



## Profile of childhood headaches in a tertiary center

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### Background

The aims of this study were to analyze the profile of childhood headache complaints in a tertiary headache center, verify the differences between children and adolescents, and provide the clinical characteristics that are related to the headaches.

### Methods

A review of 384 medical records of children aged between 4-12 years old (n=206) and adolescents (n=178) aged >12 to 18 years old. The variables evaluated were reported as percentages, compared between children and adolescents and selected the variables that were related to headaches diagnosis.

### Results

The majority of the sample were females (60.7%), diagnosis of migraine (70.3%), pulsatile pain (60.2%), episodic attacks (60.2%) and no need for imaging tests associated with the diagnosis (69.3%), which were associated with different clinical characteristics (LR X2(52); p<0.001; Log likelihood = -322.434; Pseud R2 = 0.154). The group of adolescents had a higher proportion of use of antidepressants (29.8%) as prophylactic medication than children, who on the other hand, had a higher prevalence of use of antivertiginous drugs (32%). The abortive medication used was common analgesics (37.8%) and the main outcome after treatment was discharge from the service (32%).

### Conclusion

The evaluation and the treatment for these patients should take into account the main complaints, considering the particularities of each type of headache and also the age group, in order to identify, treat the disease properly and avoid chronification and continuity in the tertiary service, referring them to less complex services.

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## Introduction

Headache is one of the most prevalent neurological symptoms that affects all age groups, both adults and childhood, and is associated with high levels of disability, leading to a worsening quality of life, and generating costs for health systems (1). Around 60% of children and adolescents are likely to have headaches, being the third leading cause of visits to the emergency department (2,3).

When it comes to primary headaches in childhood, migraine is the most common diagnosis, affecting 10% of both females and males (2,4), and about 20% of migraine children have aura (5,6). Tension-type headache (TTH) has a prevalence of 5% to 11% in this population and presents similar proportions in childhood and adulthood (4,7,8). TTH usually coexists with migraine, and can be episodic or chronic, depending on the frequency of the attacks (4,9). Secondary headaches, have a variable prevalence, ranging from 35.4% to 63.2%, among the various causes, headaches as a consequence of viral infections are the most common (3,10,11).

In treating different types of headaches in children could be made by abortive or preventive therapy, respectively at the beginning of a headache attack, and when headaches are frequent and disabling (12–14). Headache types in childhood have distinct characteristics and prevalence, but they also have similarities, such as the method of diagnosis and the kind of treatment (4,12,15). However, most of the data available about this profile does not consider distinction or the possible levels of complexity of headaches in childhood mainly in specialized care environments such as the routine of a tertiary-level hospital (11,12,16). Therefore, the aims of this study were to analyze the profile of the pediatric population diagnosed with primary and secondary headaches managed at the specialized headache service in the tertiary center, to evaluate the differences between the groups of children and adolescents, and provide the clinical characteristics that are related to the headaches.

## Methods

A retrospective study, based on a review of children's and adolescent's medical records diagnosed with primary or secondary headaches from the *Ambulatório de Cefaleia Infantil (ACEI) at the Hospital das Clínicas da Faculdade de Medicina de Ribeirão Preto – HCFMRP/USP* between 2016 and 2021. This project was approved by the Research Ethics Committee of HCFMRP/USP (CAAE: 45631321.0.0000.5440).

### Sample

The study included medical records from 2016 to 2021 of children and adolescents aged between 4 and 18 years. According to the Statute of the Child and Adolescent (ECA, Brazil) children were defined as those up to 4 and

12 incomplete years, while adolescents were those aged between 12 (complete) and 18 years (17). These individuals had a diagnosis of primary or secondary headaches, whether related to comorbidities or not, and at any stage of treatment. The analysis of the initial medical record was standardized, however, if this service did not have all the necessary information, both the follow-up evaluation and the last evaluation of the patient were analyzed. Medical records of children younger than 4 years old or older than 18 years old, as well as those with insufficient clinical information were excluded.

