

Adolescent Chronic Fatigue Syndrome: Prevalence, Incidence, and Morbidity

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KEY WORDS

chronic fatigue, adolescents, epidemiology, incidence, prevalence

ABBREVIATIONS

CFS—chronic fatigue syndrome

CDC—Centers for Disease Control and Prevention

GP—general practitioner

NIVEL—Dutch Institute for Research of Health Services

DPSU—Dutch Pediatric Surveillance Unit

CIS-20—Checklist Individual Strength

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WHAT'S KNOWN ON THIS SUBJECT: Adolescent chronic fatigue syndrome (CFS) is a disabling illness. The majority of adolescents with CFS miss significant amounts of school. Little is known about the epidemiology of CFS in adolescents.



WHAT THIS STUDY ADDS: The prevalence of adolescent chronic fatigue syndrome (CFS) diagnosed by general practitioners was approximately 111 per 100 000 (0.11%) per year and the incidence of CFS diagnosed by pediatricians was 12 per 100 000 (0.012%) per year. Adolescent CFS is a well-accepted diagnosis among pediatricians but is probably underrecognized by primary health care providers.

abstract

FREE

OBJECTIVE: To determine nationwide general practitioner (GP)-diagnosed prevalence and pediatrician–diagnosed incidence rates of adolescent chronic fatigue syndrome (CFS), and to assess CFS morbidity.

DESIGN AND SETTING: We collected data from a cross-sectional national sample among GPs and prospective registration of new patients with CFS in all pediatric hospital departments in the Netherlands.

PATIENTS AND METHODS: Study participants were adolescents aged 10 to 18 years. A representative sample of GPs completed questionnaires on the prevalence of CFS in their adolescent patients. Pediatric hospital departments prospectively reported new cases of CFS in adolescent patients. For every new reported case, a questionnaire was sent to the reporting pediatrician and the reported patient to assess CFS morbidity. Prevalence was estimated through the data from GP questionnaires and incidence was estimated on the basis of cases newly reported by pediatricians from January to December 2008.

RESULTS: Prevalence was calculated as 111 per 100 000 adolescents and incidence as 12 per 100 000 adolescents per year. Of newly reported patients with CFS, 91% scored at or above cutoff points for severe fatigue and 93% at or above the cutoff points for physical impairment. Forty-five percent of patients with CFS reported >50% school absence during the previous 6 months.

CONCLUSIONS: Clinically diagnosed incidence and prevalence rates show that adolescent CFS is uncommon compared with chronic fatigue. The primary adverse impact of CFS is extreme disability associated with considerable school absence. *Pediatrics* 2011;127:e1169–e1175

Chronic fatigue syndrome (CFS) in adolescents often has an extensive disease course that may lead to considerable school absence and long-term consequences for educational and social development.^{1–3} To assess the effects of chronic fatigue on Dutch society and adolescent health care, the determination of sound prevalence and incidence rates is mandatory. Almost all currently available estimates of incidence and prevalence were determined in adult populations. Moreover, international research has revealed a wide variation in rates, partly because of differences in patient age limits and methods (eg, settings and applied diagnostic criteria) used in various studies. In adolescents, population surveys revealed annual incidence rates of 0.5% and prevalence rates of 0.19% to 1.29%,^{4–7} with female-to-male ratios that varied from 2:1 up to 3:1.^{5,8,9} Most of these estimates were primarily determined on the basis of self-reported data obtained from patients by use of questionnaires and telephone interviews.

Several diagnostic criteria for CFS exist, of which the 1994 Centers for Disease Control and Prevention (CDC) criteria are commonly used in the Netherlands.^{10–13} According to these criteria CFS is characterized by severe and disabling new-onset fatigue that lasts for at least 6 months and is accompanied by 4 or more of the following symptoms: impaired memory or concentration, sore throat, tender cervical or axillary lymph nodes, muscle pain, multiple joint pain, new headaches, unrefreshing sleep, and postexertional malaise. Somatic and psychiatric illnesses should be excluded.¹⁰

Accurate diagnosis of CFS is a complex task that requires exclusion of other illnesses that could cause similar complaints but require different treatment. Therefore, clinical estimates of CFS prevalence and incidence can be

of value in addition to the aforementioned population surveys.

