16.8)**	**1.2**
Age at transfer of care	**17.3 (17.1)**	**1.2**
Diabetes	17.2	0.7
Rheumatology	16.2	0.5
Gastroenterology	19.0	0.9
Others	17.8	1.2
Time between ADSUME and transfer of care	**0.2 (0.0)**	**0.4**
Time between physical diagnosis and transfer of care	**8.3 (7.4)**	**8.3**

Time between psychiatric diagnosis and transfer of care	**4.0 (3.2)**	**4.0**

Among all study participants, 27.7% (n=70) were categorized as having good disease control and/or adherence, 41.5% (n=105) had some evidence of concern, and 30.0% (n=76) had poor disease control and/or adherence or more severe condition during the year preceding the transfer of care. Only 16% of adolescents with gastroenterological diseases and 14% of adolescents with diabetes had good disease control (requirements for adolescents with IBD: at least 80% of faecal calprotectin results <100 µg/g and always <300 µg/g; medication unchanged or reduced, and no inpatient care; requirements for adolescents with diabetes: mean of all HbA1C measurements across the year preceding transfer of care ≤ 53 mmol/mol including on average 4.6 measurements). In the group of adolescents with rheumatological disease, 39% had good disease control and in the group "others" 48%. Gender showed no association with different disease control groups (p=0.58) and neither did the age at diagnosis (p=0.88). Older age at transfer of care was associated with poorer disease control (p=0.045).

In this cohort, 23.3% of adolescents (n=59) had a psychiatric diagnosis of whom 37.2% (n=22) had at least two different diagnoses. Anxiety disorders were most common (n=38), and they constituted 15.0% of all participants and 64.4% of adolescents with a psychiatric diagnosis. In terms of gender differences, females were overrepresented in anxiety disorders and males in the 'other psychiatric diagnosis' group. Adolescents with diabetes had more psychiatric diagnoses (28.3% vs 20.5%; p=0.12) and had more often at least one outpatient visit in adolescent psychiatry (44.6 % vs 32.9%; p= 0.08) than adolescents with other conditions, although these differences did not reach statistical significance. Nine adolescents (3.6%) received inpatient psychiatric care and the median time per person spent in in-patient care was 22 days (range 9-956 days). There was no association between the age at physical diagnosis and psychiatric diagnosis (p=0.32).

More than half of the participants (n=142, 56.1%) were abstinent or reported only experimental substance use, see Table 3. Twenty-nine participants (11.5%) used nicotine products with eleven (4.3%) using them daily. The most frequently used products were tobacco and snuff. Approximately half of the adolescents reported using alcohol in the last year and seven (2.7%) reported use of other substances (e.g., cannabis, solvents, or medication abuse). Most of the adolescents used intoxicants for fun (80.2%) and together with friends (64.9%). The median ADSUME total score was 3.0 and the maximum score was 27 points.

Table 3. Adolescent Substance Use Measurement (ADSUME) in the past year (n=252*).

	N	%
Substance use		
Nicotine products	**29**	11.5
Alcohol	**131**	52
Abuse of medications	**3**	1.2
Cannabis	**3**	1.2
Missed school because of substance use	**5**	2
Risk behavior while intoxicated		
Hurt herself/himself	**10**	4
Hurt someone else	**5**	2
Drove a car	**3**	1.2
Passenger in a car with intoxicated driver	**3**	1.2
Had sex that regretted afterwards	**8**	3.2

* One response missing

Table 4 and Figure 1 summarize the associations between disease control, psychiatric diagnoses, substance use and family composition. Adolescents with psychiatric diagnoses more often had poor disease control and/or adherence or more severe disease/condition than adolescents without psychiatric diagnoses (p=0.01). Adolescents with psychiatric diagnoses also more frequently reported hazardous substance use than adolescents without psychiatric diagnoses (p=0.02). No direct association between disease control and substance use was

detected. Adolescents who lived with two parents (n=158, 62.5%) had significantly fewer psychiatric diagnoses than adolescents living in other kinds of families (p = 0.05).

Table 4. Family composition, disease control and substance use, by psychiatric diagnosis (n=253).

	No psychiatric diagnosis (n=194) **N (%)**	**Psychiatric diagnosis (n=59)** **N (%)**	**p**
Living with two parents	128 (66)	30 (51)	**0.05**
Disease control *			
Good control and/or adherence	59 (30)	11 (19)	0.13
Some evidence of concern	84 (43)	21 (37)	0.45
Poor control and/or adherence or more severe condition	51 (26)	25 (44)	**0.01**
ADSUME risk category **			
Abstinence or experimental use	106 (55)	36 (62)	0.37
Repetitive use	48 (24)	9 (16)	0.16
Risky use	25 (13)	2 (3)	**0.05**
Hazardous use	15 (8)	11 (19)	**0.02**

*Transfer of two adolescents has been delayed.

** One response missing

Discussion and conclusions

In this cross-sectional study of adolescents with a chronic physical disorder in the year preceding the transfer to adult health services, nearly a third had poor disease control and almost a quarter had received a psychiatric diagnosis during adolescence. Adolescents with a comorbid psychiatric diagnosis more frequently had poor control of their physical disorder and more often reported hazardous substance use than adolescents with a chronic physical disorder without a psychiatric diagnosis.

The mean age at transfer to adult health services (17.3 years) in this study is lower than reported in many studies [24-25] and nearly a year and a half younger than the mean preferred age (18.7 years) recently reported in a global study of pediatricians. [26] However, the definition for the date of transfer of care varies between studies which hinders direct comparisons. In our study, adolescents who transferred to adult health care at a younger age had better disease control than adolescents who were older at transfer. This may be due to the differences between subspecialties in the ages at transfer or different definitions of optimal disease control or they may reflect the clinicians' attempts to achieve acceptable disease control prior to the transfer of care.

Most studies of mental health in adolescents with chronic physical health disorders use brief self-report surveys instead of collecting data on the actual psychiatric diagnoses, as in our study. Few studies have specifically assessed psychiatric diagnoses at the time of transition to adult health care. Concerningly, a recent study on transition to adult health care in adolescents with juvenile idiopathic arthritis showed that psychiatric diagnoses were associated with disease activity before the transfer of care. [27] Another study reported that more than 56% of transition-aged patients with epilepsy had signs of mental illness and that psychiatric problems were an independent predictor of lower quality of life. [28] These findings have relevance to the whole transition process as the adolescent may need concurrent transition of psychiatric care in addition to the transition of physical health care.

Surprisingly, only 27.7% of the study cohort had good disease control and/or adherence of their physical disorder. The proportion of adolescents with good disease control was lowest among adolescents with diabetes and IBD. This may reflect the availability of laboratory measures of adherence for these conditions as an elevated fecal calprotectin level was the most common reason for suboptimal disease control in gastroenterological patients. It may also depict the relatively stringent threshold values in diabetes.[21] The prevalence of

suboptimal disease control before transferring adolescents to adult health care is important to note as poor disease control at transfer is associated with increased risks of poor disease control after the transfer of care, poor engagement with adult health services (higher rates of loss-to-follow-up) and psychosocial problems. [29] Optimizing health outcomes is important in all patients. However, additional strategies may be required before and after transfer to adult services in adolescents whose disease is challenging to treat, who lack motivation or skills for self-management, and who have mental health or substance use disorders. [30]

A previous Finnish study reported that adolescents with diabetes are relatively overrepresented among their peers with psychiatric diagnoses. [31] Type 1 diabetes is common in Finland and national guidelines encourage routine assessment of the need for psychological support. The higher rate of psychiatric diagnoses among adolescents with diabetes than other diagnosis groups may thus reflect better access to evaluation and treatment for mental health problems, or it could be related to the demands of diabetes in every-day life.

The association we found between poor disease control and psychiatric comorbidity may be bidirectional: living with a severe disease may increase the emotional burden experienced while mental health problems may affect motivation and self-management resources and thus worsen the control of the physical disorder. Based on this study, estimating the direction of causality is impossible. However, this connection is important to notice when managing transition-aged adolescents with physical conditions, because the adequate treatment of psychiatric problems may improve symptoms of depression and anxiety and positively influence disease control of the somatic disease and health care utilization. [32] Treating mental disorders in adolescents with physical health disorders could be viewed as an investment in quality of life, education, and employment as well as a way of reducing the long-term costs of health care. Maximizing mental health and wellbeing well before adolescents transfer to adult health services appears especially important given the association of both poor mental health

and the transfer of care itself with unsatisfactory adherence to treatment and increased rates of emergency visits and hospitalizations. [11,13,33] Thus finding effective ways to integrate collaboration of physical and psychiatric care already in children`s hospitals are essential.[34]

Adolescents living with two parents had fewer psychiatric diagnoses than their peers living in other kinds of families. This finding has also been reported among the general population of children and adolescents. [35,36] As a child's illness is a significant stressor for parents, [37] beyond attending to the young person's distress, family psychosocial supports and advocacy for interventions to minimize financial hardships also warrant consideration.

Although alcohol consumption has decreased among adolescents in many developed countries, adolescent binge drinking and the risky behavior that commonly accompany it remain significant public health problems. [38] In this study, 22.5% used intoxicants repeatedly and a further 21.0% were categorized as risky or hazardous users. Adolescents with psychiatric comorbidity more often reported hazardous use and adolescents without psychiatric diagnoses were overrepresented in the group of risky users. This may reflect that abundant use appears in both subgroups, but mental health problems may increase the likelihood of serious substance abuse. While different recruitment and assessment methods were used, these findings are similar to a US study of 14-18-yr-old adolescents attending routine care in which 18% had substance use problems and 16% had substance use disorders. [15] However, few adolescents in our cohort had used cannabis during the past year, in comparison to 13% of 15-16-yr-old students in Europe. [39] At the very least, these data affirm the importance of regularly discussing substance use and its effects with adolescents with chronic physical disorders, and especially those with mental health challenges.

A strength of this study is that we recruited a cohort of adolescents from six different hospital departments to cover a diversity of conditions. This increases the generalizability of our

results. However, this is also a limitation, especially in relation to how disease control was defined as, by definition, this differed by disorder. We also had to categorize adolescents with rare diseases subjectively, but we used two independent reviewers and the final grouping was based on consensus, so misclassification bias is unlikely. We had access to all electronic medical records in the study catchment area, including psychiatry, which enabled us to use exact diagnoses and to estimate disease control based on clinical findings and the high response rate reduces the likelihood of selection bias. Some psychiatric diagnoses may have been missed if the adolescent had moved to or from another hospital district. However, this is unlikely to change the findings, as 96% of patients lived in the hospital district at the time they were transferred to adult services. Considering substance use, we used survey data which could be more reliable than what adolescents share with health professionals. [40] Multivariate analyses were not performed because no significant differences were found in appropriate variables in independent analyses. The health care system in Finland is government-funded so all adolescents receive the same treatment despite their socioeconomic status. In countries without public health care, associations between mental health problems and poor disease control among adolescents may be even more significant.

In conclusion, our results show that psychiatric morbidity and poor disease control of chronic physical disorders are prevalent and closely intertwined among adolescents. This highlights the importance of physical health care providers preventing, identifying, and organizing treatment of mental health disorders, including around the time of transition to adult health care.

A Funding statement:

This study is supported by grants from the Foundation for Medical Research, the Helsinki University Hospital (TYH2019312), the Foundation for Pediatric Research and the Paulo Foundation.

A competing interest statement:

Authors have no conflicts of interest relevant to this article to disclose.

Contributor`s Statement:

Dr Mira Kallio collected data, carried out initial analyses, drafted the initial manuscript and reviewed and revised the manuscript. Ms Tornivuori collected data and reviewed and revised the manuscript. Drs Miettinen and Kolho participated in designing the study and reviewed and revised the manuscript. Ms Culnane and Professor Sawyer participated in study design and reviewed and revised the manuscript. Kosola designed the study, coordinated, and supervised data collection and critically reviewed the manuscript for important intellectual content. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

Checklist: STROBE.

Data sharing statement: Data available on request from the authors.

References

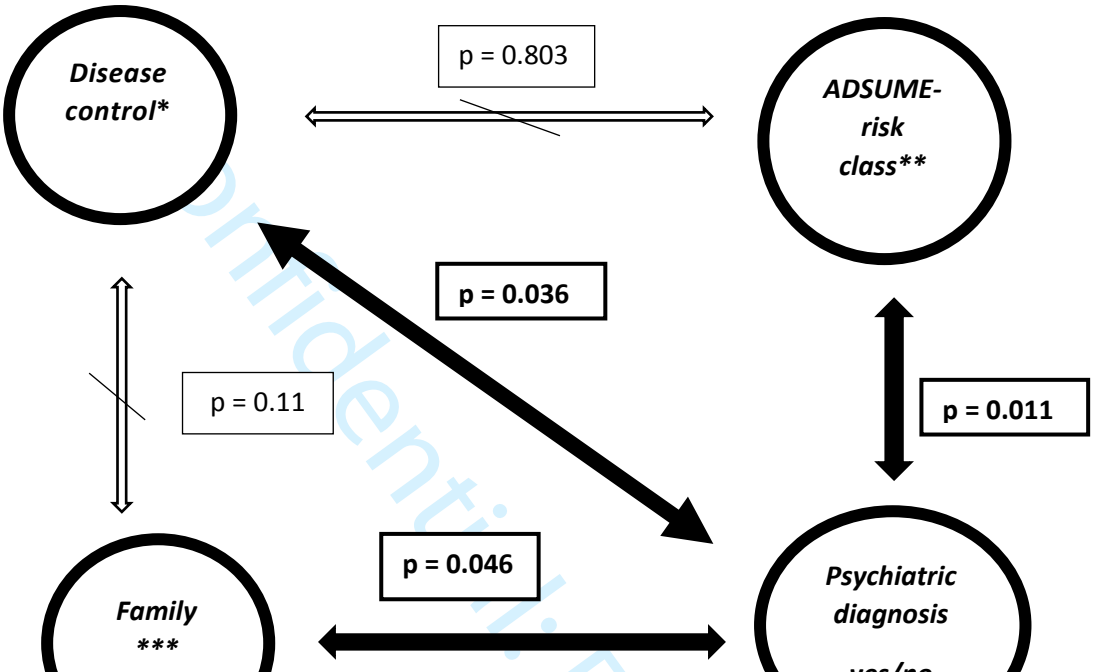
1. Raissadati A, Nieminen H, Jokinen E, Sairanen H. Progress in late results among pediatric cardiac surgery patients: A population-based 6-decade study with 98% follow-up. *Circulation*. 2015;131(4):347-353. doi:10.1161/CIRCULATIONAHA.114.011190
2. Benchimol EI, Fortinsky KJ, Gozdyra P, Van Den Heuvel M, Van Limbergen J, Griffiths AM. Epidemiology of pediatric inflammatory bowel disease: A systematic review of international trends. *Inflamm Bowel Dis*. 2011;17(1):423-429. doi:10.1002/ibd.21349

3. Patterson CC, Karuranga S, Salpea P, et al. Worldwide estimates of incidence, prevalence, and mortality of type 1 diabetes in children and adolescents: Results from the International Diabetes Federation Diabetes Atlas, 9th edition. *Diabetes Res Clin Pract.* 2019;157:107842. doi:10.1016/j.diabres.2019.107842
4. Maes M, Van Den Noortgate W, Fustolo-Gunnink SF, Rassart J, Luyckx K, Goossens L. Loneliness in Children and Adolescents with Chronic Physical Conditions: A Meta-Analysis. *J Pediatr Psychol*. 2017;42(6) :622-635. doi:10.1093/jpepsy/jsx046
5. Brady AM, Deighton J, Stansfeld S. Psychiatric outcomes associated with chronic illness in adolescence: A systematic review. *J Adolesc*. 2017;59:112-123. doi:10.1016/j.adolescence.2017.05.014
6. Robinson ME, Simard M, Larocque I, Shah J, Nakhla M, Rahme E. Risk of psychiatric disorders and suicide attempts in emerging adults with diabetes. *Diabetes Care.* 2020;43(2):484-486. doi:10.2337/dc19-1487
7. LaGrant B, Marquis BO, Berg AT, Grinspan ZM. Depression and anxiety in children with epilepsy and other chronic health conditions: National estimates of prevalence and risk factors. *Epilepsy Behav*. 2020;103 (Pt A):106828. doi:10.1016/j.yebeh.2019.106828
8. Reynolds KA, Helgeson VS. Children with diabetes compared to peers: Depressed? Distressed? A meta-analytic review. *Ann Behav Med.* 2011;42(1):29-41. doi:10.1007/s12160-011-9262-4
9. Butwicka A, Olén O, Larsson H, et al. Association of Childhood-Onset Inflammatory Bowel Disease with Risk of Psychiatric Disorders and Suicide Attempt. *JAMA Pediatr.* 2019;173(10):969-978. doi:10.1001/jamapediatrics.2019.2662
10. Malham M, Jakobsen C, Paerregaard A, Virta LJ, Kolho KL, Wewer V. The incidence of cancer and mortality in paediatric onset inflammatory bowel disease in Denmark and Finland during a 23-year period: a population-based study. *Aliment Pharmacol Ther.* 2019;50(1):33-39. doi:10.1111/apt.15258
11. Bernstein CM, Stockwell MS, Gallagher MP, Rosenthal SL, Soren K. Mental health issues in adolescents and young adults with type 1 diabetes: Prevalence and impact on glycemic control. *Clin Pediatr (Phila).* 2013;52(1):10-15. doi:10.1177/0009922812459950
12. Blount RL. Disease Activity Does Not Explain It All: How Internalizing Symptoms and Caregiver Depressive Symptoms Relate to Health-related Quality of Life Among Youth with Inflammatory Bowel Disease. *Inflamm Bowel Dis*. 2016;22(4):963-967. doi:10.1097/MIB.0000000000000686
13. Wong JJ, Sceats L, Dehghan M, et al. Depression and health care use in patients with inflammatory bowel disease. *J Crohn's Colitis.* 2019;13(1):19-26. doi:10.1093/ecco-jcc/jjy145
14. Sawyer SM, Drew S, Yeo MS, Britto MT. Adolescents with a chronic condition: challenges living, challenges treating. *Lancet.* 2007;369(9571):1481-1489. doi:10.1016/S0140-6736(07)60370-5
15. Shrier LA, Harris SK, Kurland M, Knight JR. Substance use problems and associated psychiatric symptoms among adolescents in primary care. *Pediatrics.* 2003;111(6 Pt 1):e699-e705. doi:10.1542/peds.111.6.e699
16. Deas D. Adolescent substance abuse and psychiatric comorbidities. *J Clin Psychiatry*. 2006;67 (7):e02. doi:10.4088/jcp.0706e02
17. Gray KM, Squeglia LM. Research Review: What have we learned about adolescent substance use? *J Child Psychol Psychiatry Allied Discip*. 2018;59(6):618-627. doi:10.1111/jcpp.12783

