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Childhood trauma and the use of opioids and other prescription analgesics in adolescence and young adulthood: The HUNT Study

Monica Baumann-Larsen[a,b,*], Kjersti Storheim[a,c], Helle Stangeland[b,d], John-Anker Zwart[a,b], Tore Wentzel-Larsen[d,e], Svetlana Skurtveit[f], Grete Dyb[b,d], Synne Øien Stensland[a,d]

Abstract

Opioid and nonopioid analgesics are commonly prescribed to young people to alleviate pain. Even short-term prescriptions increase the risk of persistent use and future misuse of potent analgesics, such as opioids. Childhood trauma exposure has been found to be related to pain conditions and to using more prescription analgesics. This large, prospective cohort study aimed to investigate the association of a broad range of childhood trauma exposures with prescription rates for opioid and nonopioid analgesics in adolescence and young adulthood. Self-reported data on childhood trauma exposures from adolescents (aged 13-19 years) who participated in the Young-HUNT3 Study (2006-2008, n = 8199) were linked to data from the Norwegian Prescription Database (NorPD, 2004-2021). We found that exposure to childhood trauma was consistently associated with higher prescription rates for opioids throughout adolescence and young adulthood. The highest incidence rate ratio (IRR) in adolescence was observed for sexual abuse (IRR 1.63, confidence interval [CI] 1.19-2.23). In young adulthood, the highest IRR was observed for physical violence (2.66, CI 2.27-3.12). The same overall pattern was observed for nonopioid analgesics. The more frequent prescriptions of opioid and nonopioid analgesics to participants exposed to childhood trauma suggests a higher symptom load of pain causing them to seek professional help with pain relief. Receiving potent analgesics is not without risk, and the likelihood of misuse may be elevated among trauma-exposed individuals. A trauma-informed approach to pain could be vital for guiding clinicians to the most effective and least harmful treatment for each patient.

Keywords: Childhood trauma, Pain, Opioids, Nonopioid analgesics, Adolescence, Young adulthood

1. Introduction

Opioid and nonopioid analgesics are commonly prescribed to young individuals to alleviate pain in outpatient settings.[17,18,74] Receiving prescription analgesics implies seeking help for pain management, indicating the severity of the pain condition.[27] Even short-term prescriptions increase the risk of persistent use and future misuse of potent analgesics, such as opioids,[1,35,36] and they should therefore be prescribed with great caution in all settings.[23,44] Overall, more frequent use of both opioid and nonopioid analgesics is linked to female sex, low socioeconomic status, pain in multiple sites, and psychological distress,[8,13,54,62,68,69] with prescriptions increasing sharply from midadolescence.[69] Although evidence is sparse, retrospectively assessed childhood interpersonal trauma, including sexual abuse, emotional abuse, and exposure to physical violence, has been found to be associated with using more analgesics.[6,29,64] Recent results from a large, prospective study on the relation of childhood trauma to subsequent use of over-the-counter analgesics are consistent with these findings, with results indicating an increased risk of frequent use of over-the-counter analgesics among young adults exposed to childhood trauma.[9] Trauma types representing interpersonal violence, such as bullying, sexual abuse, and physical violence, and particularly multiple types of such trauma, have been found to be especially strongly associated with frequent use of over-the-counter analgesics.[8] Such cumulative load may be of importance for the relation to analgesics use also for other trauma types.[8] Childhood trauma is associated with pain, often in combination with functional impairment as well as psychological distress, with the latter representing an independent risk factor for chronic pain.[3,5,15,72] Exposure to childhood trauma may therefore result in an increased risk of receiving prescription analgesics, including opioids.

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[a] Division of Clinical Neuroscience, Department of Research and Innovation, Oslo University Hospital, Oslo, Norway, [b] Institute of Clinical Medicine, University of Oslo, Oslo, Norway, [c] Department of Rehabilitation Science and Health Technology, Faculty of Health Sciences, Oslo Metropolitan University, Oslo, Norway, [d] Norwegian Centre for Violence and Traumatic Stress Studies, Oslo, Norway, [e] Centre for Child and Adolescent Mental Health, Eastern and Southern Norway, Oslo, Norway, [f] Department of Chronic Diseases, Norwegian Institute of Public Health, Oslo, Norway

**Corresponding author. Address: Department of Clinical Neuroscience, Oslo University Hospital, PB 4956 Nydalen, 0424 Oslo, Norway. Tel.: +47 48153345. E-mail address: monica.baumann-larsen@studmed.uio.no (M. Baumann-Larsen).*

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There is a dearth of prospective studies on the relation of childhood trauma to prescription rates for analgesics in adolescence and young adulthood. Knowledge about the potential importance of childhood trauma exposure as a risk factor for receiving prescription analgesics may inform clinical approaches to pain management for this especially vulnerable group.

In this study, we aimed to investigate the relation of a broad range of childhood trauma exposures to risk of receiving prescriptions for opioid and nonopioid analgesics in adolescence and young adulthood. We further explored whether exposure to multiple trauma types would predict an especially high prescription rate.