The primary aim of this study was to determine adolescent CFS prevalence and incidence rates as reported by general practitioners (GPs) and pediatricians, respectively, in the Netherlands. We also investigated the severity of symptoms and disability and the extent of school absence associated with CFS in adolescents and assessed the attitude of GPs and pediatricians toward the diagnosis and management of this disease.

METHODS

Prevalence Estimations Obtained From GPs

In March 2008 a questionnaire was mailed to a sample of 735 GPs, 10% of all GPs in the Netherlands, who were randomly selected by the Dutch Institute for Research of Health Services (NIVEL). The GPs were given the opportunity to respond by mail, e-mail, fax, or telephone. Reminders were sent every 3 months during the period from November 2008 to May 2009.

The GPs were asked to submit their practice size and the number of patients with CFS aged 10 to 18 years who were receiving care. Specifically, the GPs were asked to query their ICPC coding-system database (International Classification of Primary Care), which is used by all Dutch GPs, for “fatigue” and its derivatives.

Additional questions to the GPs concerned the criteria for the diagnosis and management of these patients. If a GP indicated not to have any patients with CFS, the GP was asked for a possible reason.

Population estimates were made by extrapolation of sample data to the population level, because the entire Dutch population is obliged to be registered within the practice of a GP and the average GP practice sizes are compara-

ble (~2000 patients). Furthermore, referral by a GP is mandatory for patients to access hospital care (ie, pediatric care) in the Netherlands, and in turn GPs are informed on the progress of diagnostics and/or treatment of patients referred to the hospital and other health care professionals and facilities (eg, psychologists and rehabilitation centers).

Incidence Estimations Obtained From Pediatricians

During the period from July 2007 to December 2008 all new cases of CFS in adolescents (aged 10–18 years) were assessed monthly by the Dutch Pediatric Surveillance Unit (DPSU). The DPSU is a national registry for pediatric disorders that includes all 103 pediatric hospital departments in the Netherlands and consequently reaches all pediatricians working in the Netherlands. The DPSU is 1 of 12 active pediatric-surveillance registries worldwide. Each pediatric department in the Netherlands receives a monthly (electronic) card to report new cases of various pediatric disorders. For more information on survey methods see www.inopsu.com.¹⁴ For validation of the estimated incidence number, a postal questionnaire was sent to all pediatric departments that had not reported any adolescent patients with CFS in 2008 to verify that there were no cases of CFS in adolescent patients that had not been reported. These questionnaires also queried for information on whether management of patients suspected to have CFS by these pediatricians differed from that of prospective reporting departments. Incidence was calculated as the total number of patients reported from January to December 2008.

For every prospectively reported patient with CFS, the pediatrician and patient were requested by the DPSU to complete a questionnaire. Pediatrici-

cians were asked whether they diagnosed CFS according to the 1994 CDC criteria. Patients received, through their pediatricians, an anonymized short survey regarding gender, age, duration of complaints before diagnosis, assessment of fatigue and concentration problems, functional impairment, type of complaints, and school absence. Fatigue was assessed with the self-report questionnaire Checklist Individual Strength-20 (CIS-20) subscales "fatigue severity" (8 items) and "concentration problems" (5 items). The CIS-20 is a reliable assessment tool with excellent internal consistency (Cronbach's α : 0.93) and discriminative validity for CFS.^{15,16} The cut-off point for severe fatigue was set at ≥ 40 on the subscale fatigue severity.^{16,17} Disabilities were measured by using the self-report Child Health Questionnaire-Child Form subscale "physical functioning" (9 items). This assessment tool is reliable and has been validated with good internal consistency (Cronbach's α : 0.56–0.90).^{18,19} The cutoff point for impaired physical functioning was set at ≤ 85 (healthy population's mean of 96.8 minus 2 SDs [2×5.4]).¹⁹ As a reference group, students at a Dutch secondary school (de Breul, Zeist) were invited to participate. Adolescents who were suffering from a chronic illness and adolescents currently under treatment were excluded. The participation rate was 85%. From this group of students we randomly selected individuals for a control group matched for age and gender ($n = 144$; mean age: 15.3 ± 0.6 years; 79% girls).