18. Kessler RC, Berglund P, Demler O, Jin R, Merikangas KR, Walters EE. Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the national comorbidity survey replication. *Arch Gen Psychiatry*. 2005;62(6):593-602. doi:10.1001/archpsyc.62.6.593
19. Kosola Silja, Culnane Evelyn, Loftus Hayley, et al. The Bridge study protocol: an international, observational cohort study on the transition of healthcare for adolescents with chronic conditions. *BMJ Open*. 2021;11(6):e048340. Published 2021 Jun 21. doi:10.1136/bmjopen-2020-048340
20. Backström M, Tynjälä P, Ylijoki H, et al. Finding specific 10-joint Juvenile Arthritis Disease Activity Score (JADAS10) and clinical JADAS10 cut-off values for disease activity levels in non-systemic juvenile idiopathic arthritis: A Finnish multicentre study. *Rheumatology (Oxford)*. 2016;55(4):615-623. doi:10.1093/rheumatology/kev353
21. DiMeglio LA, Acerini CL, Codner E, et al. ISPAD Clinical Practice Consensus Guidelines 2018: Glycemic control targets and glucose monitoring for children, adolescents, and young adults with diabetes. *Pediatr Diabetes*. 2018;19 Suppl 27:105-114. doi:10.1111/pedi.12737
22. Piskanen M. Promoting Adolescents` Abstinence from Substance Use. An Early Intervention Model for School and Student Health Care. Published online 2007. http://urn.fi/URN:ISBN:978-951-27-0510-8
23. Pirskanen M, Laukkanen E, Pietilä AM. A formative evaluation to develop a school health nursing early intervention model for adolescent substance use. *Public Health Nurs*. 2007;24(3):256-264. doi:10.1111/j.1525-1446.2007.00632.x
24. Lotstein DS, Seid M, Klingensmith G, et al. Transition from pediatric to adult care for youth diagnosed with type 1 diabetes in adolescence. *Pediatrics*. 2013;131(4) :e1062-e1070. doi:10.1542/peds.2012-1450
25. Akchurin OM, Melamed ML, Hashim BL, Kaskel FJ, Del Rio M. Medication adherence in the transition of adolescent kidney transplant recipients to the adult care. *Pediatr Transplant*. 2014;18(5):538-548. doi:10.1111/petr.12289
26. Sawyer SM, McNeil R, Francis KL, et al. The age of paediatrics. *Lancet Child Adolesc Heal*. 2019;3(11):822-830. doi:10.1016/S2352-4642(19)30266-4
27. Kosola S, Relas H. Patients with psychiatric diagnoses have lower quality of life than other patients with juvenile rheumatic disease: a prospective study. *Rheumatology (Oxford)*. 2021;60(12):5560-5566. doi:10.1093/rheumatology/keab150 doi:10.1093/rheumatology/keab150
28. Healy SA, Fantaneanu TA, Whiting S. The importance of mental health in improving quality of life in transition-aged patients with epilepsy. *Epilepsy Behav*. 2020;112:107324. doi:10.1016/j.yebeh.2020.107324
29. Rollo A, Salardi S, Ciavarella A, et al. Transition from pediatric to adult care. Eight years after the transition from pediatric to adult diabetes care: Metabolic control, complications and associated diseases. *J Endocrinol Invest*. 2014;37(7):653-659. doi:10.1007/s40618-014-0090-9
30. Andrade DM, Bassett AS, Bercovici E, et al. Epilepsy: Transition from pediatric to adult care. Recommendations of the Ontario epilepsy implementation task force. *Epilepsia*. 2017;58(9):1502-1517. doi:10.1111/epi.13832
31. Karukivi M, Haapasalo-Pesu K-M. The predictive effect of medical illnesses for mental health care in adolescence: a register-based study. *Adolesc Health Med Ther*. 2017;8 :95-98. doi:10.2147/ahmt.s142980

32. Bennett S, Shafran R, Coughtrey A, Walker S, Heyman I. Psychological interventions for mental health disorders in children with chronic physical illness: A systematic review. *Arch Dis Child*. 2015;100(4):308-316. doi:10.1136/archdischild-2014-307474
33. Kosola S, Ylinen E, Finne P, Rönnholm K, Ortiz F. Implementation of a transition model to adult care may not be enough to improve results: National study of kidney transplant recipients. *Clin Transplant.* 2019;33(1):e13449. doi:10.1111/ctr.13449
34. Fazel M, Townsend A, Stewart H, Pao M, Paz I, Walker J, Sawyer S.M, Sharpe M. Integrated care to address child and adolescent health in the 21st century: A clinical review. *JCPP Advances.*2021;e12045. doi:10.1002/jcv2.12045
35. Ängarne-Lindberg T, Wadsby M. Psychiatric and somatic health in relation to experience of parental divorce in childhood. *Int J Soc Psychiatry*. 2012;58(1):16-25. doi:10.1177/0020764010382372
36. Perales F, Johnson SE, Baxter J, Lawrence D, Zubrick SR. Family structure and childhood mental disorders: new findings from Australia. *Soc Psychiatry Psychiatr Epidemiol.* 2017;52(4):423-433. doi:10.1007/s00127-016-1328-y
37. Mutanen A, Kosola S, Merras-Salmio L, Kolho KL, Pakarinen MP. Long-term health-related quality of life of patients with pediatric onset intestinal failure. *J Pediatr Surg*. 2015;50(11). doi:10.1016/j.jpedsurg.2015.05.012
38. Siqueira L, Smith VC; COMMITTEE ON SUBSTANCE ABUSE. Binge Drinking. *Pediatrics*. 2015;136(3):e718-e726. doi:10.1542/peds.2015-2337
39. Molinaro S, Vicente J BE et al. ESPAD Report 2019. Results from the European School Survey Project on Alcohol and Other Drugs. Published 2020. http://espad.org/sites/espad.org/files/2020.3878_EN_04.pdf
40. Gryczynski J, Mitchell SG, Schwartz RP, et al. Disclosure of Adolescent Substance Use in Primary Care: Comparison of Routine Clinical Screening and Anonymous Research Interviews. *J Adolesc Health*. 2019;64(4):541-543. doi:10.1016/j.jadohealth.2018.10.009

Figure 1. Associations between disease control, psychiatric diagnoses, substance use (ADSUME) and family composition. P < 0.05 is considered significant.



* Good control and/or adherence, some evidence of concern or poor control and/or adherence or more severe condition

** Abstinence or experimental use, repetitive use, risky use, or hazardous use

*** Living with mother and father or with someone else (for example with only one parent, mixed family or any other third party)

BMJ Paediatrics Open

Disease control and psychiatric comorbidity among adolescents with chronic medical conditions - a single centre retrospective study

Journal:	*BMJ Paediatrics Open*
Manuscript ID	bmjpo-2022-001605.R1
Article Type:	Original research
Date Submitted by the Author:	28-Sep-2022
Complete List of Authors:	Kallio, Mira; University of Helsinki Faculty of Medicine, Department of Pediatrics Tornivuori, Anna; Turun yliopisto Miettinen, Päivi; University of Helsinki Faculty of Medicine, Department of Pediatrics Kolho, kaija-Leena; University of Helsinki Faculty of Medicine, Department of Pediatrics Culnane, Evelyn; The Royal Children's Hospital Melbourne Sawyer, Susan; The Royal Children's Hospital Melbourne Kosola, Silja; University of Helsinki Faculty of Medicine
Keywords:	Adolescent Health, Gastroenterology, Neurology, Rheumatology, Endocrinology

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

Disease control and psychiatric comorbidity among adolescents with chronic medical conditions – a single center retrospective study

Kallio Mira [a,c], Tornivuori Anna [a,b], Miettinen Päivi J. [a,c], Kolho Kaija-Leena [a,c,d], Culnane Evelyn [e], Sawyer Susan M [f,g,h] Kosola Silja [a,c]

Affiliations: [a] Department of Pediatrics, Helsinki University Hospital and University of Helsinki, Helsinki, Finland; [b] Nursing Science of University of Turku, Turku, Finland; [c] Pediatric Research Center, Helsinki University Hospital and University of Helsinki, Helsinki, Finland; [d] Faculty of Medicine and Health Technology, Tampere University, Tampere, Finland; [e] Transition Support Service, The Royal Children's Hospital, Melbourne, Australia; [f] Centre for Adolescent Health, Royal Children's Hospital, Melbourne, Australia; [g] Murdoch Children's Research Institute, Melbourne, Australia; [h] Department of Paediatrics, The University of Melbourne, Australia.

Address correspondence to: Mira Kallio, Department of Pediatrics, University of Helsinki, Biomedicum 6, Haartmaninkatu 8, 00290 Helsinki, [mira.kallio@hus.fi], +35840 778 5221.

Clinical Trial registration: Trial registration name The Bridge and registration number NCT04631965 (https://clinicaltrials.gov/ct2/show/NCT04631965).

Data Sharing Statement: Data are available upon reasonable request.

Word count: 2997 words

Abstract

Background

To investigate disease control, psychiatric comorbidity, substance use and their possible associations in adolescents with chronic medical conditions before transfer to adult health care.

Methods

We collected clinical data from the year preceding transfer of care and psychiatric data from the records of the paediatric hospital in Helsinki, Finland (population base 1.7 million). Participants were grouped into three disease and/or adherence control categories (good, some evidence of concern, poor) based on clinical data from the medical records of the year preceding the transfer of care. Participants completed the Adolescent`s Substance Use Measurement questionnaire before transfer of care and were divided into four risk subgroups accordingly.

Results

In total, 253 adolescents (mean age 17.3 years, SD 1.2) from six pediatric subspecialties participated in this study. Disease control and/or adherence were rated as good in 28% (n=70), moderate in 42% (n=105) and poor in 30% (n=76) in the year before participants transferred to adult health services. A quarter of participants had at least one psychiatric diagnosis during adolescence. Adolescents with concomitant psychiatric diagnoses more often had poor disease control of their chronic medical condition than adolescents with only a medical condition 44% vs 26% (n=25/59 vs 51/194, respectively). More than half of adolescents (56%) were abstinent or used substances infrequently; 10% (n=26) reported hazardous substance use.

Conclusions

Psychiatric comorbidity in adolescents with chronic medical conditions is common. Its negative association with disease control and possible substance use should be considered in the transition process to adult health services.

What is already known on this topic

Adolescents with chronic medical disorders have a higher prevalence of mental health disorders than their peers, but the impact of mental health disorders on disease control prior to transfer to adult health care is poorly understood.

What this study adds

Adolescents with chronic medical disorders and comorbid psychiatric diagnoses more frequently have poor control of their medical condition than those without psychiatric comorbidities which highlights the necessity of a holistic approach to care.

How this study might affect research, practice, or policy

Ensuring that mental health disorders are identified and treated is an important aspect of caring for adolescents and young adults with chronic medical conditions, including at the time they transfer to adult services. Future research to measure the potential impact of adolescent mental health disorders on transfer to adult health service is indicated.

Introduction

The landscape of chronic illness in children and adolescents with chronic medical conditions has changed. Over the past few decades, treatment success has resulted in improved survival of many of these young people, which together with an increased incidence of particular chronic medical disorders in childhood,[1-3] results in increasing numbers of adolescents requiring regular follow-up in adult health services. Living with a chronic medical condition can pose many challenges during adolescence, not least due to the requirement for regular medication and other treatments, frequent medical appointments, and the uncertainty of future treatment such as surgical procedures. These demands for health management and monitoring, together with the impact of the medical condition itself, such as pain and fatigue,[4] can reduce participation in normative activities with effects on peer relationships, extracurricular participation and school attendance.[5]

Chronic medical conditions are associated with increased rates of mental health problems.[6,7] In the US, 25% of children with epilepsy have anxiety and/or depression compared with the general population of 12-17-year-olds of whom 6% have a current diagnosis of depression and 11% anxiety.[8,9] During a decade of follow-up, 17% of Swedish children with inflammatory bowel disease (IBD) received a diagnosis of any psychiatric disorder compared with 12% of the general population.[10] Beyond diagnostic studies in clinical samples, as population surveys that assess self-reported symptoms of depression or anxiety yield even higher proportions of affected young people, [11] the proportion of adolescents with chronic medical conditions who struggle with symptoms of mental health disorders is expected to be even higher.

Mental health problems, together with pain and fatigue,[4] can affect disease control, adherence behaviors, and health-related quality of life in children and adolescents with chronic medical

conditions,[12,13] but which young people are most at risk is incompletely understood. While depression is also associated with higher health care costs and emergency department visits in children and adolescents with IBD[14] whether this reflects more severe disease or poor disease control remains unknown.

Adolescents living with chronic medical conditions often engage in risk behaviors, such as substance use.[15] Substance use in adolescence is frequently associated with other mental health disorders, and the incidence of both substance use and mental health disorders increases across adolescence and into adulthood.[16,17,18] This accumulation of risk behaviors and mental health disorders among adolescents and young adults suggests it is important to identify which adolescents with chronic medical disorders are at greatest risk so that they can be appropriately managed, including at the time they transfer to adult health services.

In this study of adolescents with different chronic medical conditions, we aimed to investigate disease control, rates of psychiatric comorbidity and risky substance use and their associations before their care is transferred to adult health services. Our hypothesis was that psychiatric comorbidity is common and associated with poorer disease control and higher rates of substance use.

Methods

Study design

This study is part of an international prospective cohort study named the Bridge, for which the study protocol is available online.[19] In this cross-sectional analysis, we combined retrospective data with questionnaire responses from one study site. Fifteen adolescents with chronic conditions participated in the design of the study questionnaires.

Ethics

This study was approved by the Ethics Committee for Women's and Children's Health and Psychiatry at the Helsinki University Hospital (HUS/1547/2017). Participants gave informed consent to link their routine clinical data with individual questionnaire responses. The Bridge trial has been registered with ClinicalTrials.gov (ID number NCT04631965).

Participants

Participants were recruited from the New Children's Hospital, Helsinki, Finland (hospital catchment area 1.7 million inhabitants) between September 2017 and August 2019. In Finland, practically all adolescents with chronic medical conditions are managed by public health services, with few cared for by private doctors. Clinicians from six different pediatric subspecialty clinics (endocrinology, gastroenterology, rheumatology, nephrology and organ transplants, neurology, and cardiology) identified adolescents who were expected to transfer to adult clinics within the coming six to twelve months. Inclusion criteria were that participants were aged 15-24 years and had a chronic medical condition that had been diagnosed at least six months earlier and was expected to require regular follow-up in adult health services. Eligible participants also needed to have sufficient cognitive and linguistic ability to communicate in Finnish, English or Swedish. Adolescents received a movie ticket (value 10 EUR) after completing the survey in acknowledgement of their time.

A research nurse, uninvolved in patient care, personally met 306 consecutive adolescents during their routine hospital visits and provided oral and written information about the Bridge study.

Demographics

Background information was obtained from the baseline survey, including gender, residential area, home language and family composition (living with two parents or any other family type).

Disease control

To determine disease control, we gathered data and laboratory test results from the electronic medical records for the year preceding the final visit at the Children's Hospital. The final visit was specified as the out-patient appointment where the clinician made a formal referral to the respective adult health service. We divided participants into one of three categories according to the condition for which they were recruited: 1) good disease control and/or adherence; 2) some evidence of concern; and 3) poor disease control and/or adherence or more severe condition (see study protocol for further details).[19] Where appropriate, we used published cut-offs for disease control. For adolescents with diabetes, a mean glycosylated hemoglobin (the mean of all measurements across the year preceding transfer of care) ≤ 53 mmol/mol was categorized as good control/adherence, 54-69 mmol/mol was considered evidence of some concern while ≥ 70 mmol/mol was deemed poor control/adherence. For adolescents with rheumatic disease, the 10-joint Juvenile Arthritis Disease Activity Score (JADAS10) was completed. For those with oligoarthritis, cut-points of ≤ 0.5 (good), 0.6-2.8 (some concern) and > 2.8 (poor) were used, while for those with polyarthritis, the cut-points were ≤ 0.7, 0.8-4 and > 4, as previously applied.[19–21] For adolescents with IBD, good control/adherence required minimal pain (Visual analog scale, VAS 1-2), at least 80% of faecal calprotectin results <100 µg/g and always <300 µg/g, medication unchanged or reduced, and no inpatient care; indicators of some evidence of concern were VAS 3-5, < 80% of faecal calprotectin results within target range or exceeded 300 ug/g even once, but no significant medication changes nor inpatient care; and for poor control/adherence any of the following: VAS ≥ 6, significant changes in medication, need for corticosteroids and/or commencement of

biological medication or an episode of inpatient care. For rare conditions without standard criteria of disease control and/or adherence, experienced clinicians subjectively categorized participants according to their symptoms, clinical and laboratory findings, need for inpatient care, and changes in medication. MK first reviewed medical records of every participant, of whom 28 (11%) were difficult to categorize. For these 28 adolescents, SK made an independent assessment of disease control. Six adolescents were categorized differently, and the final grading was based on consensus between the two reviewers. For some analyses we combined the three smallest subspecialties (neurology, cardiology, and nephrology/organ transplant) into "others".