2. Methods

2.1. Data sources

This large, prospective cohort study used self-reported data on childhood trauma exposures from adolescents (aged 13-19 years) who participated in the Young-HUNT3 Study (2006-2008)[39] linked to data from the Norwegian Prescription Database (NorPD).[28] The linkage enabled tracking of individual prescriptions for opioid and nonopioid analgesics for the participants from 2004 to 2021. The Norwegian Institute of Public Health linked the data from the Young-HUNT3 and NorPD based on the unique personal identification number of each individual, ensuring high linkage quality.[37] Prescription data were linked for all 8199 participants, including participants who did not receive analgesics prescriptions within the follow-up period. The study was approved by the Norwegian Regional Committee for Medical Research Ethics (project ID: 2017/2229).

In Young-HUNT3, all 10,464 adolescents in the region of Norway formerly called Nord-Trøndelag were invited to participate. The participation rate in Young-HUNT3 was 78% (n = 8199). Inclusion was based on written consent from participants aged 16 years or older and from the parents of those younger than 16 years, in accordance with Norwegian law. The consent to linkage of survey data to registry data was an integrated part of the consent to participate in the HUNT Study because data from the HUNT Study are extensively used in linkage studies. Participants can withdraw their consent at any time. Individuals who withdraw consent to linkage are considered nonparticipants, and they are not included in participant counts. Most adolescents completed the self-administered questionnaire during school hours.

Norwegian prescription database is an electronic registry which has obtained data on all filled prescriptions from all pharmacies in Norway since 2004.[28] Each filled prescription is registered with patient identifiers and drug information, including the date of dispensing and an Anatomical Therapeutic Chemical (ATC) code identifying the specific drug.[77] All prescriptions filled at a pharmacy, whether issued in primary or specialist care, including hospitals and institutions, are registered. Medications directly dispensed from an institution's medication inventory are not registered.

2.2. Norwegian health services and prescription subsidy program

Residents of Norway are automatically enrolled in the public health care system, covering both primary and specialist care.[66] Specialist care, including hospital care, requires a referral, while primary care services do not. The costs of health services are subsidized by the government and maintained at an affordable rate.

Prescription medications are paid for by the recipient. Analgesics can be obtained on a reimbursed prescription for chronic pain, where the cost of medication is reduced to 39% of the total cost. To qualify, the patient must have chronic, severe pain that significantly reduces quality of life and function. Validated tools must be used to assess diagnosis, pain severity, and treatment effect. Only 2% of the entire Norwegian population received an analgesic to treat chronic pain on a reimbursed prescription in 2010, corresponding to approximately 10% of those with a diagnosis of chronic pain at the time.[57]

There is a cost limit for all payments within the public health care system, including payment for consultations and reimbursed prescriptions. Once this limit is reached, further consultations and reimbursed prescriptions are free of charge. Individuals living in a low-income household can apply for reimbursement of health costs regardless of total health expenses. For individuals younger than 16 years, medication on a reimbursed prescription will be dispensed for free, irrespective of total health expenses.

While prescription medication has a fixed maximum price, the pricing of nonprescription medication is not regulated in Norway. Nonsteroid anti-inflammatory drugs (NSAIDs) and paracetamol can be purchased over the counter; however, acquiring them through a prescription can be more affordable.

2.3. Measures

2.3.1. Sociodemographics in adolescence

Data on sex and age at the time of attendance in the Young-HUNT3 Study were obtained from the Norwegian National Population Registry. *Pubertal development* was assessed using a four-item version of the pubertal development scale by Carskadon and Acebo[14]. Participants were asked 2 questions regarding household structure, and they were categorized as "living with both parents" or "living in other type of household" for the variable *Household structure*. The adolescents were asked whether they perceived their family economy as below average, average, or above average and were grouped into "family economy average or better" and "family economy below average" for the variable *Family economy*.

2.3.2. Childhood trauma

2.3.2.1. Lifetime trauma screen

Childhood exposure to potentially traumatic events, termed *childhood trauma*, was assessed in adolescence by a lifetime trauma screen derived from the University of California, Los Angeles Posttraumatic Stress Disorder Reaction Index (UCLA PTSD Reaction Index), part I,[70,71] adapted to a Norwegian context. All events were listed under the question "Did you ever experience any of these events?" Response alternatives were "never," "yes, last year," and "yes, in my life" for all items. Participants responding "yes, last year" and "yes, in my life" were labelled as exposed.

2.3.2.2. Direct interpersonal trauma

Items on exposure to direct interpersonal trauma included physical violence, bullying, and sexual abuse. Participants were classified as exposed to *physical violence* if they responded affirmatively to the statement "been subjected to violence (beaten/injured)". Participants who answered "yes" to the

statement "been threatened or physically harassed by fellow students at school over a period of time" were classified as exposed to *bullying*. Exposure to sexual abuse was measured by 2 items: "subjected to an unpleasant sexual act by a peer" and "subjected to an unpleasant sexual act by an adult." Reports of exposure to either or both were categorized as *sexual abuse*. A sum score (range 0-3) of the 3 items assessing exposure to different types of direct interpersonal trauma was computed and labelled *Interpersonal trauma, number of types*. For regression analyses, scores of 2 and 3 were combined because of low counts.