Ethics

The medical ethics committee of the University Medical Center Utrecht approved this study. Case data obtained by the GP registration surveys were anonymous; investigators did not have access to information that would allow them to identify or contact these pa-

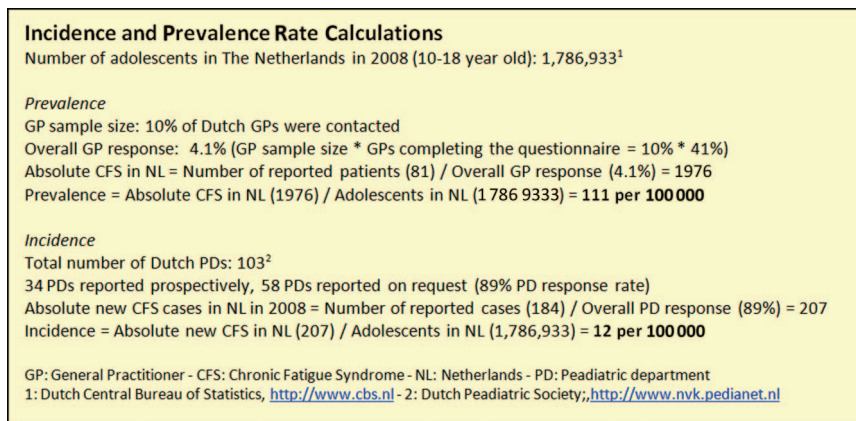


FIGURE 1

Incidence and prevalence rate calculations.

tients and their families. The requirement for informed consent was thus waived. Informed consent was obtained in all cases for which data were traceable to the individual patient, ie, the in which questionnaires were sent to the patients of reporting pediatricians.

Analysis

For estimation of the prevalence and incidence rates, the total number of adolescents in the Netherlands in 2008 was determined to be 1786 933 according to figures of the Dutch Bureau of Statistics.²⁰

Statistical analyses were performed by using SPSS version 15.0 (SPSS Inc, Chicago, IL). Outcome variables were presented as means with SDs and percentages.

RESULTS

Prevalence Estimates

A total of 354 GPs (48%) responded, of whom 304 (41%) returned a completed questionnaire. There were 81 adolescent patients with CFS reported by 42 GPs. Absolute CFS number was estimated to be 1976 adolescents nationwide. The point prevalence of adolescent CFS was calculated at 111 per 100 000 adolescents (0.11%). For details on prevalence calculation, see Fig. 1.

Incidence Estimates

Of 103 Dutch pediatric departments, 92 reported 200 adolescent patients with newly diagnosed CFS cases in 2008. Of these patients, a total of 16 were excluded because of age ($n = 3$), double report ($n = 9$), or a revised diagnosis by the reporting pediatrician ($n = 4$), leaving 184 newly reported cases.

Eleven pediatric departments did not respond to the questionnaires of the DPSU. Therefore, the overall pediatric department response rate was 89%.

Analysis of the 11 hospitals that did not report new cases of adolescent CFS did not reveal trends in hospital size, location (urban versus rural), or organization level (academic versus regular). The locations of the nonreporting hospitals seemed randomly associated, so different incidence rates of patients with CFS in these hospitals are not expected.

On the basis of the assumption that the same number of adolescents with CFS were referred to nonresponding departments the incidence rate was corrected for the 11% nonresponse. The CFS incidence rate was 12 per 100 000 adolescents per year (0.012%). For details on incidence calculation, see Fig. 1.

From all DPSU-derived reports, completed questionnaires were obtained

TABLE 1 Morbidity of Adolescents With CFS Reported by Pediatric Departments in 2008