Psychiatric diagnosis and treatment

Psychiatric diagnoses and treatment details were collected from the electronic medical records of the Helsinki University Hospital which is the only public provider of adolescent psychiatric care in the study catchment area. Data were collected from ages 13 to 18, the age range of adolescent psychiatry in the study area. These data were collected separately from the disease control data, and in a different order of patients. Psychiatric diagnoses were divided into four categories: 1) mood disorders; 2) anxiety disorders; 3) others; and 4) multiple diagnoses (i.e., diagnosis from at least two different diagnostic categories). The New Children's Hospital has no general guideline regarding psychiatric assessment and adolescents may have received referrals to adolescent psychiatry from community healthcare centers and student health services. Outpatient appointments with mental health professionals over these six years were divided into three categories: 1) no appointments; 2) one to three appointments; and 3) more than three appointments. We also recorded the age at first psychiatric diagnosis, any admissions for psychiatric inpatient care and, if so, the number of days spent in psychiatric inpatient care.

Substance use

Participants completed the Adolescent Substance Use Measurement (ADSUME), a brief measure that was developed and validated in Finland to evaluate adolescent substance use and its possible consequences during the previous year. ADSUME is reliable when compared to validated adult questionnaires (AUDIT, CRAFFT) and may even be superior in detecting hazardous substance use among adolescents.[22] Certainly, survey data is more reliable than what adolescents share with health professionals.[23] We calculated a total score (0-31 points) of the first nine questions (appendix 1) to yield a numeric score which we used in analyses. We also divided participants into subgroups according to guidelines from the Finnish Institute for Health and Welfare: 1) abstinence or experimental use, 0-3 points; 2) recurring use, 4-6 points; 3) risky use, 7-9 points; and 4) hazardous use, 10 points or more.[24]

Data analysis

Categorical data are presented as frequencies (with percentages). For continuous variables, means and standard deviations (SDs) or medians (with interquartile range) are used. Associations between disease control, psychiatric diagnoses, and family composition were compared using Fisher's exact test (two-sided). To evaluate the associations between categorical data and continuous variables we used non-parametric tests (Mann-Whitney U and Kruskal-Wallis). Data analyses were performed using IBM SPSS Statistics 25 (IBM, Somers, NY) and a p-value < 0.05 was considered significant.

Results

In total, 279 (91.2%) adolescents consented to participate, and 253 (82.7%) adolescents completed the baseline survey after a maximum of two reminders. Demographic and clinical data of the 253 study participants are summarized in Tables 1 and 2. The mean age at

diagnosis of the medical condition was 9.0 years (SD 5.3) and the mean age at first psychiatric diagnosis was 13.7 years (SD 2.7). Age at transfer differed greatly between subspecialties: rheumatology patients were the youngest to transfer (mean age 16.2 years) and gastroenterology were the oldest (mean age 19.0 years; p<0.001 for difference between groups).

Table 1. Demographic and clinical data of 253 adolescents.

Sex	**N**	**%**
Male	118	46.6
Female	132	52.2
Other	3	1.2
Pediatric subspecialty		
Diabetes	92	36.4
Rheumatology	66	26.1
Gastroenterology	45	17.8
Cardiology	19	7.5
Neurology	18	7.1
Kidney or liver disease with/without transplant	13	5.1
Lives with		
Mother and father	158	62.5
Other than with two parents	95	37.5
Disease control *		
Good control and/or adherence	70	27.7
Some evidence of concern	105	41.5
Poor control and/or adherence or more severe condition	76	30.0
Psychiatric diagnoses	**59**	**23.3**
Anxiety disorders	38	15.0
Mood disorders	18	7.1
Others **	26	10.3
Many diagnoses	22	8.7
Outpatient visits in adolescent psychiatry		
No visits	159	62.8
1-3 visits	36	14.2
More than 3 visits	58	22.9
Median ADSUME total scores (IQR) * **	**3**	**(0-6)**
Females	2	(0-6)
Males	3	(0-6)

ADSUME risk category ***	N	%
Abstinence or experimental use (0-3 points)	142	56.1
Recurring use (4-6 p)	57	22.5
Risky use (7-9 p)	27	10.7
Hazardous use (10 p or more)	26	10.3

*Data available for 251 adolescents as transfer of two adolescents was delayed.
** Others: for example, conduct disorder, attention deficit-hyperactivity disorder, psychotic disorder, eating disorders, developmental disorders.
*** One response missing.
ADSUME = Adolescent`s Substance Use Measurement; IQR = interquartile range

Table 2. Demographic and clinical data (n=253).

	Mean, years (median)	SD
Age at first medical diagnosis	**9.0 (10.1)**	**5.3**
Age at first psychiatric diagnosis	**13.7 (14.3)**	**2.7**
Age when completing the ADSUME	**17.2 (16.8)**	**1.2**
Age at transfer of care	**17.3 (17.1)**	**1.2**
Diabetes	17.2	0.7
Rheumatology	16.2	0.5
Gastroenterology	19.0	0.9
Others	17.8	1.2
Time between ADSUME and transfer of care	**0.2 (0.0)**	**0.4**
Time between medical diagnosis and transfer of care	**8.3 (7.4)**	**8.3**
Time between psychiatric diagnosis and transfer of care	**4.0 (3.2)**	**4.0**

ADSUME = Adolescent`s Substance Use Measurement

Among all study participants, 27.7% (n=70) were categorized as having good disease control and/or adherence, 41.5% (n=105) were rated as having some evidence of concern, and 30.0% (n=76) were deemed to have poor disease control and/or adherence (or more severe condition) during the year preceding the transfer of care. Only 16% of adolescents with gastroenterological diseases and 14% of adolescents with diabetes had good disease control (mean of 4.6 measurements). Among adolescents with rheumatological disease, 39% had good disease control, while it was 48% in the group of "others". Gender showed no association with different disease control groups (p=0.58) and neither did the age at diagnosis (p=0.88). Older age at transfer of care was associated with poorer disease control (p=0.045).

In this cohort, 23.3% of adolescents (n=59) had a psychiatric diagnosis, of whom 37.2% (n=22) had at least two different diagnoses. Anxiety disorders were most common (n=38), comprising 15.0% of all participants and 64.4% of adolescents with a psychiatric diagnosis. Females were overrepresented in anxiety disorders and males in the 'other psychiatric diagnosis' group. Adolescents with diabetes had more psychiatric diagnoses (28.3% vs 20.5%; p=0.12) and more often had at least one outpatient visit in adolescent psychiatry (44.6 % vs 32.9%; p= 0.08) than adolescents with other conditions, although these differences did not reach statistical significance. Nine adolescents (3.6%) received inpatient psychiatric care, with a median of 22 days (range 9-956 days) per person. Age at medical diagnosis and age at psychiatric diagnosis showed no association (p=0.32).

More than half of participants (n=142, 56.1%) were abstinent or reported only experimental substance use (Tables 1 and 3). Twenty-nine participants (11.5%) used nicotine products with eleven (4.3%) using them daily. Approximately half of the adolescents reported using alcohol in the last year. The median ADSUME total score was 3.0 and the maximum score was 27 points.

Table 3. Details of adolescent substance use in the past year (n=252*).

	N	%
Substance use		
Nicotine products	**29**	11.5
Alcohol	**131**	52
Abuse of medications	**3**	1.2
Cannabis	**3**	1.2
Missed school because of substance use	**5**	2
Risk behavior while intoxicated		
Hurt herself/himself	**10**	4
Hurt someone else	**5**	2
Drove a car	**3**	1.2
Passenger in a car with intoxicated driver	**3**	1.2
Had sex that regretted afterwards	**8**	3.2

* One response missing

Table 4 and Figure 1 summarize the associations between disease control, psychiatric diagnoses, substance use and family composition. Adolescents with psychiatric diagnoses more often had poor disease control and/or adherence or more severe disease/condition than adolescents without psychiatric diagnoses (p=0.01). Hazardous substance use was more frequent among adolescents with psychiatric diagnoses (8% vs 19%), but total ADSUME points showed no direct association with psychiatric diagnoses nor disease control. Adolescents who lived with two parents (n=158, 62.5%) had significantly fewer psychiatric diagnoses than adolescents living in other kinds of families (p = 0.05).

Table 4. Family composition, disease control and substance use, by psychiatric diagnosis (n=253).

	No psychiatric diagnosis (n=194) N (%)	**Psychiatric diagnosis (n=59)** N (%)	**p**

Living with two parents	128 (66)	30 (51)	**0.05**
Disease control *			
Good control and/or adherence	59 (30)	11 (19)	0.13
Some evidence of concern	84 (43)	21 (37)	0.45
Poor control and/or adherence or more severe condition	51 (26)	25 (44)	**0.01**
ADSUME score, median (IQR) **	3 (0-6)	0 (0-6)	0.56

*Transfer of two adolescents has been delayed.

** One response missing.

Other factors compared using Fisher's exact test, ADSUME median scores compared using the Mann-Whitney U test.

Discussion

In this cross-sectional study of adolescents with chronic medical disorders, nearly a third were assessed to have poor disease control in the year preceding transfer to adult health services and almost a quarter had received a psychiatric diagnosis during adolescence. Adolescents with a comorbid psychiatric diagnosis more frequently had poor control of their medical condition than those without a psychiatric diagnosis.

Surprisingly, only 27.7% of the study cohort were deemed to have good disease control and/or adherence of their medical condition. The proportion of adolescents with good disease control was lowest among adolescents with diabetes and IBD. This may reflect the availability of laboratory measures of adherence for these conditions. It may also depict stringent threshold values, especially in diabetes.[21] Optimizing health outcomes is important in all patients. However, additional strategies may be required in adolescents before transfer to adult health services, especially in those whose disease is challenging to treat, who lack motivation or skills for self-management, or have mental health or substance use problems.[25,26]

Most studies of mental health in adolescents with chronic medical conditions use self-report surveys to assess prevalence rather than data on psychiatric diagnoses following referral, as in our study. Regular assessment by medical professionals might have contributed to unnecessary referrals aided by the relative ease of referral to public mental health professionals. Certainly, 23% of adolescents receiving a mental health diagnosis between the ages of 13 and 18 is higher than in other diagnostic studies.[8,10] However, as the portion of adolescents with three or more outpatient visits in the department of adolescent psychiatry is almost the same as the proportion of adolescents with a psychiatric diagnosis, overdiagnosis seems unlikely.

Adolescents living with two parents had fewer psychiatric diagnoses than their peers living in other kinds of families. This finding has also been reported among the general population of children and adolescents.[27,28] As a child's illness is a significant stressor for parents,[29] family psychosocial supports and interventions to minimize financial hardship also warrant consideration.

The association between poor disease control and psychiatric comorbidity may be bidirectional: living with a severe disease may increase the emotional burden experienced, while mental health problems may affect self-management resources and thus worsen disease control. The treatment of anxiety and depression in adolescents is expected to improve symptoms and positively influence disease control and health care utilization.[30-32] Regardless of direction of association, the presence of mental health problems are relevant to the transition process as some adolescents will need concurrent transition of psychiatric and medical care.

Although alcohol consumption has decreased among adolescents in many developed countries, adolescent binge drinking and the accompanying risky behavior remain significant

public health problems.[33] In this study, 22.5% of adolescents with chronic medical conditions reported using substances regularly while a further 21.0% were categorized as risky or hazardous users. This is consistent with national Finnish data that found 15-24% of 17-18-year-old students reported monthly binge drinking.[34] Although different recruitment and assessment methods were used, our findings are also similar to a US study of 14-18-yr-old adolescents attending routine health care in which 18% had substance use problems and 16% had substance use disorders.[16] Conversely, only 1% of adolescents in our cohort had used cannabis during the past year, in comparison to 8-12% of 17-18-yr-old students in Finland.[34] These data affirm the importance of regularly discussing substance use and its effects with adolescents with chronic medical conditions especially given its potential effect on specific medical conditions, such as a reduced seizure threshold in adolescents with epilepsy or hypoglycemia in adolescents with diabetes.[35,36]

A strength of this study is the high response rate of adolescents recruited from six different hospital departments to intentionally span a range of conditions, increasing the generalizability of our results. However, this also provided some challenges, especially regarding how disease control was defined as by definition this differs by medical condition. Although the same researcher collected data on disease control and psychiatric diagnoses, we attempted to reduce bias by collecting these data on separate occasions, using separate files, and in different patient order. While we needed to categorize disease control subjectively in adolescents with rare diseases, the likelihood of misclassification was reduced by having two independent reviewers. As we had access to all electronic medical records in the study catchment area, including psychiatry, we were able to use specific psychiatric diagnoses and estimate disease control of medical conditions based on clinical and laboratory findings. While psychiatric diagnoses were made by the psychiatry department, standardized assessments were not routinely used. Further, some psychiatric diagnoses may have been

missed if the adolescent had moved to or from another hospital district. A further strength of this study is that the public health system in Finland results in adolescents receiving the same treatment regardless of socioeconomic status, with provision of psychiatric care in the private sector uncommon. In countries without public health care, associations between mental health problems and poor disease control may be even more significant. Multivariate analyses were not performed because no significant differences were found in appropriate variables in independent analyses.

Conclusions

In conclusion, psychiatric morbidity and poor disease control of chronic medical conditions are prevalent and closely intertwined among adolescents, reinforcing the importance of collaboration between medical and psychiatric care.[37] Identifying and treating mental disorders in adolescents with medical conditions could be viewed as an investment in quality of life, education, and employment as well as a way of reducing the long-term costs of health care. Maximizing mental health before adolescents transfer to adult health services appears especially important given the associations of both poor mental health and the transfer of care itself with unsatisfactory adherence to treatment and increased rates of emergency visits and hospitalizations. [12,38,39]

A Funding statement:

This study is supported by grants from the Foundation for Medical Research, the Helsinki University Hospital (TYH2019312), the Foundation for Pediatric Research and the Paulo Foundation.

A competing interest statement:

Authors have no conflicts of interest relevant to this article to disclose.

Contributor`s Statement:

Dr Mira Kallio collected data, carried out initial analyses, drafted the manuscript and reviewed and revised the manuscript. Ms Tornivuori collected data and reviewed and revised the manuscript. Drs Miettinen and Kolho participated in designing the study and reviewed and revised the manuscript. Ms Culnane and Professor Sawyer participated in study design and reviewed and revised the manuscript. Dr Kosola designed the study, coordinated, and supervised data collection and critically reviewed the manuscript for important intellectual content. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

Checklist: STROBE.

Data sharing statement: Data are available upon reasonable request.

Acknowledgments: We wish to thank all the participants of the study as well as research nurse Satu Lindström. We also acknowledge Kristiina Aalto, Eero Jokinen, Eeva-Liisa Metsähonkala, Tiina Remes and Elisa Ylinen for clinical advice regarding disease control.

References

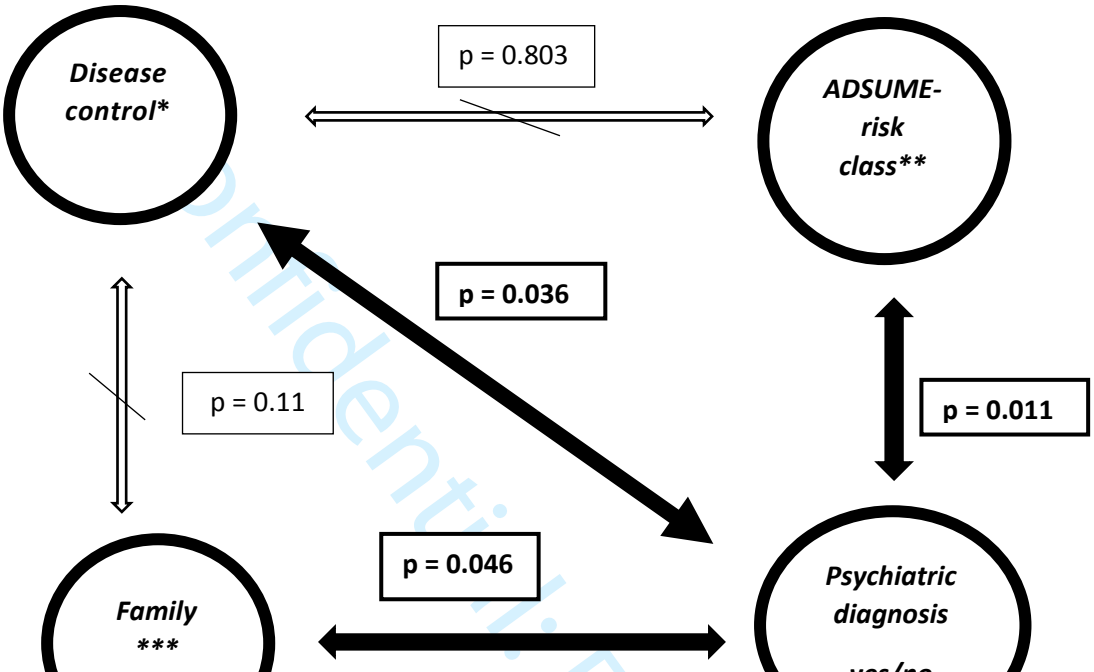
1. Raissadati A, Nieminen H, Jokinen E, Sairanen H. Progress in late results among pediatric cardiac surgery patients: A population-based 6-decade study with 98% follow-up. *Circulation.* 2015;131(4):347-353. doi:10.1161/CIRCULATIONAHA.114.011190
2. Benchimol EI, Fortinsky KJ, Gozdyra P, Van Den Heuvel M, Van Limbergen J, Griffiths AM. Epidemiology of pediatric inflammatory bowel disease: A systematic review of international trends. *Inflamm Bowel Dis.* 2011;17(1):423-429. doi:10.1002/ibd.21349
3. Patterson CC, Karuranga S, Salpea P, et al. Worldwide estimates of incidence, prevalence, and mortality of type 1 diabetes in children and adolescents: Results from the International Diabetes Federation Diabetes Atlas, 9th edition. *Diabetes Res Clin Pract.* 2019;157:107842. doi:10.1016/j.diabres.2019.107842