2.3.2.3. Other trauma

Participants were asked whether they had "seen someone else being subjected to violence," and responders answering affirmatively were classified as having been a *witness to violence.* Responders answering "yes" to either "someone in your family was seriously ill" or "the death of someone close to you" was classified as exposed to *severe illness or death of someone close*. Participants responding "yes" to experiencing "a disaster (fire, hurricane or similar)", "a serious accident (eg, serious car accident)," "painful or frightening hospital treatment for a disease or an accident," or "other experience that was very frightening, dangerous or violent" were classified as exposed to *other potentially traumatic event*. A sum score (range 0-3) of the 3 items assessing exposure to different types of other trauma was computed and labelled *other trauma, number of types*.

2.3.3. Chronic pain and psychological symptoms in adolescence

Post-traumatic stress symptoms, psychological distress, headaches, and musculoskeletal pain were assessed in Young-HUNT3; these measures are detailed in Supplementary Table 1 (available at http://links.lww.com/PAIN/B975).

2.3.4. Opioid and nonopioid prescription analgesics

Counts of all prescriptions of opioid analgesics (ATC group N02A) and the nonopioid analgesics paracetamol (ATC group N02BE), gabapentinoids (N03AX12 and N03AX16), and NSAIDs (non-steroid anti-inflammatory drugs, ATC group M01A) filled by the participants as (1) adolescents and (2) young adults in the period 2004 to 2021 served as outcome measures. The number of filled prescriptions within each analgesic group was counted for each individual. Prescriptions in adolescence (age 13-19 years) and in young adulthood (age 20-32 years) were analyzed separately, accounting for number of follow-up years (eg, an individual who was aged 13 years in 2006 would have 7 years of follow-up as an adolescent and 9 years as a young adult, while an individual who was aged 19 years in 2006 would have 3 years of follow-up as an adolescent and 13 years as a young adult). The count measure for each developmental stage was chosen based on the knowledge that prescription opioid use is relatively rare among adolescents and young adults and that very few will meet the criteria of previously used definitions for persistent use.[32,33] Prescriptions with a reimbursement code indicating palliative care (−90) were excluded.[48,49]

2.4. Statistical procedures

Descriptive data on the adolescents' sociodemographics, exposure to childhood trauma, and nonopioid analgesics prescriptions were presented stratified by the follow-up periods in which the participants received opioid prescriptions and by sex. Categorical variables were described with counts and percentages; continuous variables were described with mean and SD. The half rule was used to handle missing values, meaning that participants who answered at least half of the questions were used to calculate mean scores and sum scores. Number of types of exposure to other trauma types was presented by number of types of exposure to interpersonal trauma.

The number of prescriptions of opioids, paracetamol, NSAIDs, and gabapentinoids filled in (1) adolescence (age 13-19 years) and (2) young adulthood (age 20-32 years) served as separate outcomes in zero-inflated negative binomial regression analyses. Variation in follow-up time was accounted for by offsetting for log follow-up time, resulting in incidence rate ratios that may be interpreted as ratios between rates per year.[25] Exposure to each trauma type was assessed in separate complete case analyses, while number of trauma types was assessed in one complete case analysis including interpersonal trauma and other trauma types. For the subsample reporting trauma exposure, symptoms reported in adolescence were assessed in separate zero-inflated negative binomial regression analyses for the number of analgesics prescriptions filled in adolescence and young adulthood

All the described analyses were adjusted for the variables age, sex, *household structure*, and *family economy* as reported in adolescence.[7,46] Analyses for prescription analgesics in adolescence were additionally adjusted for *pubertal development*.[16,47] Separate and unadjusted zero-inflated negative binomial regression analyses were run to show the association of background variables to the outcomes. Statistical analyses were conducted using R version 4.2.2 and Stata version 17.0, with the R package data.table[24] for aggregating from data on individual prescriptions to number of prescriptions for participants and Stata for estimation of zero-inflated negative binomial regression models.

3. Results

3.1. Sample descriptives

Girls and boys were evenly represented among participating adolescents in the Young-HUNT3 Study (50.3% female participants, n = 4128). During the study period, about 1 in 10 participants received opioid analgesics in adolescence and 2 in 5 received opioids in young adulthood (**Table 1**, Supplementary Table 2, available at http://links.lww.com/PAIN/B975). Among nonopioids, NSAIDs were prescribed to the largest proportion of participants, both in adolescence (about 2 in 5) and in young adulthood (2 in 3), while paracetamol prescriptions were received by fewer participants than opioid prescriptions, both in adolescence and in young adulthood. Very few participants received gabapentinoid prescriptions. Participants who received opioid prescriptions in both adolescence and young adulthood were overall more exposed to childhood trauma (**Table 1**). This cohort also received more nonopioid prescription analgesics in both developmental stages. As adolescents, participants in this cohort reported more psychological and somatic symptomatology, including post-traumatic stress, psychological distress, recurrent musculoskeletal pain, and headaches. Girls reported higher childhood exposure to sexual abuse, and boys reported higher exposure to physical violence and witnessing violence (Supplementary Table 2, available at http://links.lww.com/PAIN/B975). More female participants than male participants received opioid