### Collected Data

All variables were collected using data available in each patient's medical records, which were recorded through an interview between the doctor and the child/guardian, without a structured questionnaire. The numeric data available was the age, weight and height. The other variables were presented in the clinical reports as nominal data and were described as categorical data as follow:

a) *Patient's medical history*: as normal birth or caesarean section, family history of headache (present or absent), comorbidities (presented or absent), physical examination (pain in the facial/cervical/shoulder region, atypical walk, without alteration and others), physical activity (no relation and worsening of the condition), and imaging in requested or unsolicited cases.

b) *Clinical history of headache*: diagnosis (migraine, tension-type headache, secondary, mix or inconclusive headaches), location (frontal, hemicranial, temporal, parietal, holocranial and other), laterality (unilateral, bilateral and without information), quality of pain (pulsatile, pressure or others), intensity (mild, moderate or strong), frequency (episodic, chronic and without information), associated symptoms, that could be photo/phonophobia, nausea, vomiting and others (separated into present and absent), preferred time of headache (no preferences, morning, afternoon, night or more than one period) and presence or absence of aura.

c) *Treatment*: preventive (divided by pharmacological classes: anticonvulsant, antidepressant, antiepileptic, antivertigo, antihypertensive, antipsychotic, muscle relaxant or not used), abortive medications (common analgesic, antidepressant, antipsychotic, anti-inflammatory, more than one category or not used) and response to clinical treatment (no information, discharged, referred to adult outpatient clinic, single medical record or still in treatment).

The names of all the children and adolescents analyzed in the medical records were preserved and the confidentiality of the personal data of both the family and the child was guaranteed.



### Statistical Analysis

The analyses were performed using Stata/SE 17.0 software, with a significance level set at 0.05. Numerical variables were presented in terms of mean and standard deviation. On the other hand, for categorical variables, the number of cases (absolute frequency) and the percentage in relation to the total sample (relative frequency) were reported. The sample was stratified into two distinct groups: children and adolescents. Different statistical tests were used to compare the differences between these groups. Specifically, the Mann-Whitney test was used for numerical variables such as age, weight, and height, due to the non-normality of the data, and the chi-squared ( $X^2$ ) test was applied for categorical variables.

A multinomial logistic regression was performed to analyze the association between the dependent variable diagnosis, within five categories: migraine, tension headache, secondary headache, mixed and inconclusive. The "inconclusive" category was used as a reference for comparison, offering the probability of the diagnosis being different compared to the inconclusive diagnosis.

The independent variables included were the presence of comorbidities, frequency of pain, location of pain, pain characteristics, pain intensity, presence of associated symptoms, presence of aura, types of prophylactic and abortive medication, effect of physical activity on pain, response to treatment, laterality of pain and the child and adolescent groups.

The regression coefficients estimated for each independent variable indicate the direction and magnitude of the association with each diagnosis category, controlling for the effects of the other variables in the model. The values of  $\beta$ , Likelihood, the 95% confidence interval (95%CI), and Pseud  $R^2$  were taken into account. The p-values were used to determine whether these associations were statistically significant.

In addition, a graph was presented to visualize the distribution of the number of patients according to the type of medication they were taking, providing a clear visual representation of the trends observed in the sample.

### Results

A total of 576 medical records were collected, with 192 being excluded due to incomplete information, old and non-digitized medical records, or because the patient was absent from the medical appointment. Therefore, 384 medical records were included in the analysis (Figure 1).

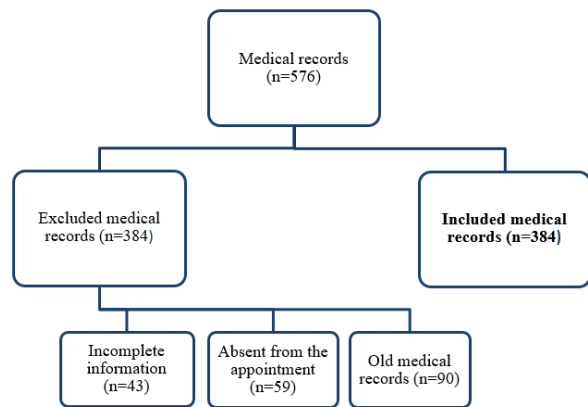


Figure 1. Flowchart of medical records evaluated and excluded.

The general sample included a pediatric population with an average age of 11.3 years, of which approximately 54% were children and 46% were adolescents. The majority of the sample (60.6%) was female patients, the most prevalent diagnosis was migraine, and aura was present in 23.3% of them. Analysis between groups also showed that the diagnosis of migraine was prevalent for both children (77.7%) and adolescents (61.7%). Unlike children, adolescents had a higher proportion of mixed and inconclusive headache diagnosis,  $p < 0.05$  (Table 1).