4. Nap-van der Vlist MM, Dalmeijer GW, Grootenhuis MA, et al. Fatigue in childhood chronic disease. *Arch Dis Child*. 2019;104(11):1090-1095. doi:10.1136/archdischild-2019-316782
5. Maes M, Van Den Noortgate W, Fustolo-Gunnink SF, Rassart J, Luyckx K, Goossens L. Loneliness in Children and Adolescents with Chronic Physical Conditions: A Meta-Analysis. *J Pediatr Psychol.* 2017;42(6) :622-635. doi:10.1093/jpepsy/jsx046
6. Brady AM, Deighton J, Stansfeld S. Psychiatric outcomes associated with chronic illness in adolescence: A systematic review. *J Adolesc.* 2017;59:112-123. doi:10.1016/j.adolescence.2017.05.014
7. Robinson ME, Simard M, Larocque I, Shah J, Nakhla M, Rahme E. Risk of psychiatric disorders and suicide attempts in emerging adults with diabetes. *Diabetes Care.* 2020;43(2):484-486. doi:10.2337/dc19-1487
8. LaGrant B, Marquis BO, Berg AT, Grinspan ZM. Depression and anxiety in children with epilepsy and other chronic health conditions: National estimates of prevalence and risk factors. *Epilepsy Behav*. 2020;103 (Pt A):106828. doi:10.1016/j.yebeh.2019.106828
9. Ghandour RM, Sherman LJ, Vladutiu CJ, et al. Prevalence and Treatment of Depression, Anxiety, and Conduct Problems in US Children. *J Pediatr*. 2019;206:256-267.e3. doi:10.1016/j.jpeds.2018.09.021
10. Butwicka A, Olén O, Larsson H, et al. Association of Childhood-Onset Inflammatory Bowel Disease with Risk of Psychiatric Disorders and Suicide Attempt. *JAMA Pediatr.* 2019;173(10):969-978. doi:10.1001/jamapediatrics.2019.2662
11. Finnish Institute for Health and Welfare. Well-being of children and young people – School Health Promotion Study 2021. Available at: https://thl.fi/en/web/thlfi-en/statistics-and-data/statistics-by-topic/social-services-children-adolescents-and-families/well-being-of-children-and-young-people-school-health-promotion-study
12. Bernstein CM, Stockwell MS, Gallagher MP, Rosenthal SL, Soren K. Mental health issues in adolescents and young adults with type 1 diabetes: Prevalence and impact on glycemic control. *Clin Pediatr (Phila).* 2013;52(1):10-15. doi:10.1177/0009922812459950
13. Blount RL. Disease Activity Does Not Explain It All: How Internalizing Symptoms and Caregiver Depressive Symptoms Relate to Health-related Quality of Life Among Youth with Inflammatory Bowel Disease. *Inflamm Bowel Dis*. 2016;22(4):963-967. doi:10.1097/MIB.0000000000000686
14. Wong JJ, Sceats L, Dehghan M, et al. Depression and health care use in patients with inflammatory bowel disease. *J Crohn's Colitis.* 2019;13(1):19-26. doi:10.1093/ecco-jcc/jjy145
15. Sawyer SM, Drew S, Yeo MS, Britto MT. Adolescents with a chronic condition: challenges living, challenges treating. *Lancet.* 2007;369(9571):1481-1489. doi:10.1016/S0140-6736(07)60370-5
16. Shrier LA, Harris SK, Kurland M, Knight JR. Substance use problems and associated psychiatric symptoms among adolescents in primary care. *Pediatrics.* 2003;111(6 Pt 1):e699-e705. doi:10.1542/peds.111.6.e699
17. Deas D. Adolescent substance abuse and psychiatric comorbidities. *J Clin Psychiatry.* 2006;67 (7):e02. doi:10.4088/jcp.0706e02
18. Kessler RC, Berglund P, Demler O, Jin R, Merikangas KR, Walters EE. Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the national comorbidity survey replication. *Arch Gen Psychiatry.* 2005;62(6):593-602. doi:10.1001/archpsyc.62.6.593

19. Kosola Silja, Culnane Evelyn, Loftus Hayley, et al. The Bridge study protocol: an international, observational cohort study on the transition of healthcare for adolescents with chronic conditions. *BMJ Open.* 2021;11(6):e048340. Published 2021 Jun 21. doi:10.1136/bmjopen-2020-048340
20. Backström M, Tynjälä P, Ylijoki H, et al. Finding specific 10-joint Juvenile Arthritis Disease Activity Score (JADAS10) and clinical JADAS10 cut-off values for disease activity levels in non-systemic juvenile idiopathic arthritis: A Finnish multicentre study. *Rheumatology (Oxford).* 2016;55(4):615-623. doi:10.1093/rheumatology/kev353
21. DiMeglio LA, Acerini CL, Codner E, et al. ISPAD Clinical Practice Consensus Guidelines 2018: Glycemic control targets and glucose monitoring for children, adolescents, and young adults with diabetes. *Pediatr Diabetes.* 2018;19 Suppl 27:105-114. doi:10.1111/pedi.12737
22. Piskanen M. Promoting Adolescents` Abstinence from Substance Use. An Early Intervention Model for School and Student Health Care. Published online 2007. http://urn.fi/URN:ISBN:978-951-27-0510-8
23. Gryczynski J, Mitchell SG, Schwartz RP, et al. Disclosure of Adolescent Substance Use in Primary Care: Comparison of Routine Clinical Screening and Anonymous Research Interviews. *J Adolesc Health.* 2019;64(4):541-543. doi:10.1016/j.jadohealth.2018.10.009
24. Pirskanen M, Laukkanen E, Pietilä AM. A formative evaluation to develop a school health nursing early intervention model for adolescent substance use. *Public Health Nurs.* 2007;24(3):256-264. doi:10.1111/j.1525-1446.2007.00632.x
25. Andrade DM, Bassett AS, Bercovici E, et al. Epilepsy: Transition from pediatric to adult care. Recommendations of the Ontario epilepsy implementation task force. *Epilepsia.* 2017;58(9):1502-1517. doi:10.1111/epi.13832
26. Healy SA, Fantaneanu TA, Whiting S. The importance of mental health in improving quality of life in transition-aged patients with epilepsy. Epilepsy Behav. 2020;112:107324. doi:10.1016/j.yebeh.2020.107324
27. Ängarne-Lindberg T, Wadsby M. Psychiatric and somatic health in relation to experience of parental divorce in childhood. Int J Soc Psychiatry. 2012;58(1):16-25. doi:10.1177/0020764010382372
28. Perales F, Johnson SE, Baxter J, Lawrence D, Zubrick SR. Family structure and childhood mental disorders: new findings from Australia. Soc Psychiatry Psychiatr Epidemiol. 2017;52(4):423-433. doi:10.1007/s00127-016-1328-y
29. Mutanen A, Kosola S, Merras-Salmio L, Kolho KL, Pakarinen MP. Long-term health-related quality of life of patients with pediatric onset intestinal failure. J Pediatr Surg. 2015;50(11). doi:10.1016/j.jpedsurg.2015.05.012
30. Bennett S, Shafran R, Coughtrey A, Walker S, Heyman I. Psychological interventions for mental health disorders in children with chronic physical illness: A systematic review. *Arch Dis Child.* 2015;100(4):308-316. doi:10.1136/archdischild-2014-307474
31. Thabrew H, Stasiak K, Hetrick SE, Wong S, Huss JH, Merry SN. E-Health interventions for anxiety and depression in children and adolescents with long-term physical conditions. *Cochrane Database Syst Rev*. 2018;8(8):CD012489. Published 2018 Aug 15. doi:10.1002/14651858.CD012489.pub2
32. Lehtimaki S, Martic J, Wahl B, Foster KT, Schwalbe N. Evidence on Digital Mental Health Interventions for Adolescents and Young People: Systematic Overview. *JMIR Ment Health*. 2021;8(4):e25847. Published 2021 Apr 29. doi:10.2196/25847
33. Siqueira L, Smith VC; COMMITTEE ON SUBSTANCE ABUSE. Binge Drinking. *Pediatrics.* 2015;136(3):e718-e726. doi:10.1542/peds.2015-2337

34. Helakorpi S, Kivimaki H. Well-being of children and young people – School Health Promotion study 2021: Large share of children and young people satisfied with their lives – a sense of loneliness has become more common. Statistical report 42/2021, National Institute for Health and Welfare, Finland. Available at https://www.julkari.fi/handle/10024/143418 . Downloaded Sep 6, 2022.
35. Samokhvalov AV, Irving H, Mohapatra S, Rehm J. Alcohol consumption, unprovoked seizures, and epilepsy: a systematic review and meta-analysis. *Epilepsia*. 2010;51(7):1177-1184. doi:10.1111/j.1528-1167.2009.02426.x
36. Tetzschner R, Nørgaard K, Ranjan A. Effects of alcohol on plasma glucose and prevention of alcohol-induced hypoglycemia in type 1 diabetes-A systematic review with GRADE. *Diabetes Metab Res Rev*. 2018;34(3):10.1002/dmrr.2965. doi:10.1002/dmrr.2965
37. Fazel M, Townsend A, Stewart H, Pao M, Paz I, Walker J, Sawyer S.M, Sharpe M. Integrated care to address child and adolescent health in the 21st century: A clinical review. *JCPP Advances*.2021;e12045. doi:10.1002/jcv2.12045
38. Kosola S, Ylinen E, Finne P, Rönnholm K, Ortiz F. Implementation of a transition model to adult care may not be enough to improve results: National study of kidney transplant recipients. Clin Transplant. 2019;33(1):e13449. doi:10.1111/ctr.13449
39. Rollo A, Salardi S, Ciavarella A, et al. Transition from pediatric to adult care. Eight years after the transition from pediatric to adult diabetes care: Metabolic control, complications and associated diseases. J Endocrinol Invest. 2014;37(7):653-659. doi:10.1007/s40618-014-0090-9

Figure 1. Associations between disease control, psychiatric diagnoses, substance use (ADSUME) and family composition. P < 0.05 is considered significant.



* Good control and/or adherence, some evidence of concern or poor control and/or adherence or more severe condition

** Abstinence or experimental use, repetitive use, risky use, or hazardous use

*** Living with mother and father or with someone else (for example with only one parent, mixed family or any other third party)

Appendix 1. Adolescents Substance Use Measurement (ADSUME)

1. Do you smoke (including tobacco, cannabis and e-cigarettes)?
    a. No
    b. Occasionally
    c. Daily
2. Have you tried or used following substances during the past year? (If not, there is no need to answer the next questions)
    a. Alcohol
    b. Medication to get high
    c. Illegal drugs
    d. Alcohol together with other substances
    e. Inhaled chemicals `sniffing`
3. How many times have you tried or used other substances than tobacco during last year?
    a. 1-3 times
    b. 4-6 times
    c. about once in a month
    d. 2-3 times per month
    e. once a week or more often
4. How many drinks do you usually have at a time?
    a. 1-2 drinks
    b. 3-4 drinks
    c. 5-6 drinks
    d. 7 drinks or more
5. Have you ever been late to school or work, left in the middle of the day or stayed home from school or work because of substance use?
    a. Never
    b. Once
    c. 2-3 times
    d. 4 or more times
6. Have you encountered any of these situations when you have been under the influence of alcohol or drugs during the past year?
    a. I have hurt myself or someone else has hurt me
    b. I have hurt someone else
    c. I have been a passenger in a vehicle with a driver who was under the influence
    d. I have driven a vehicle under the influence
    e. I have broken or stolen someone else's property
    f. I have had a sexual relationship that I regret afterwards
7. How often have you been in these situations (described before)?
    a. Once
    b. Twice
    c. More Often
8. Have you ever had a blackout (i.e., trouble remembering what happened due to substance use)?
    a. Once
    b. Twice
    c. More Often
9. Have you ever passed out because of substance use?
    a. Once
    b. Twice
    c. More Often

BMJ Paediatrics Open

Disease control and psychiatric comorbidity among adolescents with chronic medical conditions - a single centre retrospective study

Journal:	*BMJ Paediatrics Open*
Manuscript ID	bmjpo-2022-001605.R2
Article Type:	Original research
Date Submitted by the Author:	15-Nov-2022
Complete List of Authors:	Kallio, Mira; University of Helsinki Faculty of Medicine, Department of Pediatrics Tornivuori, Anna; Turun yliopisto Miettinen, Päivi; University of Helsinki Faculty of Medicine, Department of Pediatrics Kolho, kaija-Leena; University of Helsinki Faculty of Medicine, Department of Pediatrics Culnane, Evelyn; The Royal Children's Hospital Melbourne Sawyer, Susan; The Royal Children's Hospital Melbourne Kosola, Silja; University of Helsinki Faculty of Medicine
Keywords:	Adolescent Health, Gastroenterology, Neurology, Rheumatology, Endocrinology

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

Disease control and psychiatric comorbidity among adolescents with chronic medical conditions – a single center retrospective study

Kallio Mira [a,c], Tornivuori Anna [a,b], Miettinen Päivi J. [a,c], Kolho Kaija-Leena [a,c,d], Culnane Evelyn [e], Sawyer Susan M [f,g,h] Kosola Silja [a,c]

Affiliations: [a] Department of Pediatrics, Helsinki University Hospital and University of Helsinki, Helsinki, Finland; [b] Nursing Science of University of Turku, Turku, Finland; [c] Pediatric Research Center, Helsinki University Hospital and University of Helsinki, Helsinki, Finland; [d] Faculty of Medicine and Health Technology, Tampere University, Tampere, Finland; [e] Transition Support Service, The Royal Children's Hospital, Melbourne, Australia; [f] Centre for Adolescent Health, Royal Children's Hospital, Melbourne, Australia; [g] Murdoch Children's Research Institute, Melbourne, Australia; [h] Department of Paediatrics, The University of Melbourne, Australia.

Address correspondence to: Mira Kallio, Department of Pediatrics, University of Helsinki, Biomedicum 6, Haartmaninkatu 8, 00290 Helsinki, [mira.kallio@hus.fi], +35840 778 5221.

Clinical Trial registration: Trial registration name The Bridge and registration number NCT04631965 (https://clinicaltrials.gov/ct2/show/NCT04631965).

Data Sharing Statement: Data are available upon reasonable request.

Word count: 2797

Abstract

Background

To investigate disease control, psychiatric comorbidity, substance use and their possible associations in adolescents with chronic medical conditions before transfer to adult health care.

Methods

We collected clinical data from the year preceding transfer of care and psychiatric data from the records of the paediatric hospital in Helsinki, Finland (population base 1.7 million). Participants were grouped into three disease and/or adherence control categories (good, some evidence of concern, poor) based on clinical data from the medical records of the year preceding the transfer of care. Participants completed the Adolescent`s Substance Use Measurement questionnaire before transfer of care and were divided into four risk subgroups accordingly.

Results

In total, 253 adolescents (mean age 17.3 years, SD 1.2) from six pediatric subspecialties participated in this study. Disease control and/or adherence were rated as good in 28% (n=70), moderate in 42% (n=105) and poor in 30% (n=76) in the year before participants transferred to adult health services. A quarter of participants had at least one psychiatric diagnosis during adolescence. Adolescents with concomitant psychiatric diagnoses more often had poor disease control of their chronic medical condition than adolescents with only a medical condition 44% vs 26% (n=25/59 vs 51/194, respectively). More than half of adolescents (56%) were abstinent or used substances infrequently; 10% (n=26) reported hazardous substance use.

Conclusions

Psychiatric comorbidity in adolescents with chronic medical conditions is common. Its negative association with disease control and possible substance use should be considered in the transition process to adult health services.

What is already known on this topic

Adolescents with chronic medical disorders have a higher prevalence of mental health disorders than their peers, but the impact of mental health disorders on disease control prior to transfer to adult health care is poorly understood.

What this study adds

Adolescents with chronic medical disorders and comorbid psychiatric diagnoses more frequently have poor control of their medical condition than those without psychiatric comorbidities which highlights the necessity of a holistic approach to care.

How this study might affect research, practice, or policy

Ensuring that mental health disorders are identified and treated is an important aspect of caring for adolescents and young adults with chronic medical conditions, including at the time they transfer to adult services. Future research to measure the potential impact of adolescent mental health disorders on transfer to adult health service is indicated.

Introduction

The landscape of chronic illness in children and adolescents with chronic medical conditions has changed. Over the past few decades, treatment success has resulted in improved survival of many of these young people, which together with an increased incidence of particular chronic medical disorders in childhood,[1-3] results in increasing numbers of adolescents requiring regular follow-up in adult health services. Living with a chronic medical condition can pose many challenges during adolescence, not least due to the requirement for regular medication and other treatments, frequent medical appointments, and the uncertainty of future treatment such as surgical procedures. These demands for health management and monitoring, together with the impact of the medical condition itself, such as pain and fatigue,[4] can reduce participation in normative activities with effects on peer relationships, extracurricular participation and school attendance.[5]

Chronic medical conditions are associated with increased rates of mental health problems.[6,7] In the US, 25% of children with epilepsy have anxiety and/or depression compared with the general population of 12-17-year-olds of whom 6% have a current diagnosis of depression and 11% anxiety.[8,9] During a decade of follow-up, 17% of Swedish children with inflammatory bowel disease (IBD) received a diagnosis of any psychiatric disorder compared with 12% of the general population.[10] Population surveys that assess self-reported symptoms of depression or anxiety yield even higher proportions of affected young people. [11] So the proportion of adolescents with chronic medical conditions who struggle with symptoms of mental health disorders is expected to be even higher.

Mental health problems, together with pain and fatigue,[4] can affect disease control, adherence behaviors, and health-related quality of life in children and adolescents with chronic medical conditions. [12,13] For example, depression is associated with higher health care costs and

emergency department visits in children and adolescents with IBD [14], but which young people are most at risk is still incompletely understood.

Adolescents living with chronic medical conditions often engage in risk behaviors, such as substance use.[15] Substance use in adolescence is frequently associated with other mental health disorders, and the incidence of both substance use and mental health disorders increases across adolescence and into adulthood.[16,17,18] This accumulation of risk behaviors and mental health disorders among adolescents and young adults suggests it is important to identify which adolescents with chronic medical disorders are at greatest risk so that they can be appropriately managed, including at the time they transfer to adult health services.