Table 1

Number and proportion of participants receiving opioid analgesics in adolescence or young adulthood by background factors, trauma, and history of nonopioid analgesics.

	n	All	No prescription opioids in adolescence or young adulthood	Prescription opioids in adolescence only	Prescription opioids in young adulthood only	Prescription opioids in adolescence and young adulthood
		n (%)/mean (SD)	n (%)/mean (SD)	n (%)/mean (SD)	n (%)/mean (SD)	n (%)/mean (SD)
All participants	8199	8199	4314 (52.6)	378 (4.6)	2947 (35.9)	560 (6.8)
Female participants	4128	4128 (50.3)	1962 (47.5)	208 (5.04)	1601 (38.8)	357 (8.7)
Male participants	4071	4071 (49.7)	2352 (57.8)	170 (4.2)	1346 (33.1)	203 (5.0)
Age at Young-HUNT3, mean (min 12.7, max 20.9)	8199	15.9 (1.7)	15.8 (1.7)	15.6 (1.7)	16.0 (1.7)	16.0 (1.7)
Pubertal development score, mean (range 1-4)	7511	3.1 (0.7)	3.1 (0.7)	3.1 (0.6)	3.1 (0.7)	3.2 (0.6)
Socioeconomic factors						
Family economy below average	7636	708 (9.3)	351 (8.7)	27 (7.6)	266 (9.7)	64 (12.1)
Household, not living with both parents	8104	3776 (46.6)	1874 (43.9)	173 (46.3)	1433 (49.2)	296 (53.6)
Direct interpersonal trauma						
By type						
Bullying	7803	628 (8.1)	284 (6.9)	22 (6.0)	257 (9.2)	65 (12.0)
Physical violence	7809	789 (10.1)	340 (8.3)	29 (7.9)	340 (12.2)	80 (14.8)
Sexual abuse	7829	430 (5.5)	189 (4.6)	18 (4.9)	165 (5.9)	58 (10.7)
By number of types	7833					
No events		6464 (82.5)	3512 (85.1)	313 (84.6)	2226 (79.7)	413 (76.1)
1 type		987 (12.6)	457 (11.1)	48 (13.0)	407 (14.6)	75 (13.8)
≥2 types		382 (4.9)	158 (3.8)	9 (2.4)	160 (5.7)	55 (10.1)
Other trauma						
By type						
Witness to violence	7812	1810 (23.2)	869 (21.1)	82 (22.4)	692 (24.8)	167 (30.9)
Disease or death of someone close	7848	5757 (73.4)	2979 (72.0)	278 (75.1)	2073 (74.1)	427 (78.8)
Severe accident, disaster, or other traumatic event	7848	2481 (31.6)	1168 (28.2)	115 (31.0)	959 (34.3)	239 (44.0)
By number of types	7863					
No events		1657 (21.1)	942 (22.7)	72 (19.4)	570 (20.3)	73 (13.4)
1 type		3307 (42.1)	1803 (43.5)	168 (45.3)	1133 (40.4)	203 (37.4)
2 types		1956 (24.9)	990 (23.9)	86 (23.2)	709 (25.3)	171 (31.5)
3 types		943 (12.0)	411 (9.9)	45 (12.1)	391 (14.0)	96 (17.7)
≥1 nonopioid prescriptions in adolescence	8199					
Paracetamol		646 (7.9)	193 (4.5)	89 (23.5)	215 (7.3)	149 (26.6)
NSAIDs		3196 (39.0)	1243 (28.8)	270 (71.4)	1234 (41.9)	449 (80.2)
Gabapentinoids		21 (0.3)	<5	<5	<5	9 (1.6)
≥1 nonopioid prescriptions in young adulthood	8199					
Paracetamol		2439 (29.8)	669 (15.5)	73 (19.3)	1370 (46.5)	327 (58.4)
NSAIDs		5472 (66.7)	2238 (51.9)	235 (62.2)	2491 (84.5)	508 (90.7)
Gabapentinoids		178 (2.2)	18 (0.4)	<5	108 (3.7)	47 (8.4)

(*continued on next page*)

Table 1 (*continued*)

	n	All	No prescription opioids in adolescence or young adulthood	Prescription opioids in adolescence only	Prescription opioids in young adulthood only	Prescription opioids in adolescence and young adulthood
		n (%)/mean (SD)	n (%)/mean (SD)	n (%)/mean (SD)	n (%)/mean (SD)	n (%)/mean (SD)
Symptoms reported in adolescence						
Psychological distress (SCL-5, 1-4)	7961	1.50 (0.55)	1.46 (0.51)	1.49 (0.56)	1.54 (0.58)	1.64 (0.65)
Post-traumatic stress symptoms (0-3)	5016	0.82 (0.99)	0.73 (0.93)	0.82 (0.98)	0.90 (1.05)	1.00 (1.07)
Musculoskeletal pain, weekly	8035	2748 (34.2)	1190 (28.2)	139 (37.5)	1124 (38.9)	295 (53.5)
Headaches, weekly	7619	617 (8.10)	226 (5.6)	39 (11.1)	274 (10.0)	78 (15.1)

NSAIDs, nonsteroid anti-inflammatory drugs SCL-5, Hopkins Symptom Checklist, short version with five items.