	CFS		Healthy Peers		P
Age, mean, SD	15.2 (1.9)		15.3 (0.6)		.556 ^a
Gender, % girls	85		79		.250 ^b
Duration of symptoms, mean (SD), mo	17 (18.1)		—		
Onset of disease, %					
Acute	10		—		
Gradual	68		—		
Postinfectious	22		—		
CIS-20, mean (SD)					
Subscale fatigue severity (range: 8–56)	49.8 (6.4)		22.6 (10.7)		.000 ^a
Subscale concentration problems (range: 5–35)	26.5 (6.9)		16.3 (7.1)		.000 ^a
Child Health Questionnaire, mean (SD)					
Subscale physical functioning (range: 0–100)	58.6 (20.4)		95.1 (7.6)		.000 ^a
School absence, %	Previous 2 wk	Previous 6 mo	Previous 2 wk	Previous 6 mo	
Mean (SD)	58.5 (33.0)	54.2 (29.1)	1.5 (3.9)	4.9 (6.9)	.000 ^a
Minimal (<5%)	7.1	4.0	91.2	75.6	
Mild (5%–15%)	4.0	5.0	5.9	18.5	
Considerable (15%–50%)	34.3	46.5	2.9	5.9	
Severe (50%–75%)	18.2	15.8	0.0	0.0	
Almost complete to complete (75%–100%)	36.4	28.7	0.0	0.0	
Reported CDC symptoms, %					
Mean (SD) (range: 0–8)	5.0 (1.6)		—		
Unrefreshing sleep, %	84.4		—		
Postexertional malaise lasting >24 h, %	79.7		—		
Memory and/or concentration problems, %	78.9		—		
Headaches, %	78.1		—		
Muscle pain, %	59.4		—		
Joint pain, %	48.4		—		
Sore throat, %	43.0		—		
Tender lymph nodes, %	31.3		—		

^a Independent Student *t* test.^b χ^2 -test/Fisher's Exact test.

for 81% of patient questionnaires and 96% of pediatrician questionnaires. In all reported cases the CFS diagnosis was in compliance with CDC criteria.

Demographics and Morbidity

Demographic characteristics were obtained from 184 CFS cases. The average age of illness onset was 15 years (SD: ± 1.9 years), with a female-to-male ratio of 5:1. Median illness duration from start of complaints until diagnosis was 17 months (SD: ± 18.1 months), but illness duration ranged widely (6–110 months). In 22% of patients the illness started after an acute episode of infectious disease (of these patients 52% had a current or recent Epstein Barr virus infection); 10% of patients had an acute noninfectious onset. The remaining majority of patients (68%) had a gradual onset of the symptom pattern over weeks to months. The morbidity of patients compared to their healthy peers is summa-

rized in Table 1. Most patients (91%) scored at or above the cutoff point of 40 for severe fatigue (mean: 49.8) on the CIS-20 fatigue-severity subscale. Most patients (93%) also scored at or beyond the cutoff point of 85 on the Health Questionnaire-Child Form physical-functioning subscale. School absence was high: $\sim 90\%$ of patients with CFS reported “considerable” (defined as 15%–50% school absence) to complete school absence in the previous 2 weeks and 6 months (Fig. 2). The mean number of concurrently present CDC symptoms was 5, with “unrefreshing sleep” the most commonly reported (84.4%) and “tender lymph nodes” the least reported (31.3%).

Attitudes to Diagnosis and Disease Management

Among contacted GPs, 7% indicated that they were too busy to cooperate or never cooperated with postal surveys. Forty-three percent of GPs re-

ported that they themselves diagnosed adolescent CFS in their patients, and 1 of 3 of these GPs used CDC criteria. CFS in adolescents was accepted as a distinct diagnosis by 51% of all responding GPs. For detailed information on GP attitudes, see Table 2.

Ninety-six percent of the consulted pediatric departments regarded CFS as a distinct diagnosis, and 92% used CDC criteria for diagnosing CFS. Of the departments who had never diagnosed CFS in an adolescent patient, 1 stated that this diagnosis is applicable only in adults and 3 that this diagnosis is inadequate. For CFS treatment, patients were referred to a psychologist, physical therapist, rehabilitation center, and/or a tertiary care center.

DISCUSSION

This study was the first, to our knowledge, in which nationwide cross-sectional prevalence data as well as

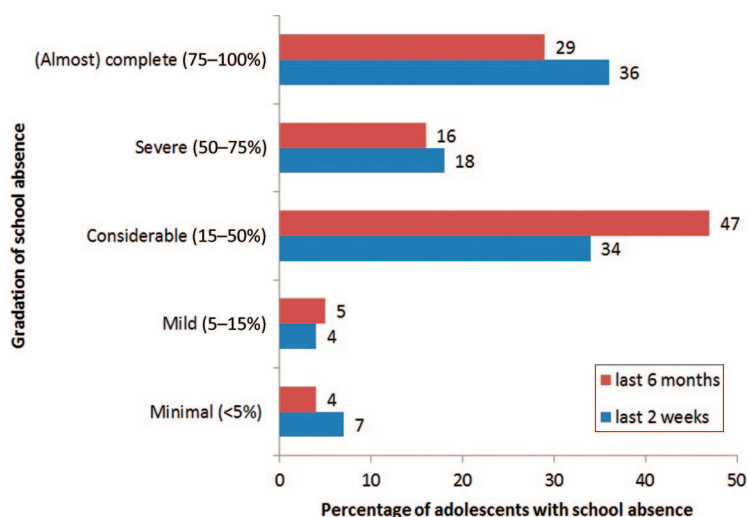


FIGURE 2
Distribution of school absence.