In this study of adolescents with different chronic medical conditions, we aimed to investigate disease control, rates of psychiatric comorbidity and risky substance use and their associations before adolescent care is transferred to adult health services. Our hypothesis was that psychiatric comorbidity is common and associated with poorer disease control and higher rates of substance use.

Methods

Study design

This study is part of an international prospective cohort study named the Bridge, for which the study protocol is available online.[19] In this cross-sectional analysis, we combined retrospective data with questionnaire responses from one study site. Fifteen adolescents with chronic conditions participated in the design of the study questionnaires.

Ethics

This study was approved by the Ethics Committee for Women's and Children's Health and Psychiatry at the Helsinki University Hospital (HUS/1547/2017). Participants gave informed consent to link their routine clinical data with individual questionnaire responses. The Bridge trial has been registered with ClinicalTrials.gov (ID number NCT04631965).

Participants

Participants were recruited from the New Children's Hospital, Helsinki, Finland (hospital catchment area 1.7 million inhabitants) between September 2017 and August 2019. In Finland, practically all adolescents with chronic medical conditions are managed by public health services, with few cared for by private doctors. Clinicians from six different pediatric subspecialty clinics (endocrinology, gastroenterology, rheumatology, nephrology and organ transplants, neurology, and cardiology) identified adolescents who were expected to transfer to adult clinics within the coming six to twelve months. Inclusion criteria were that participants were aged 15-24 years and had a chronic medical condition that had been diagnosed at least six months earlier and was expected to require regular follow-up in adult health services. Eligible participants also needed to have sufficient cognitive and linguistic ability to communicate in Finnish, English or Swedish. Adolescents received a movie ticket (value 10 EUR) after completing the survey in acknowledgement of their time.

A research nurse, uninvolved in patient care, personally met 306 consecutive adolescents during their routine hospital visits and provided oral and written information about the Bridge study.

Demographics

Background information was obtained from the baseline survey, including gender, residential area, home language and family composition (living with two parents or any other family type).

Disease control

To determine disease control, we gathered data and laboratory test results from the electronic medical records for the year preceding the final visit at the New Children's Hospital. The final visit was specified as the out-patient appointment where the clinician made a formal referral to the respective adult health service. We divided participants into one of three categories according to the condition for which they were recruited: 1) good disease control and/or adherence; 2) some evidence of concern; and 3) poor disease control and/or adherence or more severe condition (see study protocol for further details).[19] Where appropriate, we used published cut-offs for disease control. For adolescents with diabetes, a mean glycosylated hemoglobin (the mean of all measurements across the year preceding transfer of care) ≤ 53 mmol/mol was categorized as good control/adherence, 54-69 mmol/mol was considered evidence of some concern while ≥ 70 mmol/mol were classified as having poor control/adherence. For adolescents with rheumatic disease, the 10-joint Juvenile Arthritis Disease Activity Score (JADAS10) was completed. For those with oligoarthritis, cut-points of ≤ 0.5 (good), 0.6-2.8 (some concern) and > 2.8 (poor) were used, while for those with polyarthritis, the cut-points were ≤ 0.7, 0.8-4 and > 4, as previously applied.[19–21] For adolescents with IBD, good control/adherence required minimal pain (Visual analog scale, VAS 1-2), at least 80% of faecal calprotectin results <100 µg/g and always <300 µg/g, medication unchanged or reduced, and no inpatient care; indicators of some evidence of concern were VAS 3-5, < 80% of faecal calprotectin results within target range or exceeded 300 ug/g even once, but no significant medication changes nor inpatient care; and for poor control/adherence any of the following: VAS ≥ 6, significant changes in medication, need for corticosteroids and/or commencement of biological medication or an episode of inpatient care. For rare conditions without standard criteria of disease control and/or adherence, experienced clinicians subjectively categorized participants according to their symptoms,

clinical and laboratory findings, need for inpatient care, and changes in medication. MK first reviewed medical records of every participant, of whom 28 (11%) were difficult to categorize. For these 28 adolescents, SK made an independent assessment of disease control. Six adolescents were categorized differently, and the final grading was based on consensus between the two reviewers. For some analyses we combined the three smallest subspecialties (neurology, cardiology, and nephrology/organ transplant) into "others".

Psychiatric diagnosis and treatment

Psychiatric diagnoses and treatment details were collected from the electronic medical records of the Helsinki University Hospital which is the only public provider of adolescent psychiatric care in the study catchment area. Data were collected from ages 13 to 18, the age range of adolescent psychiatry in the study area. These data were collected separately from the disease control data, and in a different order of patients. Psychiatric diagnoses were divided into four categories: 1) mood disorders; 2) anxiety disorders; 3) others; and 4) multiple diagnoses (i.e., diagnosis from at least two different diagnostic categories). The New Children's Hospital has no general guideline regarding psychiatric assessment and adolescents may have received referrals to adolescent psychiatry from community healthcare centers and student health services. Outpatient appointments with mental health professionals over these six years were divided into three categories: 1) no appointments; 2) one to three appointments; and 3) more than three appointments. We also recorded the age at first psychiatric diagnosis, any admissions for psychiatric inpatient care and, if so, the number of days spent in psychiatric inpatient care.

Substance use

Participants completed the Adolescent Substance Use Measurement (ADSUME), a brief measure that was developed and validated in Finland to evaluate adolescent substance use and

its possible consequences during the previous year. ADSUME is reliable when compared to validated adult questionnaires (AUDIT, CRAFFT) and may even be superior in detecting hazardous substance use among adolescents.[22] We calculated a total score (0-31 points) of the first nine questions (appendix 1) to yield a numeric score which we used in analyses. We also divided participants into subgroups according to guidelines from the Finnish Institute for Health and Welfare: 1) abstinence or experimental use, 0-3 points; 2) recurring use, 4-6 points; 3) risky use, 7-9 points; and 4) hazardous use, 10 points or more.[23]

Data analysis

Categorical data are presented as frequencies (with percentages). For continuous variables, means and standard deviations (SDs) or medians (with interquartile range) are used. Associations between disease control, psychiatric diagnoses, and family composition were compared using Fisher's exact test (two-sided). To evaluate the associations between categorical data and continuous variables we used non-parametric tests (Mann-Whitney U and Kruskal-Wallis). Finally, ordinal logistic regression with disease control as the dependent variable was conducted. Data analyses were performed using IBM SPSS Statistics 25 (IBM, Somers, NY) and a p-value < 0.05 was considered significant.

Results

In total, 279 (91.2%) adolescents consented to participate, and 253 (82.7%) adolescents completed the baseline survey after a maximum of two reminders. Demographic and clinical data of the 253 study participants are summarized in Tables 1 and 2. The mean age at diagnosis of the medical condition was 9.0 years (SD 5.3) and the mean age at first psychiatric diagnosis was 13.7 years (SD 2.7). Age at transfer differed greatly between subspecialties: rheumatology patients were the youngest to transfer (mean age 16.2 years) and

gastroenterology were the oldest (mean age 19.0 years; p<0.001 for difference between groups).

Table 1. Demographic and clinical data of 253 adolescents.

Gender	**N**	**%**
Male	118	46.6
Female	132	52.2
Other	3	1.2
Pediatric subspecialty		
Diabetes	92	36.4
Rheumatology	66	26.1
Gastroenterology	45	17.8
Cardiology	19	7.5
Neurology	18	7.1
Kidney or liver disease with/without transplant	13	5.1
Lives with		
Mother and father	158	62.5
Other than with two parents	95	37.5
Disease control *		
Good control and/or adherence	70	27.7
Some evidence of concern	105	41.5
Poor control and/or adherence or more severe condition	76	30.0
Psychiatric diagnoses	**59**	**23.3**
Anxiety disorders	38	15.0
Mood disorders	18	7.1
Others **	26	10.3
Many diagnoses	22	8.7
Outpatient visits in adolescent psychiatry		
No visits	159	62.8
1-3 visits	36	14.2
More than 3 visits	58	22.9
Median ADSUME total scores (IQR) * **	**3**	**(0-6)**
Females	2	(0-6)
Males	3	(0-6)
ADSUME risk category * **	**N**	**%**
Abstinence or experimental use (0-3 points)	142	56.1
Recurring use (4-6 p)	57	22.5
Risky use (7-9 p)	27	10.7
Hazardous use (10 p or more)	26	10.3

*Data available for 251 adolescents as transfer of two adolescents was delayed.
** Others: for example, conduct disorder, attention deficit-hyperactivity disorder, psychotic disorder, eating disorders, developmental disorders.
*** One response missing.
ADSUME = Adolescent`s Substance Use Measurement; IQR = interquartile range

Table 2. Demographic and clinical data (n=253).

	Mean, years (median)	**SD**
Age at first medical diagnosis	**9.0 (10.1)**	**5.3**
Age at first psychiatric diagnosis	**13.7 (14.3)**	**2.7**
Age when completing the ADSUME	**17.2 (16.8)**	**1.2**
Age at transfer of care	**17.3 (17.1)**	**1.2**
Diabetes	17.2	0.7
Rheumatology	16.2	0.5
Gastroenterology	19.0	0.9
Others	17.8	1.2
Time between ADSUME and transfer of care	**0.2 (0.0)**	**0.4**
Time between medical diagnosis and transfer of care	**8.3 (7.4)**	**8.3**
Time between psychiatric diagnosis and transfer of care	**4.0 (3.2)**	**4.0**

ADSUME = Adolescent`s Substance Use Measurement

Among all study participants, 27.7% (n=70) were categorized as having good disease control and/or adherence, 41.5% (n=105) were rated as having some evidence of concern, and 30.0% (n=76) were classified as having poor disease control and/or adherence (or more severe

condition) during the year preceding the transfer of care. Only 16% of adolescents with gastroenterological diseases and 14% of adolescents with diabetes had good disease control (mean of 4.6 measurements). Among adolescents with rheumatological disease, 39% had good disease control, while it was 48% in the group of "others". Gender and age at diagnosis showed no association with different disease control groups. Older age at transfer of care was associated with poorer disease control (p=0.045).

In this cohort, 23.3% of adolescents (n=59) had a psychiatric diagnosis, of whom 37.2% (n=22) had at least two different diagnoses. Anxiety disorders were most common (n=38), comprising 15.0% of all participants and 64.4% of adolescents with a psychiatric diagnosis. Females were overrepresented in anxiety disorders and males in the 'other psychiatric diagnosis' group. Nine adolescents (3.6%) received inpatient psychiatric care, with a median of 22 days (range 9-956 days) per person. Age at medical diagnosis and age at psychiatric diagnosis showed no association (p=0.32).

More than half of participants (n=142, 56.1%) were abstinent or reported only experimental substance use (Table 1). Approximately half of the adolescents reported using alcohol in the last year. The median ADSUME total score was 3.0 and the maximum score was 27 points.

Table 3 and Figure 1 summarize the associations between disease control, psychiatric diagnoses, substance use and family composition. Adolescents with psychiatric diagnoses more often had poor disease control and/or adherence or more severe disease/condition than adolescents without psychiatric diagnoses (p=0.01). Hazardous substance use was more frequent among adolescents with psychiatric diagnoses (8% vs 19%), but total ADSUME points showed no direct association with psychiatric diagnoses nor disease control. Adolescents who lived with two parents (n=158, 62.5%) had fewer psychiatric diagnoses than

adolescents living in other kinds of families (p = 0.05). In ordinal regression, only psychiatric diagnoses were significant for disease control (Table 4).

Table 3. Family composition, disease control and substance use, by psychiatric diagnosis (n=253).

	No psychiatric diagnosis (n=194) **N (%)**	**Psychiatric diagnosis (n=59)** **N (%)**	**p**
Living with two parents	128 (66)	30 (51)	**0.05**
Disease control *			
Good control and/or adherence	59 (30)	11 (19)	0.13
Some evidence of concern	84 (43)	21 (37)	0.45
Poor control and/or adherence or more severe condition	51 (26)	25 (44)	**0.01**
ADSUME score, median (IQR) **	3 (0-6)	0 (0-6)	0.56

*Transfer of two adolescents has been delayed

** One response missing.

Other factors compared using Fisher's exact test, ADSUME median scores compared using the Mann-Whitney U test.

Table 4. Results of ordinal regression with disease control (good, moderate, or poor) as the dependent variable.

						95% CI	
	Estimate	SE	Wald	df	p	Lower	Upper
Threshold: poor to moderate dc	-0.879	0.248	12.588	1	<0.001	-1.364	-0.393
Threshold: moderate to good dc	0.958	0.249	14.800	1	<0.001	0.470	1.445
Male vs. female	-0.189	0.238	0.633	1	0.426	-0.656	0.277
Two parents vs. other family	0.364	0.246	2.193	1	0.139	-0.118	0.847
Psychiatric dg vs. no dg	-0.689	0.289	5.700	1	0.017	-1.254	-0.123

Goodness of fit: Pearson chi-squared 11.380 with 11 degrees of freedom; significance 0.412.

Pseudo r squared: Cox and Snell 0.036, Nagelkerke 0.041.

CI = confidence interval, SE = standard error, df = degress of freedom, dc = disease control, dg = diagnosis

Please note: age at transfer could not be included in the model because it lead to empty cells in more than half (56%) of cases.

Discussion

In this cross-sectional study of adolescents with chronic medical conditions, nearly a third were assessed to have poor disease control in the year preceding transfer to adult health services and almost a quarter had received a psychiatric diagnosis during adolescence. Adolescents with a comorbid psychiatric diagnosis more frequently had poor control of their medical condition than those without a psychiatric diagnosis.

In our study, 23% of the adolescents received a mental health diagnosis between the ages of 13 and 18. Adolescents living with two parents had fewer psychiatric diagnoses than their peers living in other kinds of families. The protective effect of living in a nuclear family when considering psychiatric morbidity has also been reported among the general population of children and adolescents.[24,25]. Overall, the prevalence of psychiatric diagnoses was higher in our study than in other diagnostic studies.[8,10] Regular assessment by medical professionals might have contributed to unnecessary referrals aided by the relative ease of referral to public mental health professionals. However, as the portion of adolescents with three or more outpatient visits in the department of adolescent psychiatry is comparable to the proportion of adolescents with a psychiatric diagnosis, overdiagnosis seems unlikely.

In this study, 22.5% of adolescents reported using substances regularly while a further 21.0% were categorized as risky or hazardous users. This is consistent with national Finnish data that found 15-24% of 17-18-year-old students reported monthly binge drinking.[26] Conversely, only 1% of adolescents in our cohort had used cannabis during the past year, in comparison to 8-12% of 17-18-yr-old students in Finland.[26] Although alcohol consumption has decreased among adolescents in many developed countries, adolescent binge drinking and the accompanying risky behavior remain significant public health problems.[27]

The association between poor disease control and psychiatric comorbidity found in our study may be bidirectional: mental health problems may affect self-management resources and thus worsen disease control, while living with a severe disease may increase the emotional burden experienced. The burden of a chronic condition also includes a sense of interrupted social maturation for which substance use can sometimes present as a means of catching up although adolescents are aware of the harmful effects of substance use. [28]

Considering the modest proportion of adolescents with good disease control before transfer of care, additional strategies may be required to optimize health outcomes in adolescents whose disease is challenging to treat, who lack motivation or skills for self-management, or have mental health or substance use problems.[29,30] The treatment of anxiety and depression in adolescents is expected to improve symptoms and positively influence disease control and health care utilization.[31-33] while some adolescents will need concurrent transition of psychiatric and medical care. A child's illness is a significant stressor for parents,[34] and family psychosocial supports and interventions to minimize financial hardship also warrant consideration. Our data affirms the importance of regularly discussing substance use and its effects with adolescents with chronic medical conditions especially given its potential effect on specific medical conditions, such as a reduced seizure threshold in adolescents with epilepsy or hypoglycemia in adolescents with diabetes.[35,36]

A strength of this study is the high response rate of adolescents recruited from six different hospital departments to intentionally span a range of conditions, increasing the generalizability of our results. However, this also provided some challenges, especially regarding how disease control was defined as by definition this differs by medical condition. Although the same researcher collected data on disease control and psychiatric diagnoses, we attempted to reduce bias by collecting these data on separate occasions, using separate files, and in different patient order. While we needed to categorize disease control subjectively in

adolescents with rare diseases, the likelihood of misclassification was reduced by having two independent reviewers. As we had access to all electronic medical records in the study catchment area, including psychiatry, we were able to use specific psychiatric diagnoses and estimate disease control of medical conditions based on clinical and laboratory findings. While psychiatric diagnoses were made by the psychiatry department, standardized assessments were not routinely used. Further, some psychiatric diagnoses may have been missed if the adolescent had moved to or from another hospital district. The public health system in Finland results in adolescents receiving the same treatment regardless of socioeconomic status, with provision of psychiatric care in the private sector uncommon. In countries without public health care, associations between mental health problems and poor disease control may be even more significant than in our study.

Conclusions

In conclusion, psychiatric morbidity and poor disease control of chronic medical conditions are prevalent and closely intertwined among adolescents, reinforcing the importance of collaboration between medical and psychiatric care.[37] Maximizing mental health before adolescents transfer to adult health services appears especially important given the associations of both poor mental health and the transfer of care itself with unsatisfactory adherence to treatment and increased rates of emergency visits and hospitalizations. [12,38,39]

A Funding statement:

This study is supported by grants from the Foundation for Medical Research, the Helsinki University Hospital (TYH2019312), the Foundation for Pediatric Research and the Paulo Foundation.

A competing interest statement:

Authors have no conflicts of interest relevant to this article to disclose.

Contributor`s Statement:

Dr Mira Kallio collected data, carried out initial analyses, drafted the manuscript and reviewed and revised the manuscript. Ms Tornivuori collected data and reviewed and revised the manuscript. Drs Miettinen and Kolho participated in designing the study and reviewed and revised the manuscript. Ms Culnane and Professor Sawyer participated in study design and reviewed and revised the manuscript. Dr Kosola designed the study, coordinated, and supervised data collection and critically reviewed the manuscript for important intellectual content. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

Checklist: STROBE.