Table 1. Patients' clinical characteristics of the total sample and differences between children and adolescents groups (n=384)

Demographic characteristics (mean/SD)	Total sample (n=384)	CH (n=206)	AD (n=178)	P value
Age (years)	11.3 (3.5)	8.5 (2.0)	14.4 (1.9)	<0.001
Sex (female) (n/%)	232 (60.4)	113 (54.8)	120 (67.4)	0.012
Weight (kg) (n=135)*	44.6 (18.0)	37.1 (14.3)	56.9 (16.9)	<0.001
Height (cm) (n=47)**	144.1 (15.4)	134.7 (13.7)	155.6 (7.8)	<0.001
<b>Diagnosis (n/%)</b>				
Migraine	270 (70.3)	160 (77.7)	110 (61.7)	
Tension-type	10 (2.6)	4 (1.9)	6 (3.3)	
Secondary headache	29 (7.6)	12 (5.8)	17 (9.6)	0.018
Mixed headache	36 (9.4)	13 (6.3)	23 (12.9)	
Inconclusive	39 (10.2)	17 (8.3)	22 (12.5)	

CH: children; AD: adolescents; SD: standard deviation; kg: kilogram; cm: centimeters. \*Weight sample size= 84 children and 51 adolescents. \*\*Height sample size= 26 children and 21 adolescents.



Regarding the clinical presentation of headache, the sample showed pulsatile pain as the most prevalent (60.2%). There was a difference between groups in type of pain and headache frequency,  $p < 0.05$ . All data regarding the clinical characteristics of headaches in children and adolescents can be seen in Table 2.

Table 2. Clinical characteristics of headaches in the general sample, children and adolescents (n/%) (n=384)

	Total Sample (n=384)	CR (n=206)	AD (n=178)	X <sup>2</sup>	P value
<b>Pain type</b>					
Pulsatile	231 (60.2)	108 (52.4)	123 (69.1)	11.433	0.003
Pressure	83 (21.6)	55 (26.7)	28 (15.7)		
Others	70 (19.2)	43 (20.9)	27 (15.2)		
<b>Localization</b>					
Frontal	134 (34.9)	77 (37.4)	57 (32.0)	3.522	0.620
Temporal	53 (13.8)	23 (11.2)	30 (16.9)		
Hemicranial	22 (5.7)	12 (5.8)	10 (5.6)		
Parietal	21 (5.5)	11 (5.3)	10 (5.6)		
Holocranial	31 (8.1)	15 (7.3)	16 (9.0)		
Others	123 (32.0)	68 (33.0)	55 (30.9)		
<b>Laterality</b>					
Bilateral	261 (68.0)	148 (71.8)	113 (63.5)	3.144	0.208
Unilateral	103 (26.8)	48 (23.3)	55 (30.9)		
No information	20 (5.2)	10 (4.9)	10 (5.6)		
<b>Headache frequency</b>					
Episodic	231 (60.2)	133 (64.6)	98 (55.0)	11.328	0.003
Chronic	145 (37.7)	73 (35.4)	72 (40.5)		
No information	8 (2.1)	0 (0.0)	8 (4.5)		
<b>Intensity</b>					
Mild	39 (10.2)	25 (12.2)	14 (7.8)		
Moderate	137 (35.7)	80 (38.8)	57 (32.0)	5.122	0.077
Strong	208 (54.2)	101 (49.0)	107 (60.2)		
<b>Associated symptoms</b>					
Yes	330 (85.9)	175 (85.0)	155 (87.1)		
No	54 (14.1)	31 (15.0)	23 (12.9)	0.357	0.550
<b>Preferred timing</b>					
No timing	186 (48.4)	102 (49.5)	84 (47.2)		
Morning	50 (13.0)	22(10.7)	28 (15.7)		
Afternoon	101 (26.3)	57 (27.7)	44 (24.7)	2.800	0.592
Night	34 (8.9)	17 (8.3)	17 (9.6)		
More than one	13 (3.4)	8 (3.8)	5 (2.8)		

CR: children; AD: adolescents.

Of the total sample, only 30.7% were asked to undergo imaging tests, and among the groups, adolescents had a higher proportion of these requests,  $p < 0.05$ . Regarding the other variables analyzed, there were no significant differences between the groups for family history, comorbidities, physical examination and worsening of symptoms with physical activity,  $p > 0.05$  (Table 3).

Table 3. Sociodemographic and clinical characteristics of total sample and the subgroups of children and adolescents (n/%) (n=384)