TABLE 2 GPs' Attitudes Toward and Management of Adolescent CFS According to Questionnaire Responses

		Answers	GP Responses, n (%)
Total GPs with adolescent patients with CFS			42 (13.8)
Who diagnosed the patient?	Myself (GP)		18 (42.9)
	Pediatrician		22 (52.4)
	Other		10 (23.8)
If you diagnosed the patient yourself ^a Which criteria did you use?	CDC criteria		6 (33.3)
	Other		12 (66.7)
Did you refer this patient?	Yes, to a pediatrician		11 (61.1)
	Yes, but not to a pediatrician		4 (22.2)
	No		3 (16.7)
How do you register this chronically fatigued patient? ^b	CFS		22 (52.4)
	Chronic fatigue		6 (14.3)
	Fatigue/weakness		15 (35.7)
	Malaise		2 (4.8)
	Other		2 (4.8)
Total GPs with no adolescent patients with CFS			262 (86.2)
For what reason do you not have any adolescent patients with CFS in your practice? ^b	There are no adolescents in my practice that can be considered to have this diagnosis		161 (61.5)
	I only consider this diagnosis in adults		26 (9.9)
	I find this diagnosis inadequate		98 (37.4)
	I don't acknowledge this diagnosis		33 (12.6)
	Other		17 (6.5)

^a Percentages of GPs who diagnosed CFS in their own patients.

^b Multiple answers could apply per GP.

prospective incidence data on adolescent patients with CFS were collected and in which CFS diagnosis was primarily confirmed by either a GP or a pediatrician. We estimated the GP-diagnosed prevalence of adolescent CFS to be 111 per 100 000 adolescents (0.11%) per year and the pediatrician-

diagnosed incidence of adolescent CFS to be 12 per 100 000 adolescents (0.012%) per year. Fatigue severity and physical impairment as well as school absence were found to be remarkably high in adolescents with CFS. These data strongly suggest that adolescent CFS should be regarded as a serious

illness with corresponding consequences such as delay in educational and social development.

Strengths and Weaknesses

Both for prevalence rates and incidence rates we made use of the independent institutes NIVEL and DPSU, which use reliable methods to assess the impact of nationwide public health issues. To determine reliable prevalence numbers, a representative sample of GPs was selected by NIVEL to allow for extrapolation. In regard to the validity of prevalence rates, we assumed that the GPs, as a gatekeepers of health care, were well informed by health care professionals involved in the diagnostic process and treatment of CFS in adolescents, which suggests that the prevalence estimates were accurately reported. The data present in Table 2 do indeed show that almost 75% of the CFS diagnoses in adolescents were made by health care professionals other than the GP. Unfortunately, although we sent several reminders and GPs had the option to respond by mail, e-mail, or telephone, the GP response rate remained low (48%) and possibly introduced a selection bias.

The nationwide response rate on adolescent CFS incidence among pediatric departments that was prospectively derived by the DPSU was high (89%). Furthermore, the rate of adherence to CDC criteria (92%) suggested that Dutch pediatricians adequately diagnosed CFS in adolescents. Although CFS seemed to be diagnosed adequately by pediatricians in our study, underreferral to pediatricians by the GPs might have led to an underestimation of incidence. However, if a GP does not diagnose CFS in adolescents this does not necessarily mean the GP is reluctant to refer a severely fatigued and disabled adolescent to a pediatrician or other health care professional. Our study does not supply data on the referral pattern of the GP.

Determination of prevalence rates in pediatric practices would have led to an underdetermination of CFS prevalence, because after the diagnostic process pediatricians referred adolescents for treatment to specialized psychologists or to a rehabilitation center.