Data sharing statement: Data are available upon reasonable request.

Acknowledgments: We wish to thank all the participants of the study as well as research nurse Satu Lindström. We also acknowledge Kristiina Aalto, Eero Jokinen, Eeva-Liisa Metsähonkala, Tiina Remes and Elisa Ylinen for clinical advice regarding disease control.

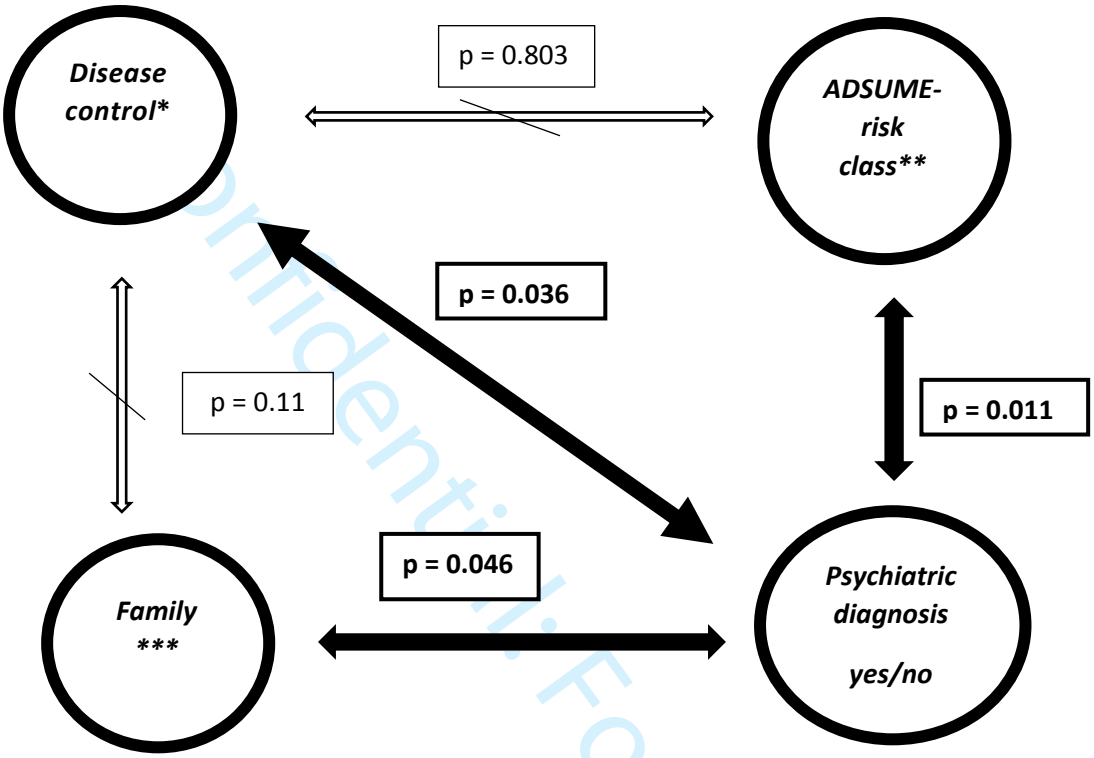
References

1. Raissadati A, Nieminen H, Jokinen E, Sairanen H. Progress in late results among pediatric cardiac surgery patients: A population-based 6-decade study with 98% follow-up. *Circulation.* 2015;131(4):347-353. doi:10.1161/CIRCULATIONAHA.114.011190
2. Benchimol EI, Fortinsky KJ, Gozdyra P, Van Den Heuvel M, Van Limbergen J, Griffiths AM. Epidemiology of pediatric inflammatory bowel disease: A systematic review of international trends. *Inflamm Bowel Dis.* 2011;17(1):423-429. doi:10.1002/ibd.21349
3. Patterson CC, Karuranga S, Salpea P, et al. Worldwide estimates of incidence, prevalence, and mortality of type 1 diabetes in children and adolescents: Results from the International Diabetes Federation Diabetes Atlas, 9th edition. *Diabetes Res Clin Pract.* 2019;157:107842. doi:10.1016/j.diabres.2019.107842
4. Nap-van der Vlist MM, Dalmeijer GW, Grootenhuis MA, et al. Fatigue in childhood chronic disease. *Arch Dis Child*. 2019;104(11):1090-1095. doi:10.1136/archdischild-2019-316782
5. Maes M, Van Den Noortgate W, Fustolo-Gunnink SF, Rassart J, Luyckx K, Goossens L. Loneliness in Children and Adolescents with Chronic Physical Conditions: A Meta-Analysis. *J Pediatr Psychol.* 2017;42(6) :622-635. doi:10.1093/jpepsy/jsx046
6. Brady AM, Deighton J, Stansfeld S. Psychiatric outcomes associated with chronic illness in adolescence: A systematic review. *J Adolesc.* 2017;59:112-123. doi:10.1016/j.adolescence.2017.05.014
7. Robinson ME, Simard M, Larocque I, Shah J, Nakhla M, Rahme E. Risk of psychiatric disorders and suicide attempts in emerging adults with diabetes. *Diabetes Care.* 2020;43(2):484-486. doi:10.2337/dc19-1487
8. LaGrant B, Marquis BO, Berg AT, Grinspan ZM. Depression and anxiety in children with epilepsy and other chronic health conditions: National estimates of prevalence and risk factors. *Epilepsy Behav*. 2020;103 (Pt A):106828. doi:10.1016/j.yebeh.2019.106828
9. Ghandour RM, Sherman LJ, Vladutiu CJ, et al. Prevalence and Treatment of Depression, Anxiety, and Conduct Problems in US Children. *J Pediatr*. 2019;206:256-267.e3. doi:10.1016/j.jpeds.2018.09.021
10. Butwicka A, Olén O, Larsson H, et al. Association of Childhood-Onset Inflammatory Bowel Disease with Risk of Psychiatric Disorders and Suicide Attempt. *JAMA Pediatr.* 2019;173(10):969-978. doi:10.1001/jamapediatrics.2019.2662
11. Finnish Institute for Health and Welfare. Well-being of children and young people – School Health Promotion Study 2021. Available at: https://thl.fi/en/web/thlfi-en/statistics-and-data/statistics-by-topic/social-services-children-adolescents-and-families/well-being-of-children-and-young-people-school-health-promotion-study
12. Bernstein CM, Stockwell MS, Gallagher MP, Rosenthal SL, Soren K. Mental health issues in adolescents and young adults with type 1 diabetes: Prevalence and impact on glycemic control. *Clin Pediatr (Phila).* 2013;52(1):10-15. doi:10.1177/0009922812459950
13. Blount RL. Disease Activity Does Not Explain It All: How Internalizing Symptoms and Caregiver Depressive Symptoms Relate to Health-related Quality of Life Among Youth with Inflammatory Bowel Disease. *Inflamm Bowel Dis*. 2016;22(4):963-967. doi:10.1097/MIB.0000000000000686

14. Wong JJ, Sceats L, Dehghan M, et al. Depression and health care use in patients with inflammatory bowel disease. *J Crohn's Colitis.* 2019;13(1):19-26. doi:10.1093/ecco-jcc/jjy145
15. Sawyer SM, Drew S, Yeo MS, Britto MT. Adolescents with a chronic condition: challenges living, challenges treating. *Lancet.* 2007;369(9571):1481-1489. doi:10.1016/S0140-6736(07)60370-5
16. Shrier LA, Harris SK, Kurland M, Knight JR. Substance use problems and associated psychiatric symptoms among adolescents in primary care. *Pediatrics.* 2003;111(6 Pt 1):e699-e705. doi:10.1542/peds.111.6.e699
17. Deas D. Adolescent substance abuse and psychiatric comorbidities. *J Clin Psychiatry.* 2006;67 (7):e02. doi:10.4088/jcp.0706e02
18. Kessler RC, Berglund P, Demler O, Jin R, Merikangas KR, Walters EE. Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the national comorbidity survey replication. *Arch Gen Psychiatry.* 2005;62(6):593-602. doi:10.1001/archpsyc.62.6.593
19. Kosola Silja, Culnane Evelyn, Loftus Hayley, et al. The Bridge study protocol: an international, observational cohort study on the transition of healthcare for adolescents with chronic conditions. *BMJ Open.* 2021;11(6):e048340. Published 2021 Jun 21. doi:10.1136/bmjopen-2020-048340
20. Backström M, Tynjälä P, Ylijoki H, et al. Finding specific 10-joint Juvenile Arthritis Disease Activity Score (JADAS10) and clinical JADAS10 cut-off values for disease activity levels in non-systemic juvenile idiopathic arthritis: A Finnish multicentre study. *Rheumatology (Oxford).* 2016;55(4):615-623. doi:10.1093/rheumatology/kev353
21. DiMeglio LA, Acerini CL, Codner E, et al. ISPAD Clinical Practice Consensus Guidelines 2018: Glycemic control targets and glucose monitoring for children, adolescents, and young adults with diabetes. *Pediatr Diabetes.* 2018;19 Suppl 27:105-114. doi:10.1111/pedi.12737
22. Piskanen M. Promoting Adolescents` Abstinence from Substance Use. An Early Intervention Model for School and Student Health Care. Published online 2007. http://urn.fi/URN:ISBN:978-951-27-0510-8
23. Pirskanen M, Laukkanen E, Pietilä AM. A formative evaluation to develop a school health nursing early intervention model for adolescent substance use. *Public Health Nurs.* 2007;24(3):256-264. doi:10.1111/j.1525-1446.2007.00632.x
24. Ängarne-Lindberg T, Wadsby M. Psychiatric and somatic health in relation to experience of parental divorce in childhood. Int J Soc Psychiatry. 2012;58(1):16-25. doi:10.1177/0020764010382372
25. Perales F, Johnson SE, Baxter J, Lawrence D, Zubrick SR. Family structure and childhood mental disorders: new findings from Australia. Soc Psychiatry Psychiatr Epidemiol. 2017;52(4):423-433. doi:10.1007/s00127-016-1328-y
26. Helakorpi S, Kivimaki H. Well-being of children and young people – School Health Promotion study 2021: Large share of children and young people satisfied with their lives – a sense of loneliness has become more common. Statistical report 42/2021, National Institute for Health and Welfare, Finland. Available at https://www.julkari.fi/handle/10024/143418 . Downloaded Sep 6, 2022.
27. Siqueira L, Smith VC; COMMITTEE ON SUBSTANCE ABUSE. Binge Drinking. *Pediatrics.* 2015;136(3):e718-e726. doi:10.1542/peds.2015-2337
28. Weitzman ER, Salimian PK, Rabinow L, Levy S. Perspectives on substance use among youth with chronic medical conditions and implications for clinical guidance

and prevention: A qualitative study. *PLoS One*. 2019;14(1):e0209963. Published 2019 Jan 23. doi:10.1371/journal.pone.0209963
29. Andrade DM, Bassett AS, Bercovici E, et al. Epilepsy: Transition from pediatric to adult care. Recommendations of the Ontario epilepsy implementation task force. *Epilepsia.* 2017;58(9):1502-1517. doi:10.1111/epi.13832
30. Healy SA, Fantaneanu TA, Whiting S. The importance of mental health in improving quality of life in transition-aged patients with epilepsy. Epilepsy Behav. 2020;112:107324. doi:10.1016/j.yebeh.2020.107324
31. Bennett S, Shafran R, Coughtrey A, Walker S, Heyman I. Psychological interventions for mental health disorders in children with chronic physical illness: A systematic review. *Arch Dis Child.* 2015;100(4):308-316. doi:10.1136/archdischild-2014-307474
32. Thabrew H, Stasiak K, Hetrick SE, Wong S, Huss JH, Merry SN. E-Health interventions for anxiety and depression in children and adolescents with long-term physical conditions. *Cochrane Database Syst Rev*. 2018;8(8):CD012489. Published 2018 Aug 15. doi:10.1002/14651858.CD012489.pub2
33. Lehtimaki S, Martic J, Wahl B, Foster KT, Schwalbe N. Evidence on Digital Mental Health Interventions for Adolescents and Young People: Systematic Overview. *JMIR Ment Health*. 2021;8(4):e25847. Published 2021 Apr 29. doi:10.2196/25847
34. Mutanen A, Kosola S, Merras-Salmio L, Kolho KL, Pakarinen MP. Long-term health-related quality of life of patients with pediatric onset intestinal failure. J Pediatr Surg. 2015;50(11). doi:10.1016/j.jpedsurg.2015.05.012
35. Samokhvalov AV, Irving H, Mohapatra S, Rehm J. Alcohol consumption, unprovoked seizures, and epilepsy: a systematic review and meta-analysis. *Epilepsia*. 2010;51(7):1177-1184. doi:10.1111/j.1528-1167.2009.02426.x
36. Tetzschner R, Nørgaard K, Ranjan A. Effects of alcohol on plasma glucose and prevention of alcohol-induced hypoglycemia in type 1 diabetes-A systematic review with GRADE. *Diabetes Metab Res Rev*. 2018;34(3):10.1002/dmrr.2965. doi:10.1002/dmrr.2965
37. Fazel M, Townsend A, Stewart H, Pao M, Paz I, Walker J, Sawyer S.M, Sharpe M. Integrated care to address child and adolescent health in the 21st century: A clinical review. *JCPP Advances*.2021;e12045. doi:10.1002/jcv2.12045
38. Kosola S, Ylinen E, Finne P, Rönnholm K, Ortiz F. Implementation of a transition model to adult care may not be enough to improve results: National study of kidney transplant recipients. Clin Transplant. 2019;33(1):e13449. doi:10.1111/ctr.13449
39. Rollo A, Salardi S, Ciavarella A, et al. Transition from pediatric to adult care. Eight years after the transition from pediatric to adult diabetes care: Metabolic control, complications and associated diseases. J Endocrinol Invest. 2014;37(7):653-659. doi:10.1007/s40618-014-0090-9

Figure 1. Associations between disease control, psychiatric diagnoses, substance use (ADSUME) and family composition. P < 0.05 is considered significant.



* Good control and/or adherence, some evidence of concern or poor control and/or adherence or more severe condition

** Abstinence or experimental use, repetitive use, risky use, or hazardous use

*** Living with mother and father or with someone else (for example with only one parent, mixed family or any other third party)

Appendix 1. Adolescents Substance Use Measurement (ADSUME)

1. Do you smoke (including tobacco, cannabis and e-cigarettes)?
    a. No
    b. Occasionally
    c. Daily
2. Have you tried or used following substances during the past year? (If not, there is no need to answer the next questions)
    a. Alcohol
    b. Medication to get high
    c. Illegal drugs
    d. Alcohol together with other substances
    e. Inhaled chemicals `sniffing`
3. How many times have you tried or used other substances than tobacco during last year?
    a. 1-3 times
    b. 4-6 times
    c. about once in a month
    d. 2-3 times per month
    e. once a week or more often
4. How many drinks do you usually have at a time?
    a. 1-2 drinks
    b. 3-4 drinks
    c. 5-6 drinks
    d. 7 drinks or more
5. Have you ever been late to school or work, left in the middle of the day or stayed home from school or work because of substance use?
    a. Never
    b. Once
    c. 2-3 times
    d. 4 or more times
6. Have you encountered any of these situations when you have been under the influence of alcohol or drugs during the past year?
    a. I have hurt myself or someone else has hurt me
    b. I have hurt someone else
    c. I have been a passenger in a vehicle with a driver who was under the influence
    d. I have driven a vehicle under the influence
    e. I have broken or stolen someone else's property
    f. I have had a sexual relationship that I regret afterwards
7. How often have you been in these situations (described before)?
    a. Once
    b. Twice
    c. More Often
8. Have you ever had a blackout (i.e., trouble remembering what happened due to substance use)?
    a. Once
    b. Twice
    c. More Often
9. Have you ever passed out because of substance use?
    a. Once
    b. Twice
    c. More Often

BMJ Paediatrics Open

Disease control and psychiatric comorbidity among adolescents with chronic medical conditions – a single center retrospective study

Journal:	*BMJ Paediatrics Open*
Manuscript ID	bmjpo-2022-001605.R3
Article Type:	Original research
Date Submitted by the Author:	12-Jan-2023
Complete List of Authors:	Kallio, Mira; University of Helsinki Faculty of Medicine, Department of Pediatrics Tornivuori, Anna; Turun yliopisto Miettinen, Päivi; University of Helsinki Faculty of Medicine, Department of Pediatrics Kolho, kaija-Leena; University of Helsinki Faculty of Medicine, Department of Pediatrics Culnane, Evelyn; The Royal Children's Hospital Melbourne Sawyer, Susan; The Royal Children's Hospital Melbourne Kosola, Silja; University of Helsinki Faculty of Medicine
Keywords:	Adolescent Health, Gastroenterology, Neurology, Rheumatology, Endocrinology

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

Disease control and psychiatric comorbidity among adolescents with chronic medical conditions – a single center retrospective study

Kallio Mira [a,c], Tornivuori Anna [a,b], Miettinen Päivi J. [a,c], Kolho Kaija-Leena [a,c,d], Culnane Evelyn [e], Sawyer Susan M [f,g,h] Kosola Silja [a,c]

Affiliations: [a] Department of Pediatrics, Helsinki University Hospital and University of Helsinki, Helsinki, Finland; [b] Nursing Science of University of Turku, Turku, Finland; [c] Pediatric Research Center, Helsinki University Hospital and University of Helsinki, Helsinki, Finland; [d] Faculty of Medicine and Health Technology, Tampere University, Tampere, Finland; [e] Transition Support Service, The Royal Children's Hospital, Melbourne, Australia; [f] Centre for Adolescent Health, Royal Children's Hospital, Melbourne, Australia; [g] Murdoch Children's Research Institute, Melbourne, Australia; [h] Department of Paediatrics, The University of Melbourne, Australia.