Table 2

Zero-inflated negative binomial regression analyses for number of prescriptions of analgesics in adolescence and young adulthood by type of traumatic events and number of types of direct interpersonal trauma and other trauma types.

	n	Opioids		Nonopioid analgesics			
		Opioids		Paracetamol		NSAIDs	
		IRR (95% CI)	*P*	IRR (95% CI)	*P*	IRR (95% CI)	*P*
Adolescence (age 12-19)		n = 938		n = 646		n = 3196	
Direct interpersonal trauma							
Bullying	7244	1.46 (1.10, 1.94)	0.009	1.33 (0.93, 1.89)	0.113	1.21 (1.04, 1.41)	0.013
Sexual abuse	7266	1.63 (1.19, 2.23)	0.002	1.08 (0.71, 1.65)	0.718	1.26 (1.06, 1.50)	0.011
Physical violence	7244	1.50 (1.17, 1.94)	0.002	1.07 (0.76, 1.50)	0.693	1.05 (0.91, 1.21)	0.510
Other trauma types							
Witness to violence	7245	1.17 (0.97, 1.41)	0.099	0.98 (0.77, 1.26)	0.902	1.04 (0.94, 1.15)	0.461
Severe illness or death of someone close	7269	1.37 (1.13, 1.66)	0.001	1.56 (1.23, 1.99)	<0.001	1.34 (1.21, 1.48)	<0.001
Severe accident, disaster, or other traumatic event	7274	1.59 (1.35, 1.88)	<0.001	1.57 (1.28, 1.94)	<0.001	1.30 (1.19, 1.42)	<0.001
Direct interpersonal trauma, number of types							
1 type	7270	0.83 (0.64, 1.07)	0.141	0.70 (0.51, 0.97)	0.033	0.93 (0.81, 1.06)	0.248
≥2 types	7270	1.61 (1.13, 2.29)	0.008	1.22 (0.76, 1.95)	0.419	1.18 (0.97, 1.44)	0.106
Other trauma, number of types							
1 type	7270	1.24 (0.99, 1.56)	0.067	1.49 (1.13, 2.00)	0.005	1.27 (1.13, 1.42)	<0.001
2 types	7270	1.76 (1.37, 2.27)	<0.001	1.88 (1.38, 2.57)	<0.001	1.45 (1.28, 1.65)	<0.001
3 types	7270	1.63 (1.19, 2.22)	0.002	1.92 (1.29, 2.87)	0.001	1.48 (1.25, 1.74)	<0.001
Young adulthood (age 20-32)		n = 3507		n = 2439		n = 5472	
Direct interpersonal trauma							
Bullying	7455	1.72 (1.43, 2.06)	<0.001	2.20 (1.82, 2.67)	<0.001	1.49 (1.34, 1.66)	<0.001
Sexual abuse	7480	1.59 (1.28, 1.98)	<0.001	1.38 (1.10, 1.75)	0.006	1.24 (1.08, 1.41)	0.002
Physical violence	7460	2.66 (2.27, 3.12)	<0.001	1.95 (1.63, 2.32)	<0.001	1.32 (1.19, 1.46)	<0.001
Other trauma types							
Witness to violence	7461	1.96 (1.74, 2.21)	<0.001	1.51 (1.32, 1.72)	<0.001	1.20 (1.11, 1.29)	<0.001
Severe illness or death of someone close	7485	1.17 (1.04, 1.31)	0.008	1.39 (1.22, 1.58)	<0.001	1.21 (1.13, 1.30)	<0.001
Severe accident, disaster, or other traumatic event	7490	1.69 (1.52, 1.88)	<0.001	1.62 (1.44, 1.82)	<0.001	1.24 (1.17, 1.33)	<0.001
Direct interpersonal trauma, number of types							
1 type	7484	1.40 (1.20, 1.64)	<0.001	1.35 (1.15, 1.60)	<0.001	1.23 (1.12, 1.36)	<0.001
≥2 types	7484	1.94 (1.53, 2.46)	<0.001	2.07 (1.61, 2.66)	<0.001	1.35 (1.16, 1.56)	<0.001
Other trauma, number of types							
1 type	7484	1.02 (0.89, 1.17)	0.761	1.26 (1.08, 1.47)	0.003	1.16 (1.06, 1.26)	0.001
2 types	7484	1.48 (1.27, 1.72)	<0.001	1.58 (1.33, 1.87)	<0.001	1.28 (1.16, 1.41)	<0.001
3 types	7484	1.82 (1.49, 2.21)	<0.001	1.84 (1.49, 2.27)	<0.001	1.33 (1.19, 1.50)	<0.001

Complete case analyses adjusted for age, sex, household structure, and family economy as reported in adolescence. Analyses for prescriptions received in adolescence are additionally adjusted for pubertal development. Trauma types were assessed in separate analyses, while number of types was assessed in 1 analysis including interpersonal trauma and other trauma types. Number of participants included in analyses is the same for all analgesics because data on filled prescriptions were available for all participants.