	Total Sample (n=384)	CR (n=206)	AD (n=178)	X <sup>2</sup>	P value
<b>Birth type</b>					
Normal	139 (36.2)	67 (32.5)	72 (40.4)		
Cesarean	173 (45.1)	105 (50.9)	68 (38.2)	6.307	0.043
No information	72 (18.8)	34 (16.6)	38 (21.4)		
<b>Family history</b>					
Present	221 (57.6)	121 (58.7)	100 (56.2)	0.255	0.613
Absent	163 (42.5)	85 (41.3)	78 (43.8)		
<b>Comorbidities</b>					
Present	250 (65.1)	135 (67.3)	109 (61.2)	1.100	0.294
Absent	134 (34.9)	71 (32.7)	69 (38.8)		
<b>Request for imaging test</b>					
No	266 (69.3)	154 (74.8)	112 (62.9)	6.284	0.012
Yes	118 (30.7)	52 (25.2)	66 (37.1)		
<b>Physical examination</b>					
No change	182 (47.4)	110 (53.4)	72 (40.4)		
Atypical gait	125 (32.6)	61 (29.6)	64 (36.0)	7.084	0.069
Facial/cervical/ shoulder pain	34 (8.9)	14 (6.8)	20 (11.2)		
Other	43 (11.2)	21 (10.2)	22 (12.4)		
<b>Physical Activity</b>					
Unrelated	216 (56.3)	116 (56.3)	100 (56.2)	0.001	0.979
Worsening	168 (43.8)	90 (43.7)	78 (43.8)		

CH: children; AD: adolescent.



The total sample and the children and adolescents' groups showed a higher prevalence of not using abortive medications. However, when used, common analgesics were more frequent in both groups,  $p < 0.001$  (Figure 2).

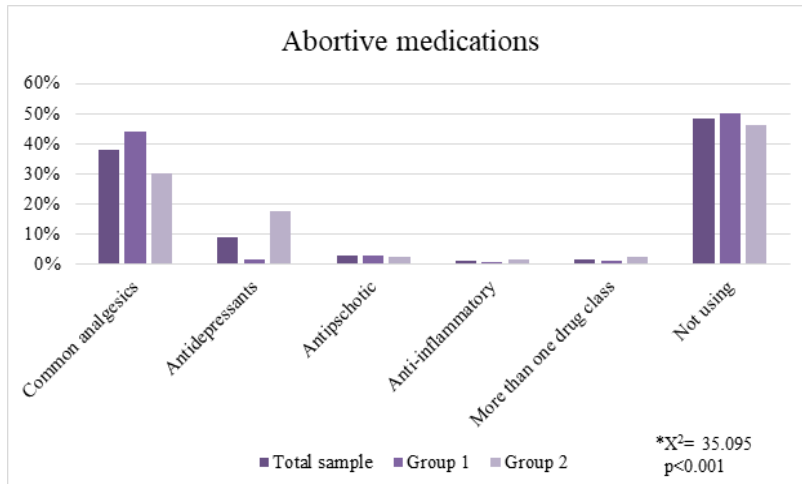


Figure 2. The percentage of abortive medications in the total sample, children (Group 1) and adolescents (Group 2) (n=384).

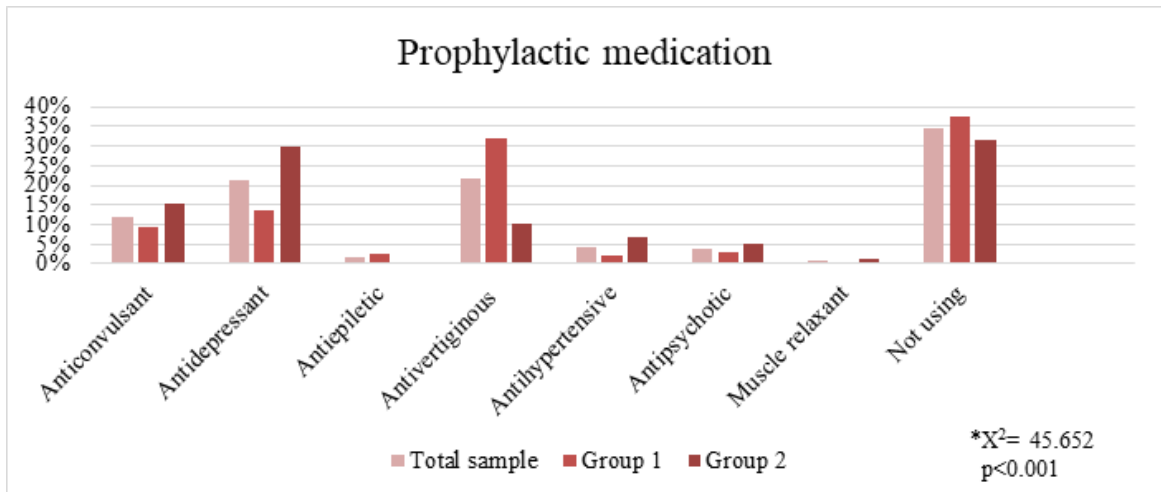


Figure 3. The percentage of prophylactic medication in the total sample, children (Group 1) and adolescents (Group 2) (n=384).