Address correspondence to: Mira Kallio, Department of Pediatrics, University of Helsinki, Biomedicum 6, Haartmaninkatu 8, 00290 Helsinki, [mira.kallio@hus.fi], +35840 778 5221.

Clinical Trial registration: Trial registration name The Bridge and registration number NCT04631965 (https://clinicaltrials.gov/ct2/show/NCT04631965).

Data Sharing Statement: Data are available upon reasonable request.

Word count: 2797

Abstract

Background

To investigate disease control, psychiatric comorbidity, substance use and their possible associations in adolescents with chronic medical conditions before transfer to adult health care.

Methods

We collected clinical data from the year preceding transfer of care and psychiatric data from the records of the paediatric hospital in Helsinki, Finland (population base 1.7 million). Participants were grouped into three disease and/or adherence control categories (good, some evidence of concern, poor) based on clinical data from the medical records of the year preceding the transfer of care. Participants completed the Adolescent`s Substance Use Measurement questionnaire before transfer of care and were divided into four risk subgroups accordingly.

Results

In total, 253 adolescents (mean age 17.3 years, SD 1.2) from six pediatric subspecialties participated in this study. Disease control and/or adherence were rated as good in 28% (n=70), moderate in 42% (n=105) and poor in 30% (n=76) in the year before participants transferred to adult health services. A quarter of participants had at least one psychiatric diagnosis during adolescence. Adolescents with concomitant psychiatric diagnoses more often had poor disease control of their chronic medical condition than adolescents with only a medical condition 44% vs 26% (n=25/59 vs 51/194, respectively). More than half of adolescents (56%) were abstinent or used substances infrequently; 10% (n=26) reported hazardous substance use.

Conclusions

Psychiatric comorbidity in adolescents with chronic medical conditions is common. Its negative association with disease control and possible substance use should be considered in the transition process to adult health services.

What is already known on this topic

Adolescents with chronic medical disorders have a higher prevalence of mental health disorders than their peers, but the impact of mental health disorders on disease control prior to transfer to adult health care is poorly understood.

What this study adds

Adolescents with chronic medical disorders and comorbid psychiatric diagnoses more frequently have poor control of their medical condition than those without psychiatric comorbidities which highlights the necessity of a holistic approach to care.

How this study might affect research, practice, or policy

Ensuring that mental health disorders are identified and treated is an important aspect of caring for adolescents and young adults with chronic medical conditions, including at the time they transfer to adult services. Future research to measure the potential impact of adolescent mental health disorders on transfer to adult health service is indicated.

Introduction

The landscape of chronic illness in children and adolescents with chronic medical conditions has changed. Over the past few decades, treatment success has resulted in improved survival of many of these young people, which together with an increased incidence of particular chronic medical disorders in childhood,[1-3] results in increasing numbers of adolescents requiring regular follow-up in adult health services. Living with a chronic medical condition can pose many challenges during adolescence, not least due to the requirement for regular medication and other treatments, frequent medical appointments, and the uncertainty of future treatment such as surgical procedures. These demands for health management and monitoring, together with the impact of the medical condition itself, such as pain and fatigue,[4] can reduce participation in normative activities with effects on peer relationships, extracurricular participation and school attendance.[5]

Chronic medical conditions are associated with increased rates of mental health problems.[6,7] In the US, 25% of children with epilepsy have anxiety and/or depression compared with the general population of 12-17-year-olds of whom 6% have a current diagnosis of depression and 11% anxiety.[8,9] During a decade of follow-up, 17% of Swedish children with inflammatory bowel disease (IBD) received a diagnosis of any psychiatric disorder compared with 12% of the general population.[10] Population surveys that assess self-reported symptoms of depression or anxiety yield even higher proportions of affected young people. [11] So the proportion of adolescents with chronic medical conditions who struggle with symptoms of mental health disorders is expected to be even higher.

Mental health problems, together with pain and fatigue,[4] can affect disease control, adherence behaviors, and health-related quality of life in children and adolescents with chronic medical conditions. [12,13] For example, depression is associated with higher health care costs and

emergency department visits in children and adolescents with IBD [14], but which young people are most at risk is still incompletely understood.

Adolescents living with chronic medical conditions often engage in risk behaviors, such as substance use.[15] Substance use in adolescence is frequently associated with other mental health disorders, and the incidence of both substance use and mental health disorders increases across adolescence and into adulthood.[16,17,18] This accumulation of risk behaviors and mental health disorders among adolescents and young adults suggests it is important to identify which adolescents with chronic medical disorders are at greatest risk so that they can be appropriately managed, including at the time they transfer to adult health services.

In this study of adolescents with different chronic medical conditions, we aimed to investigate disease control, rates of psychiatric comorbidity and risky substance use and their associations before adolescent care is transferred to adult health services. Our hypothesis was that psychiatric comorbidity is common and associated with poorer disease control and higher rates of substance use.

Methods

Study design

This study is part of an international prospective cohort study named the Bridge, for which the study protocol is available online.[19] In this cross-sectional analysis, we combined retrospective data with questionnaire responses from one study site.

Patient and Public Involvement

Fifteen adolescents with chronic conditions participated in the design of the study questionnaires.

Ethics

This study was approved by the Ethics Committee for Women's and Children's Health and Psychiatry at the Helsinki University Hospital (HUS/1547/2017). Participants gave informed consent to link their routine clinical data with individual questionnaire responses. The Bridge trial has been registered with ClinicalTrials.gov (ID number NCT04631965).

Participants

Participants were recruited from the New Children's Hospital, Helsinki, Finland (hospital catchment area 1.7 million inhabitants) between September 2017 and August 2019. In Finland, practically all adolescents with chronic medical conditions are managed by public health services, with few cared for by private doctors. Clinicians from six different pediatric subspecialty clinics (endocrinology, gastroenterology, rheumatology, nephrology and organ transplants, neurology, and cardiology) identified adolescents who were expected to transfer to adult clinics within the coming six to twelve months. Inclusion criteria were that participants were aged 15-24 years and had a chronic medical condition that had been diagnosed at least six months earlier and was expected to require regular follow-up in adult health services. Eligible participants also needed to have sufficient cognitive and linguistic ability to communicate in Finnish, English or Swedish. Adolescents received a movie ticket (value 10 EUR) after completing the survey in acknowledgement of their time.

A research nurse, uninvolved in patient care, personally met 306 consecutive adolescents during their routine hospital visits and provided oral and written information about the Bridge study.

Demographics

Background information was obtained from the baseline survey, including gender, residential area, home language and family composition (living with two parents or any other family type).

Disease control

To determine disease control, we gathered data and laboratory test results from the electronic medical records for the year preceding the final visit at the New Children's Hospital. The final visit was specified as the out-patient appointment where the clinician made a formal referral to the respective adult health service. We divided participants into one of three categories according to the condition for which they were recruited: 1) good disease control and/or adherence; 2) some evidence of concern; and 3) poor disease control and/or adherence or more severe condition (see study protocol for further details).[19] Where appropriate, we used published cut-offs for disease control. For adolescents with diabetes, a mean glycosylated hemoglobin (the mean of all measurements across the year preceding transfer of care) ≤ 53 mmol/mol was categorized as good control/adherence, 54-69 mmol/mol was considered evidence of some concern while ≥ 70 mmol/mol were classified as having poor control/adherence. For adolescents with rheumatic disease, the 10-joint Juvenile Arthritis Disease Activity Score (JADAS10) was completed. For those with oligoarthritis, cut-points of ≤ 0.5 (good), 0.6-2.8 (some concern) and > 2.8 (poor) were used, while for those with polyarthritis, the cut-points were ≤ 0.7, 0.8-4 and > 4, as previously applied.[19–21] For adolescents with IBD, good control/adherence required minimal pain (Visual analog scale, VAS 1-2), at least 80% of faecal calprotectin results <100 µg/g and always <300 µg/g, medication unchanged or reduced, and no inpatient care; indicators of some evidence of concern were VAS 3-5, < 80% of faecal calprotectin results within target range or exceeded 300 ug/g even once, but no significant medication changes nor inpatient care; and for poor control/adherence any of the following: VAS ≥ 6, significant changes in medication, need for

corticosteroids and/or commencement of biological medication or an episode of inpatient care. For rare conditions without standard criteria of disease control and/or adherence, experienced clinicians subjectively categorized participants according to their symptoms, clinical and laboratory findings, need for inpatient care, and changes in medication. MK first reviewed medical records of every participant, of whom 28 (11%) were difficult to categorize. For these 28 adolescents, SK made an independent assessment of disease control. Six adolescents were categorized differently, and the final grading was based on consensus between the two reviewers. For some analyses we combined the three smallest subspecialties (neurology, cardiology, and nephrology/organ transplant) into "others".

Psychiatric diagnosis and treatment

Psychiatric diagnoses and treatment details were collected from the electronic medical records of the Helsinki University Hospital which is the only public provider of adolescent psychiatric care in the study catchment area. Data were collected from ages 13 to 18, the age range of adolescent psychiatry in the study area. These data were collected separately from the disease control data, and in a different order of patients. Psychiatric diagnoses were divided into four categories: 1) mood disorders; 2) anxiety disorders; 3) others; and 4) multiple diagnoses (i.e., diagnosis from at least two different diagnostic categories). The New Children's Hospital has no general guideline regarding psychiatric assessment and adolescents may have received referrals to adolescent psychiatry from community healthcare centers and student health services. Outpatient appointments with mental health professionals over these six years were divided into three categories: 1) no appointments; 2) one to three appointments; and 3) more than three appointments. We also recorded the age at first psychiatric diagnosis, any admissions for psychiatric inpatient care and, if so, the number of days spent in psychiatric inpatient care.

Substance use

Participants completed the Adolescent Substance Use Measurement (ADSUME), a brief measure that was developed and validated in Finland to evaluate adolescent substance use and its possible consequences during the previous year. ADSUME is reliable when compared to validated adult questionnaires (AUDIT, CRAFFT) and may even be superior in detecting hazardous substance use among adolescents.[22] We calculated a total score (0-31 points) of the first nine questions (appendix 1) to yield a numeric score which we used in analyses. We also divided participants into subgroups according to guidelines from the Finnish Institute for Health and Welfare: 1) abstinence or experimental use, 0-3 points; 2) recurring use, 4-6 points; 3) risky use, 7-9 points; and 4) hazardous use, 10 points or more.[23]

Data analysis

Categorical data are presented as frequencies (with percentages). For continuous variables, means and standard deviations (SDs) or medians (with interquartile range) are used. Associations between disease control, psychiatric diagnoses, and family composition were compared using Fisher's exact test (two-sided). To evaluate the associations between categorical data and continuous variables we used non-parametric tests (Mann-Whitney U and Kruskal-Wallis). Finally, ordinal logistic regression with disease control as the dependent variable was conducted. Data analyses were performed using IBM SPSS Statistics 25 (IBM, Somers, NY) and a p-value < 0.05 was considered significant.

Results

In total, 279 (91.2%) adolescents consented to participate, and 253 (82.7%) adolescents completed the baseline survey after a maximum of two reminders. Demographic and clinical data of the 253 study participants are summarized in Tables 1 and 2. The mean age at

diagnosis of the medical condition was 9.0 years (SD 5.3) and the mean age at first psychiatric diagnosis was 13.7 years (SD 2.7). Age at transfer differed greatly between subspecialties: rheumatology patients were the youngest to transfer (mean age 16.2 years) and gastroenterology were the oldest (mean age 19.0 years; p<0.001 for difference between groups).

Table 1. Demographic and clinical data of 253 adolescents.

Gender	**N**	**%**
Male	118	46.6
Female	132	52.2
Other	3	1.2
Pediatric subspecialty		
Diabetes	92	36.4
Rheumatology	66	26.1
Gastroenterology	45	17.8
Cardiology	19	7.5
Neurology	18	7.1
Kidney or liver disease with/without transplant	13	5.1
Lives with		
Mother and father	158	62.5
Other than with two parents	95	37.5
Disease control *		
Good control and/or adherence	70	27.7
Some evidence of concern	105	41.5
Poor control and/or adherence or more severe condition	76	30.0
Psychiatric diagnoses	**59**	**23.3**
Anxiety disorders	38	15.0
Mood disorders	18	7.1
Others **	26	10.3
Many diagnoses	22	8.7
Outpatient visits in adolescent psychiatry		
No visits	159	62.8
1-3 visits	36	14.2
More than 3 visits	58	22.9
Median ADSUME total scores (IQR) * **	**3**	**(0-6)**
Females	2	(0-6)
Males	3	(0-6)

ADSUME risk category ***	N	%
Abstinence or experimental use (0-3 points)	142	56.1
Recurring use (4-6 p)	57	22.5
Risky use (7-9 p)	27	10.7
Hazardous use (10 p or more)	26	10.3

*Data available for 251 adolescents as transfer of two adolescents was delayed.
** Others: for example, conduct disorder, attention deficit-hyperactivity disorder, psychotic disorder, eating disorders, developmental disorders.
*** One response missing.
ADSUME = Adolescent`s Substance Use Measurement; IQR = interquartile range

Table 2. Demographic and clinical data (n=253).

	Mean, years (median)	SD
Age at first medical diagnosis	**9.0 (10.1)**	**5.3**
Age at first psychiatric diagnosis	**13.7 (14.3)**	**2.7**
Age when completing the ADSUME	**17.2 (16.8)**	**1.2**
Age at transfer of care	**17.3 (17.1)**	**1.2**
Diabetes	17.2	0.7
Rheumatology	16.2	0.5
Gastroenterology	19.0	0.9
Others	17.8	1.2
Time between ADSUME and transfer of care	**0.2 (0.0)**	**0.4**
Time between medical diagnosis and transfer of care	**8.3 (7.4)**	**8.3**
Time between psychiatric diagnosis and transfer of care	**4.0 (3.2)**	**4.0**

ADSUME = Adolescent`s Substance Use Measurement

Among all study participants, 27.7% (n=70) were categorized as having good disease control and/or adherence, 41.5% (n=105) were rated as having some evidence of concern, and 30.0% (n=76) were classified as having poor disease control and/or adherence (or more severe condition) during the year preceding the transfer of care. Only 16% of adolescents with gastroenterological diseases and 14% of adolescents with diabetes had good disease control (mean of 4.6 measurements). Among adolescents with rheumatological disease, 39% had good disease control, while it was 48% in the group of "others". Gender and age at diagnosis showed no association with different disease control groups. Older age at transfer of care was associated with poorer disease control (p=0.045).

In this cohort, 23.3% of adolescents (n=59) had a psychiatric diagnosis, of whom 37.2% (n=22) had at least two different diagnoses. Anxiety disorders were most common (n=38), comprising 15.0% of all participants and 64.4% of adolescents with a psychiatric diagnosis. Females were overrepresented in anxiety disorders and males in the 'other psychiatric diagnosis' group. Nine adolescents (3.6%) received inpatient psychiatric care, with a median of 22 days (range 9-956 days) per person. Age at medical diagnosis and age at psychiatric diagnosis showed no association (p=0.32).

More than half of participants (n=142, 56.1%) were abstinent or reported only experimental substance use (Table 1). Approximately half of the adolescents reported using alcohol in the last year. The median ADSUME total score was 3.0 and the maximum score was 27 points.

Table 3 and Figure 1 summarize the associations between disease control, psychiatric diagnoses, substance use and family composition. Adolescents with psychiatric diagnoses more often had poor disease control and/or adherence or more severe disease/condition than adolescents without psychiatric diagnoses (p=0.01). Hazardous substance use was more frequent among adolescents with psychiatric diagnoses (8% vs 19%), but total ADSUME

points showed no direct association with psychiatric diagnoses nor disease control.

Adolescents who lived with two parents (n=158, 62.5%) had fewer psychiatric diagnoses than adolescents living in other kinds of families (p = 0.05). In ordinal regression, only psychiatric diagnoses were significant for disease control (Table 4).

Table 3. Family composition, disease control and substance use, by psychiatric diagnosis (n=253).

	No psychiatric diagnosis (n=194) **N (%)**	**Psychiatric diagnosis (n=59)** **N (%)**	**p**
Living with two parents	128 (66)	30 (51)	**0.05**
Disease control *			
Good control and/or adherence	59 (30)	11 (19)	0.13
Some evidence of concern	84 (43)	21 (37)	0.45
Poor control and/or adherence or more severe condition	51 (26)	25 (44)	**0.01**
ADSUME score, median (IQR) **	3 (0-6)	0 (0-6)	0.56

*Transfer of two adolescents has been delayed

** One response missing.

Other factors compared using Fisher's exact test, ADSUME median scores compared using the Mann-Whitney U test.

Table 4. Results of ordinal regression with disease control (good, moderate, or poor) as the dependent variable.

						95% CI	
	Estimate	S.E.	Wald	df	p	Lower	Upper
Threshold: poor to moderate dc	-2.963	1.718	2.975	1	0.085	-6.330	0.404
Threshold: moderate to good dc	-1.111	1.708	0.423	1	0.516	-4.459	2.237
Male vs. female	-0.147	0.240	0.377	1	0.539	-0.617	0.323
Two parents vs. other family	0.359	0.246	2.116	1	0.146	-0.125	0.842
Psychiatric dg vs. no dg	0.636	0.291	4.794	1	**0.029**	0.067	1.206
Age (continuous)	-0.158	0.096	2.675	1	0.102	-0.347	0.031

Pseudo r squared: Cox and Snell 0.046, Nagelkerke 0.052.

CI = confidence interval, SE = standard error, df = degress of freedom, dc = disease control, dg = diagnosis

Discussion

In this cross-sectional study of adolescents with chronic medical conditions, nearly a third were assessed to have poor disease control in the year preceding transfer to adult health services and almost a quarter had received a psychiatric diagnosis during adolescence. Adolescents with a comorbid psychiatric diagnosis more frequently had poor control of their medical condition than those without a psychiatric diagnosis.