IRR, incidence rate ratio; NSAIDs, nonsteroid anti-inflammatory drugs.

Table 3

Zero-inflated negative binomial regression analyses for number of prescriptions of analgesics in adolescence and young adulthood by symptoms as reported in adolescence.

	n	Opioids		Nonopioid analgesics			
		Opioids		Paracetamol		NSAIDs	
		IRR (95% CI)	*P*	IRR (95% CI)	*P*	IRR (95% CI)	*P*
Analgesics use in adolescence							
Psychological distress	5807	1.06 (0.91, 1.24)	0.460	1.07 (0.87, 1.30)	0.537	1.07 (0.98, 1.16)	0.128
Posttraumatic stress symptoms	4753	1.05 (0.95, 1.40)	0.338	1.11 (0.99, 1.25)	0.064	1.13 (1.07, 1.19)	<0.001
Musculoskeletal pain	5790	1.35 (1.24, 1.47)	<0.001	1.56 (1.42, 1.72)	<0.001	1.29 (1.24, 1.35)	<0.001
Headaches	5447	1.54 (1.15, 2.06)	0.003	1.91 (1.35, 2.70)	<0.001	1.86 (1.60, 2.17)	<0.001
Analgesics use in young adulthood							
Psychological distress	5954	1.48 (1.33, 1.64)	<0.001	1.26 (1.13, 1.42)	<0.001	1.17 (1.10, 1.25)	<0.001
Posttraumatic stress symptoms	4858	1.31 (1.23, 1.40)	<0.001	1.17 (1.09, 1.25)	<0.001	1.10 (1.06, 1.14)	<0.001
Musculoskeletal pain	5939	1.47 (1.39, 1.55)	<0.001	1.49 (1.40, 1.58)	<0.001	1.26 (1.22, 1.30)	<0.001
Headaches	5586	1.88 (1.54, 2.29)	<0.001	2.38 (1.94, 2.93)	<0.001	1.67 (1.48, 1.88)	<0.001

Subsample analysis among participants exposed to childhood trauma.
Complete case analyses adjusted for age, sex, household structure, and family economy. Analyses for analgesics use in adolescence were additionally adjusted for pubertal development.
IRR, incidence rate ratio; NSAIDs, nonsteroid anti-inflammatory drugs.

and nonopioid analgesics, both in adolescence and in young adulthood, and girls reported more chronic pain and psychological symptoms than boys. There was considerable overlap of exposure to different trauma types, with a substantial subgroup reporting exposure to the maximum number of types for both interpersonal trauma and other trauma (Supplementary Table 3, available at http://links.lww.com/PAIN/B975).

3.2. Results from regression analyses

The results from the regression analyses showed significant and consistent relationships between the broad range of childhood trauma exposures and higher prescription rates for opioid analgesics in both the shorter term, during adolescence, and the longer term, during young adulthood (**Table 2**). Patterns were similar for paracetamol and NSAIDs, although less distinct in adolescence than in young adulthood. Childhood trauma exposure was generally significantly related to higher prescription rates for NSAIDs in adolescence, whereas prescriptions for paracetamol were only significantly linked to prior exposure to *severe illness or death of someone close* and *severe accidents, disasters, or other event* (**Table 2**). In young adulthood, childhood trauma was significantly associated with higher prescription rates for both NSAIDs and paracetamol (**Table 2**).

Exposure to more than one type of direct interpersonal trauma predicted particularly high prescription rates for both opioid and nonopioid analgesics across adolescence and young adulthood, suggesting a dose-response relationship (**Table 2**). A similar trend was observed for other trauma types (**Table 2**).

Among trauma-exposed participants, psychological and somatic symptoms, including post-traumatic stress, psychological distress, recurrent musculoskeletal pain, and headaches experienced in adolescence, were found to be significantly associated with higher prescription rates for opioids, paracetamol, and NSAIDs in young adulthood. Although less distinct, a similar trend was observed for prescriptions received in adolescence, most prominent for pain (**Table 3**). Prescriptions of gabapentinoids were limited in both adolescence and young adulthood, and the results for gabapentinoids were less reliable (Supplementary Table 4, available at http://links.lww.com/PAIN/B975). Background factors adjusted for were significantly related to the outcomes (**Table 4**).