Comparison With Other Studies

The estimated rates of the occurrence of CFS in adolescents that we report were lower than those found in previous studies. However, most recent studies on CFS incidence and prevalence rates in adolescents are based on population surveys performed with methods that were different from those used in our study.

Rimes et al used telephone questionnaires in a random adolescent population sample to longitudinally determine the incidence and prevalence of disabling fatigue. A validated questionnaire was used to assess psychological/psychiatric diagnoses, but no physical examinations or investigations to exclude physical causes of fatigue were performed. In 824 adolescents, 4 new cases of CFS were reported, ie, a incidence rate of 0.5%.⁷

Chalder et al determined the prevalence of adolescent CFS in a cross-sectional interview study, in which diagnosis based on CDC criteria (by interview only) was compared with self-report by patients and parental report. Prevalence rates were, respectively, 0.19%, 0.57%, and 0.038%. There was no concordance between parental report that a child had CFS and operationally defined CFS (CDC criteria).⁴ These findings illustrate the effect of the use of different diagnostic methods.

Jones et al also conducted a random digit-dialing survey in which adolescents with CFS-like illness were identified. Of all identified adolescents (31 of 8586) only 35.5% volunteered to undergo clinical evaluation. None of

these adolescents met the CFS case definition. The authors extracted an estimated adolescent CFS prevalence of the adult population of 50 per 100 000.⁶ Farmer et al used 2 twin registries to derive life-time prevalence estimates of chronic fatigue in adolescents. Selected families were sent questionnaires and parents were interviewed by telephone. Recorded physician diagnoses were reviewed on paper by an independent doctor, but patients did not undergo an additional medical examination. When the diagnosis was made in adherence to CDC criteria, the CFS incidence was 1.29%. When fatigue duration was only 3 months, the incidence increased to 1.90%. For fatigue without any of the 4 accompanying symptoms the incidence increased to 2.43%.⁵ These findings illustrate the effect of applied criteria on CFS incidence. Adherence to the UK NICE (National Institute for Health and Clinical Excellence) criteria leads to higher incidence rates, because the diagnosis of CFS according to NICE guidelines requires symptoms that persist for only 3 months instead of 6 months.²¹

Demographical data from the newly reported patients with CFS regarding age of onset and gender ratio are in line with earlier studies.^{1,4,8,9,22} Our findings support previous evidence on the disabling character of this illness and high level of school absence.^{1,8,9,22–24} Our data regarding GPs attitudes toward adolescent CFS are in line with results of previous studies of CFS attitudes in adults in the Netherlands. Among GPs, 58%–98% accepted CFS as a recognizable clinical entity^{25–27} and 48%–66% felt unconfident in diagnosing CFS.^{26,27}

Implications of the Findings

Although both prevalence and incidence rates are possibly underestimated, this does not change the fact that adolescent CFS seems uncommon in comparison with the high prevalence of severe fa-

tigue in the Netherlands. A recent study showed a prevalence rate of adolescent severe fatigue of 20.5% in girls and 6.5% in boys, of whom 80% and 61.5%, respectively, reported fatigue lasting ≥ 1 month and 46.9% and 35.2% for ≥ 3 months.¹⁷ These data support the theory that CFS is a specific clinical entity in the spectrum of chronic and severe fatigue. The burden to society mainly consists of the associated extensive school absence and its long-lasting and disabling effects.

Although CFS in adolescent patients seemed to be diagnosed adequately by pediatricians in our study, underreporting remains a point of attention in clinical studies. Results of a recent population-based study in the Netherlands showed a 1% prevalence rate of adult self-reported CFS. Strikingly, 70% of these adults consulted their GP for their complaints of fatigue, but GPs diagnosed CFS in only 6.7% of these patients.²⁸ We suggest that all adolescents who consult their GP for a complaint of severe and long-lasting fatigue should be referred to a pediatrician for proper disease diagnosis and initiation of treatment.

CONCLUSIONS

Adolescent CFS is an uncommon illness compared with chronic fatigue. The primary adverse impact of CFS in adolescents is its extremely disabling character and associated high rates of school absenteeism. In contrast to the high acceptance of adolescent CFS among pediatricians, CFS is probably underrecognized by other primary health care providers.

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L. Kimpen and Elise M. van de Putte
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