In our study, 23% of the adolescents received a mental health diagnosis between the ages of 13 and 18. Adolescents living with two parents had fewer psychiatric diagnoses than their peers living in other kinds of families. The protective effect of living in a nuclear family when considering psychiatric morbidity has also been reported among the general population of children and adolescents.[24,25]. Overall, the prevalence of psychiatric diagnoses was higher in our study than in other diagnostic studies.[8,10] Regular assessment by medical professionals might have contributed to unnecessary referrals aided by the relative ease of referral to public mental health professionals. However, as the portion of adolescents with three or more outpatient visits in the department of adolescent psychiatry is comparable to the proportion of adolescents with a psychiatric diagnosis, overdiagnosis seems unlikely.

In this study, 22.5% of adolescents reported using substances regularly while a further 21.0% were categorized as risky or hazardous users. This is consistent with national Finnish data that found 15-24% of 17-18-year-old students reported monthly binge drinking.[26] Conversely, only 1% of adolescents in our cohort had used cannabis during the past year, in comparison to 8-12% of 17-18-yr-old students in Finland.[26] Although alcohol consumption has decreased

among adolescents in many developed countries, adolescent binge drinking and the accompanying risky behavior remain significant public health problems.[27]

The association between poor disease control and psychiatric comorbidity found in our study may be bidirectional: mental health problems may affect self-management resources and thus worsen disease control, while living with a severe disease may increase the emotional burden experienced. The burden of a chronic condition also includes a sense of interrupted social maturation for which substance use can sometimes present as a means of catching up although adolescents are aware of the harmful effects of substance use. [28]

Considering the modest proportion of adolescents with good disease control before transfer of care, additional strategies may be required to optimize health outcomes in adolescents whose disease is challenging to treat, who lack motivation or skills for self-management, or have mental health or substance use problems.[29,30] The treatment of anxiety and depression in adolescents is expected to improve symptoms and positively influence disease control and health care utilization.[31-33] while some adolescents will need concurrent transition of psychiatric and medical care. A child's illness is a significant stressor for parents,[34] and family psychosocial supports and interventions to minimize financial hardship also warrant consideration. Our data affirms the importance of regularly discussing substance use and its effects with adolescents with chronic medical conditions especially given its potential effect on specific medical conditions, such as a reduced seizure threshold in adolescents with epilepsy or hypoglycemia in adolescents with diabetes.[35,36]

A strength of this study is the high response rate of adolescents recruited from six different hospital departments to intentionally span a range of conditions, increasing the generalizability of our results. However, this also provided some challenges, especially regarding how disease control was defined as by definition this differs by medical condition.

Although the same researcher collected data on disease control and psychiatric diagnoses, we attempted to reduce bias by collecting these data on separate occasions, using separate files, and in different patient order. While we needed to categorize disease control subjectively in adolescents with rare diseases, the likelihood of misclassification was reduced by having two independent reviewers. As we had access to all electronic medical records in the study catchment area, including psychiatry, we were able to use specific psychiatric diagnoses and estimate disease control of medical conditions based on clinical and laboratory findings. While psychiatric diagnoses were made by the psychiatry department, standardized assessments were not routinely used. Further, some psychiatric diagnoses may have been missed if the adolescent had moved to or from another hospital district. The public health system in Finland results in adolescents receiving the same treatment regardless of socioeconomic status, with provision of psychiatric care in the private sector uncommon. In countries without public health care, associations between mental health problems and poor disease control may be even more significant than in our study.

Conclusions

In conclusion, psychiatric morbidity and poor disease control of chronic medical conditions are prevalent and closely intertwined among adolescents, reinforcing the importance of collaboration between medical and psychiatric care.[37] Maximizing mental health before adolescents transfer to adult health services appears especially important given the associations of both poor mental health and the transfer of care itself with unsatisfactory adherence to treatment and increased rates of emergency visits and hospitalizations. [12,38,39]

A Funding statement:

This study is supported by grants from the Foundation for Medical Research, the Helsinki University Hospital (TYH2019312), the Foundation for Pediatric Research and the Paulo Foundation.

A competing interest statement:

Authors have no conflicts of interest relevant to this article to disclose.

Contributor`s Statement:

Dr Mira Kallio collected data, carried out initial analyses, drafted the manuscript and reviewed and revised the manuscript. Ms Tornivuori collected data and reviewed and revised the manuscript. Drs Miettinen and Kolho participated in designing the study and reviewed and revised the manuscript. Ms Culnane and Professor Sawyer participated in study design and reviewed and revised the manuscript. Dr Kosola designed the study, coordinated, and supervised data collection and critically reviewed the manuscript for important intellectual content. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

Checklist: STROBE.

Data sharing statement: Data are available upon reasonable request.

Acknowledgments: We wish to thank all the participants of the study as well as research nurse Satu Lindström. We also acknowledge Kristiina Aalto, Eero Jokinen, Eeva-Liisa Metsähonkala, Tiina Remes and Elisa Ylinen for clinical advice regarding disease control.

References

1. Raissadati A, Nieminen H, Jokinen E, Sairanen H. Progress in late results among pediatric cardiac surgery patients: A population-based 6-decade study with 98% follow-up. *Circulation.* 2015;131(4):347-353. doi:10.1161/CIRCULATIONAHA.114.011190
2. Benchimol EI, Fortinsky KJ, Gozdyra P, Van Den Heuvel M, Van Limbergen J, Griffiths AM. Epidemiology of pediatric inflammatory bowel disease: A systematic review of international trends. *Inflamm Bowel Dis.* 2011;17(1):423-429. doi:10.1002/ibd.21349
3. Patterson CC, Karuranga S, Salpea P, et al. Worldwide estimates of incidence, prevalence, and mortality of type 1 diabetes in children and adolescents: Results from the International Diabetes Federation Diabetes Atlas, 9th edition. *Diabetes Res Clin Pract.* 2019;157:107842. doi:10.1016/j.diabres.2019.107842
4. Nap-van der Vlist MM, Dalmeijer GW, Grootenhuis MA, et al. Fatigue in childhood chronic disease. *Arch Dis Child*. 2019;104(11):1090-1095. doi:10.1136/archdischild-2019-316782
5. Maes M, Van Den Noortgate W, Fustolo-Gunnink SF, Rassart J, Luyckx K, Goossens L. Loneliness in Children and Adolescents with Chronic Physical Conditions: A Meta-Analysis. *J Pediatr Psychol.* 2017;42(6) :622-635. doi:10.1093/jpepsy/jsx046
6. Brady AM, Deighton J, Stansfeld S. Psychiatric outcomes associated with chronic illness in adolescence: A systematic review. *J Adolesc.* 2017;59:112-123. doi:10.1016/j.adolescence.2017.05.014
7. Robinson ME, Simard M, Larocque I, Shah J, Nakhla M, Rahme E. Risk of psychiatric disorders and suicide attempts in emerging adults with diabetes. *Diabetes Care.* 2020;43(2):484-486. doi:10.2337/dc19-1487
8. LaGrant B, Marquis BO, Berg AT, Grinspan ZM. Depression and anxiety in children with epilepsy and other chronic health conditions: National estimates of prevalence and risk factors. *Epilepsy Behav*. 2020;103 (Pt A):106828. doi:10.1016/j.yebeh.2019.106828
9. Ghandour RM, Sherman LJ, Vladutiu CJ, et al. Prevalence and Treatment of Depression, Anxiety, and Conduct Problems in US Children. *J Pediatr*. 2019;206:256-267.e3. doi:10.1016/j.jpeds.2018.09.021
10. Butwicka A, Olén O, Larsson H, et al. Association of Childhood-Onset Inflammatory Bowel Disease with Risk of Psychiatric Disorders and Suicide Attempt. *JAMA Pediatr.* 2019;173(10):969-978. doi:10.1001/jamapediatrics.2019.2662
11. Finnish Institute for Health and Welfare. Well-being of children and young people – School Health Promotion Study 2021. Available at: https://thl.fi/en/web/thlfi-en/statistics-and-data/statistics-by-topic/social-services-children-adolescents-and-families/well-being-of-children-and-young-people-school-health-promotion-study
12. Bernstein CM, Stockwell MS, Gallagher MP, Rosenthal SL, Soren K. Mental health issues in adolescents and young adults with type 1 diabetes: Prevalence and impact on glycemic control. *Clin Pediatr (Phila).* 2013;52(1):10-15. doi:10.1177/0009922812459950
13. Blount RL. Disease Activity Does Not Explain It All: How Internalizing Symptoms and Caregiver Depressive Symptoms Relate to Health-related Quality of Life Among Youth with Inflammatory Bowel Disease. *Inflamm Bowel Dis*. 2016;22(4):963-967. doi:10.1097/MIB.0000000000000686

14. Wong JJ, Sceats L, Dehghan M, et al. Depression and health care use in patients with inflammatory bowel disease. *J Crohn's Colitis.* 2019;13(1):19-26. doi:10.1093/ecco-jcc/jjy145
15. Sawyer SM, Drew S, Yeo MS, Britto MT. Adolescents with a chronic condition: challenges living, challenges treating. *Lancet.* 2007;369(9571):1481-1489. doi:10.1016/S0140-6736(07)60370-5
16. Shrier LA, Harris SK, Kurland M, Knight JR. Substance use problems and associated psychiatric symptoms among adolescents in primary care. *Pediatrics.* 2003;111(6 Pt 1):e699-e705. doi:10.1542/peds.111.6.e699
17. Deas D. Adolescent substance abuse and psychiatric comorbidities. *J Clin Psychiatry.* 2006;67 (7):e02. doi:10.4088/jcp.0706e02
18. Kessler RC, Berglund P, Demler O, Jin R, Merikangas KR, Walters EE. Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the national comorbidity survey replication. *Arch Gen Psychiatry.* 2005;62(6):593-602. doi:10.1001/archpsyc.62.6.593
19. Kosola Silja, Culnane Evelyn, Loftus Hayley, et al. The Bridge study protocol: an international, observational cohort study on the transition of healthcare for adolescents with chronic conditions. *BMJ Open.* 2021;11(6):e048340. Published 2021 Jun 21. doi:10.1136/bmjopen-2020-048340
20. Backström M, Tynjälä P, Ylijoki H, et al. Finding specific 10-joint Juvenile Arthritis Disease Activity Score (JADAS10) and clinical JADAS10 cut-off values for disease activity levels in non-systemic juvenile idiopathic arthritis: A Finnish multicentre study. *Rheumatology (Oxford).* 2016;55(4):615-623. doi:10.1093/rheumatology/kev353
21. DiMeglio LA, Acerini CL, Codner E, et al. ISPAD Clinical Practice Consensus Guidelines 2018: Glycemic control targets and glucose monitoring for children, adolescents, and young adults with diabetes. *Pediatr Diabetes.* 2018;19 Suppl 27:105-114. doi:10.1111/pedi.12737
22. Piskanen M. Promoting Adolescents` Abstinence from Substance Use. An Early Intervention Model for School and Student Health Care. Published online 2007. http://urn.fi/URN:ISBN:978-951-27-0510-8
23. Pirskanen M, Laukkanen E, Pietilä AM. A formative evaluation to develop a school health nursing early intervention model for adolescent substance use. *Public Health Nurs.* 2007;24(3):256-264. doi:10.1111/j.1525-1446.2007.00632.x
24. Ängarne-Lindberg T, Wadsby M. Psychiatric and somatic health in relation to experience of parental divorce in childhood. Int J Soc Psychiatry. 2012;58(1):16-25. doi:10.1177/0020764010382372
25. Perales F, Johnson SE, Baxter J, Lawrence D, Zubrick SR. Family structure and childhood mental disorders: new findings from Australia. Soc Psychiatry Psychiatr Epidemiol. 2017;52(4):423-433. doi:10.1007/s00127-016-1328-y
26. Helakorpi S, Kivimaki H. Well-being of children and young people – School Health Promotion study 2021: Large share of children and young people satisfied with their lives – a sense of loneliness has become more common. Statistical report 42/2021, National Institute for Health and Welfare, Finland. Available at https://www.julkari.fi/handle/10024/143418 . Downloaded Sep 6, 2022.
27. Siqueira L, Smith VC; COMMITTEE ON SUBSTANCE ABUSE. Binge Drinking. *Pediatrics.* 2015;136(3):e718-e726. doi:10.1542/peds.2015-2337
28. Weitzman ER, Salimian PK, Rabinow L, Levy S. Perspectives on substance use among youth with chronic medical conditions and implications for clinical guidance

and prevention: A qualitative study. *PLoS One*. 2019;14(1):e0209963. Published 2019 Jan 23. doi:10.1371/journal.pone.0209963
29. Andrade DM, Bassett AS, Bercovici E, et al. Epilepsy: Transition from pediatric to adult care. Recommendations of the Ontario epilepsy implementation task force. *Epilepsia.* 2017;58(9):1502-1517. doi:10.1111/epi.13832
30. Healy SA, Fantaneanu TA, Whiting S. The importance of mental health in improving quality of life in transition-aged patients with epilepsy. Epilepsy Behav. 2020;112:107324. doi:10.1016/j.yebeh.2020.107324
31. Bennett S, Shafran R, Coughtrey A, Walker S, Heyman I. Psychological interventions for mental health disorders in children with chronic physical illness: A systematic review. *Arch Dis Child.* 2015;100(4):308-316. doi:10.1136/archdischild-2014-307474
32. Thabrew H, Stasiak K, Hetrick SE, Wong S, Huss JH, Merry SN. E-Health interventions for anxiety and depression in children and adolescents with long-term physical conditions. *Cochrane Database Syst Rev*. 2018;8(8):CD012489. Published 2018 Aug 15. doi:10.1002/14651858.CD012489.pub2
33. Lehtimaki S, Martic J, Wahl B, Foster KT, Schwalbe N. Evidence on Digital Mental Health Interventions for Adolescents and Young People: Systematic Overview. *JMIR Ment Health*. 2021;8(4):e25847. Published 2021 Apr 29. doi:10.2196/25847
34. Mutanen A, Kosola S, Merras-Salmio L, Kolho KL, Pakarinen MP. Long-term health-related quality of life of patients with pediatric onset intestinal failure. J Pediatr Surg. 2015;50(11). doi:10.1016/j.jpedsurg.2015.05.012
35. Samokhvalov AV, Irving H, Mohapatra S, Rehm J. Alcohol consumption, unprovoked seizures, and epilepsy: a systematic review and meta-analysis. *Epilepsia*. 2010;51(7):1177-1184. doi:10.1111/j.1528-1167.2009.02426.x
36. Tetzschner R, Nørgaard K, Ranjan A. Effects of alcohol on plasma glucose and prevention of alcohol-induced hypoglycemia in type 1 diabetes-A systematic review with GRADE. *Diabetes Metab Res Rev*. 2018;34(3):10.1002/dmrr.2965. doi:10.1002/dmrr.2965
37. Fazel M, Townsend A, Stewart H, Pao M, Paz I, Walker J, Sawyer S.M, Sharpe M. Integrated care to address child and adolescent health in the 21st century: A clinical review. *JCPP Advances*.2021;e12045. doi:10.1002/jcv2.12045
38. Kosola S, Ylinen E, Finne P, Rönnholm K, Ortiz F. Implementation of a transition model to adult care may not be enough to improve results: National study of kidney transplant recipients. Clin Transplant. 2019;33(1):e13449. doi:10.1111/ctr.13449
39. Rollo A, Salardi S, Ciavarella A, et al. Transition from pediatric to adult care. Eight years after the transition from pediatric to adult diabetes care: Metabolic control, complications and associated diseases. J Endocrinol Invest. 2014;37(7):653-659. doi:10.1007/s40618-014-0090-9

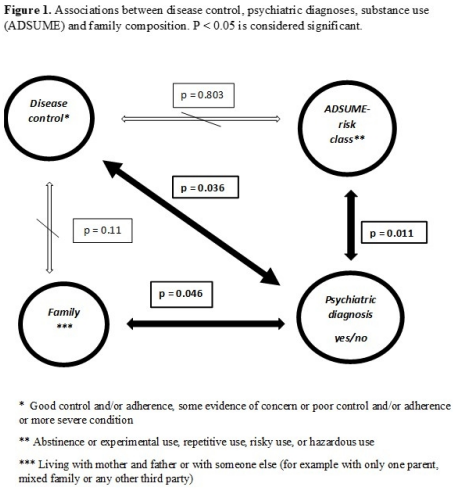


Figure 1. Associations between disease control, psychiatric diagnoses, substance use (ADSUME) and family composition. P < 0.05 is considered significant.

338x190mm (96 x 96 DPI)

Appendix 1. Adolescents Substance Use Measurement (ADSUME)

1. Do you smoke (including tobacco, cannabis and e-cigarettes)?
    a. No
    b. Occasionally
    c. Daily
2. Have you tried or used following substances during the past year? (If not, there is no need to answer the next questions)
    a. Alcohol
    b. Medication to get high
    c. Illegal drugs
    d. Alcohol together with other substances
    e. Inhaled chemicals `sniffing`
3. How many times have you tried or used other substances than tobacco during last year?
    a. 1-3 times
    b. 4-6 times
    c. about once in a month
    d. 2-3 times per month
    e. once a week or more often
4. How many drinks do you usually have at a time?
    a. 1-2 drinks
    b. 3-4 drinks
    c. 5-6 drinks
    d. 7 drinks or more
5. Have you ever been late to school or work, left in the middle of the day or stayed home from school or work because of substance use?
    a. Never
    b. Once
    c. 2-3 times
    d. 4 or more times
6. Have you encountered any of these situations when you have been under the influence of alcohol or drugs during the past year?
    a. I have hurt myself or someone else has hurt me
    b. I have hurt someone else
    c. I have been a passenger in a vehicle with a driver who was under the influence
    d. I have driven a vehicle under the influence
    e. I have broken or stolen someone else's property
    f. I have had a sexual relationship that I regret afterwards
7. How often have you been in these situations (described before)?
    a. Once
    b. Twice
    c. More Often
8. Have you ever had a blackout (i.e., trouble remembering what happened due to substance use)?
    a. Once
    b. Twice
    c. More Often
9. Have you ever passed out because of substance use?
    a. Once
    b. Twice
    c. More Often