Table 4

Zero-inflated negative binomial regression analyses for number of prescriptions of analgesics in adolescence and young adulthood by background factors as reported in adolescence.

	n	Opioids		Nonopioid analgesics			
		Opioids		Paracetamol		NSAIDs	
		IRR (95% CI)	*P*	IRR (95% CI)	*P*	IRR (95% CI)	*P*
Analgesics use in adolescence							
Age	8199	1.10 (1.05, 1.15)	<0.001	0.92 (0.87, 0.97)	<0.001	1.04 (1.01, 1.06)	0.002
Sex, female	8199	1.97 (1.69, 2.30)	<0.001	1.58 (1.31, 1.89)	<0.001	1.69 (1.56, 1.83)	<0.001
Pubertal development score	7511	1.42 (1.26, 1.60)	<0.001	0.95 (0,82, 1.09)	0.465	1.22 (1.15, 1.30)	<0.001
Family economy below average	7636	1.93 (1.51, 2.46)	<0.001	1.22 (0.89, 1.67)	0.225	1.10 (0.96, 1.27)	0.170
Household structure, not living with both parents	8104	1.30 (1.12, 1.52)	0.001	1.33 (1.11, 1.60)	0.002	1.01 (0.94, 1.10)	0.694
Analgesics use in young adulthood							
Age	8199	1.22 (1.19, 1.26)	<0.001	1.22 (1.19, 1.26)	<0.001	1.22 (1.20, 1.24)	<0.001
Sex, female	8199	1.71 (1.55, 1.89)	<0.001	2.22 (1.99, 2.47)	<0.001	1.50 (1.41, 1.60)	<0.001
Family economy below average	7636	2.13 (1.79, 2.52)	<0.001	1.56 (1.29, 1.89)	<0.001	1.29 (1.16, 1.449)	<0.001
Household structure, not living with both parents	8104	1.77 (1.61, 1.95)	<0.001	1.43 (1.28, 1.60)	<0.001	1.21 (1.14, 1.29)	<0.001

Background factors were assessed in unadjusted, separate complete case analyses.
IRR, incidence rate ratio; NSAIDs, nonsteroid anti-inflammatory drugs.

4. Discussion

To our knowledge, this is the first prospective study investigating the relationship between childhood trauma exposure and prescription rates for opioid and nonopioid analgesics in adolescence and young adulthood. Overall, we found that exposure to childhood trauma was consistently and significantly related to higher prescription rates for opioids throughout adolescence and young adulthood. Although somewhat less pronounced in adolescence, similar patterns were observed for nonopioid analgesics. A higher cumulative load of trauma was linked to higher prescription rates for both opioid and nonopioid analgesics, suggesting a dose-response relationship.

Our finding that opioids are more commonly prescribed to adolescents and young adults exposed to childhood trauma is consistent with the results from studies where childhood trauma exposure has been assessed retrospectively.[6,64] Our results suggest that trauma-exposed young people may be overrepresented in the subgroup exposed to high-risk opioid prescription practices. Such practices, including the prescription of higher doses, longer duration and use of long-acting drugs, are still common in populations of young people where the overall prescription rate is decreasing.[17,61] The risk of addiction and misuse may be higher among trauma-exposed individuals,[19,65,76] and great caution is warranted when prescribing opioids to this group.

Socioeconomic factors increasing risk of trauma exposure may also increase risk of receiving long-term opioid prescriptions.[52] Despite national variations in prescription practices, it is observed that patients with psychosocial problems receive more opioid prescriptions than individuals without such problems.[13,58,62] This study was conducted in Norway, where prescription rates for opioids are generally low[33] and health care is accessible and affordable.[66] While this could mitigate the impact of socioeconomic differences in health, health care utilization still differs with socioeconomic status.[34] This could affect the health care received, including analgesics prescriptions. A recent study on adults in Norway found that socioeconomic factors remain strongly associated with long-term opioid use, also when accounting for pain conditions and mental health diagnoses.[52] Our finding that childhood trauma exposure was associated with higher analgesics prescription rates after adjustment for socioeconomic factors could indicate that the higher prevalence of childhood trauma among children growing up with a lower socioeconomic status is a driving force behind the observed higher risk of long-term opioid use in this group.

The higher prescription rates for nonopioid analgesics among participants exposed to childhood trauma is consistent with previous findings from studies on adults where trauma has been assessed retrospectively.[64] The higher prescription rates for both opioid and nonopioid analgesics among trauma-exposed participants found in this study could indicate a higher symptom load of pain in this group, and we found that pain in adolescence was related to higher prescription rates throughout adolescence and young adulthood for trauma-exposed participants. There are indications that exposure to childhood trauma may increase the risk of persistent pain, although most studies on the subject assess childhood trauma retrospectively,[21,63] possibly introducing bias,[20,45] and prospective findings are conflicting.[43,59,60] Trauma reactions such as sleep disturbances, hypervigilance, and avoidance are symptoms considered to be relevant for the maintenance and exacerbation of pain conditions,[7,10,38,51,53,56] and our finding that post-traumatic stress symptoms were related to higher prescription rates in young adulthood among trauma-exposed participants aligns with this. Childhood interpersonal trauma is considered a predisposing factor for alterations in pain signaling leading to chronic pain.[26] Neurobiological findings indicate that early life stress contributes to alterations in pathways involved in pain signaling.[10,11,50] A higher cumulative load of stress and comorbidities may increase the risk of pain chronification,[10] which supports our finding that exposure to multiple types of trauma was particularly predictive of a higher prescription rate. This finding also aligns with studies indicating that exposure to multiple types of interpersonal trauma is more predictive of future health outcomes than any individual trauma type.[2,12,40] Our finding that prescription rates for analgesics tended to be higher already in adolescence among trauma-exposed participants is consistent with previous findings that pain may present as an early symptom after trauma exposure.[30,73] The higher prescription rates found for analgesics in young adulthood aligns with prior knowledge of the lasting detrimental effect of trauma on health, where psychological and somatic comorbidities may increasingly add to the burden of coping with pain.[4,5,10]

In addition to the mechanisms outlined above, linking trauma exposure to pain, exposure to childhood trauma is associated with risk behavior and more frequent injuries.[31,41,55] This may result in more encounters with health care services for acute pain management.

The overlap of trauma exposure and a higher symptom load of pain is increasingly recognized.[7,30] A trauma-informed approach to pain management could help identify the best treatment for each patient and may be particularly important for young people. This study showed that several young people exposed to childhood trauma turned to health care services for help with pain relief. This group often refrains from seeking psychosocial treatment regardless of high needs,[67,75] and the assessment of trauma exposure in young people seeking professional help with pain management could be the first step in providing trauma-specific health care to trauma-exposed individuals.

4.1. Strengths and limitations

The strengths of this study include the large sample size, prospective design, and access to longitudinal prescription data for the participants over a period of 18 years. The high participation rate in the adolescent survey and survey questions derived from validated instruments allowed for a thorough assessment of exposures. This study was conducted in a geographical region without metropolitan areas and with low immigration[39]; however, previous studies have found similar rates of long-term opioid use regardless of such characteristics.[58] Although health care is highly accessible and affordable in Norway, the associations revealed in this study seem to conform with patterns found in populations with different health care systems,[6,7,58,64] and we therefore consider that these associations may be generalized to other populations. The universal mechanisms outlined above also supports the generalizability of results across populations with different prescription rates.

A limitation of our study is the lack of information regarding other treatments offered to these young people, which prevents us from making assumptions about the individual appropriateness of the prescribed analgesics.

Participants may have encountered traumatic events in adolescence after the completion of the adolescent survey, leading to them being misclassified as unexposed. This could lead to an underestimation of the true incidence rate ratio (IRR). The trauma measure used in this study relies on self-report and is a subjective measure. Reports from caregivers or health care

providers would only capture events the adolescents had disclosed, and adolescents do not always tell adults about trauma exposure.[42] Alternative objective measures such as court records would not capture all the events of interest in this study. Considering the sensitivity of the subject, social desirability bias is a concern. Our findings may also be subject to recall bias, a systematic difference in reporting between groups.

The trauma measure used does not allow for distinction between exposures according to their degree of severity. While it is likely that relevant traumatic events are captured by the measures used, events with a low potential for causing trauma-related symptoms cannot be distinguished from events with a high potential for causing trauma-related symptoms.

It is also a limitation that although the UCLA PTSD Reaction Index is a validated instrument, it has not been validated in Norwegian.

The small group of adolescents not in school (n = 493) were underrepresented among survey participants (23.3% participation). This may have led to a slight underestimation of the true IRR because dropping out of school has generally been found to be associated with poorer health.[22] The significant associations of socioeconomic factors to higher prescription rates for NSAIDs and paracetamol (**Table 4**) could be confounded by the lower price of prescription medications compared with the same medication purchased over the counter.

Registry data from NorPD used in this article are on filled prescriptions. Thus, we do not know whether the medication was actually used after it was obtained from the pharmacy. Paracetamol and NSAIDs are also available without a prescription, and this may affect the prescription rates observed for these nonopioid analgesics. Medication received during hospital stays or in institutions is not registered in NorPD.

4.2. Conclusion and implications

The consistently and significantly higher prescription rates for opioid and nonopioid analgesics to participants exposed to childhood trauma likely reflects a higher symptom load of pain. Psychological symptoms debuting in adolescence may also be of importance for the observed higher prescription rates among trauma-exposed individuals. Among prescription analgesics, opioids may be particularly detrimental for trauma-exposed young people because of an elevated risk of misuse and addiction. A trauma-informed approach to pain may help guide clinicians to the most effective and least harmful treatment for each patient. This approach may also provide an opportunity to offer trauma-specific treatment to a group which often refrains from seeking psychosocial treatment.

Conflict of interest statement

The authors have no conflicts of interest to declare.

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Unfortunately, the authors are not able to share the data analyzed in this study, as they belong to the third parties, the Trøndelag Health Study and Norwegian Institute of Public Health (NorPD). The linked data set was generated for the Killing Pain project after obtaining necessary permits.

Data availability: The authors do not have permission to share the data analyzed in this study, as it belong to third parties, the Trøndelag Health Study and Norwegian Institute of Public Health.

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