The majority of patients were discharged from the clinic (32%), as were children (33.9%) and adolescents (29.8%). Due to the age of the adolescents, 9.6% were transferred to the adult outpatient clinic (*Ambulatório de Cefaleia e Dor Craniofacial do Hospital das Clínicas de Ribeirão Preto, São Paulo* (ACEF)) and continued to be treated there (Table 4).

Table 4. Response to headache treatment in the total sample, children and adolescents' groups (n/%)

Response to treatment	General Sample (n=384)	CR (n=206)	AD (n=178)	$\chi^2$	P value
Discharge	123 (32.0)	70 (33.9)	53 (29.8)	23.042	<0.001
Transferred to ACEF	17 (4.4)	-	17 (9.6)		
In treatment	90 (23.4)	56 (27.1)	34 (19.1)		
Single medical record	75 (19.5)	39 (18.9)	36 (20.2)		
Abandonment	79 (20.6)	41 (19.9)	38 (21.3)		

CH: children; AD: adolescent; ACEF: *Ambulatório de Cefaleia e Dor Craniofacial do Hospital das Clínicas de Ribeirão Preto, São Paulo*



When multinomial logistic regression (LR X<sup>2</sup>(52);  $p < 0.001$ ; Log likelihood = -322.434; Pseud R<sup>2</sup> = 0.1535) was carried out, selecting the types of diagnosis as the dependent variable, the probability of having a diagnosis of migraine was significantly influenced by the presence of aura ( $\beta = 2.27$ ;  $p = 0.030$ ; 95%CI: 0.22;4.31) and the use of prophylactic medication ( $\beta = -0.16$ ;  $p = 0.022$ ; 95%CI: -0.30;-0.02).

The presence of associated symptoms ( $\beta = -2.71$ ;  $p = 0.004$ ; 95%CI= -4.56;-0.86) proved to be statistically significant, suggesting that the presence of these symptoms are related to the decreased probability of tension headache compared to inconclusive diagnosis. There were no significant independent variables associated with secondary headaches.

The frequency of pain ( $\beta: 1.02$ ;  $p=0.042$ ; 95%CI: 0.04;2.02), the presence of aura ( $\beta: 2.87$ ;  $p=0.009$ ; 95%CI: 0.71;5.04) and physical activity ( $\beta: -1.71$ ;  $p= 0.028$ ; 95%CI: -2.23; -0.12) were statistically significant, which means that these variables are associated with an increase in the probability of diagnosis of mixed headache compared to the inconclusive diagnosis.

## Discussion

Considering the total sample, the majority were female, diagnosis of migraine, pulsatile pain, episodic attacks and no need for imaging tests associated with the diagnosis, which were associated with different clinical characteristics. In relation to the subgroups, what stood out most was the diagnosis, which after migraine, the group of adolescents had a higher proportion of other diagnosis, such as mixed headache. Most of the sample did not use abortive medication, however, those who did, usually took common analgesics. The adolescents group use of antidepressants as prophylactic medication and the children group, on the other hand, had a higher prevalence of use of antivertiginous drugs. The main outcome after treatment was discharge from the service, followed by continuing treatment in hospital, with the highest prevalence of remaining in treatment being in the children's group, and adolescents were transferred to the adult service due to their age.

The overall sample indicated that females were the most affected in both age groups, with a higher proportion of females in adolescents (67.4%) than in the sample of children (54.8%), which is consistent with studies showing that the prevalence of headaches rises in females with age (7,18,19). This may be due to an elevation in certain hormones, such as estrogen, which are related to an increase in headache frequency (20,21).

Migraine diagnosis was the most common in the total sample, corroborating with Kilic et al.(22), in which 51% of the patients in the tertiary hospital were diagnosed with migraine. However, when analyzed with questionnaires

and in non-specialized hospital centers, others types of headaches such as mixed, secondary and tension-type headache were most prevalent (16,23), but they were not as frequent as migraine in childhood, which corroborates with previously published data that this is a common differentiation in health centers (11,12,22). This difference may be due to the fact that migraine is a highly disabling type of headache (23), so these patients would be more present in the specialized headache centers in tertiary hospitals. Migraine with aura was found in 23% of cases, aura is a neurological symptom associated with migraine, and its incidence causes these patients to have attacks earlier than those without aura (24).

Considering the headache characteristics, pulsatile pain was the most common type of pain in children and adolescents, and it was also observed that the majority of patients with primary headaches had pulsatile and burning pain (22), and whereas the fact that the most part of these sample were patients with migraine, this is in accordance with the ICHD-3 (15). Regarding the frequency of attacks, episodic headache was associated with children, also seen in a different study (25). The clinical implications of these results suggest that because most of the children had episodic headaches, this would make it easier to manage the treatment and thus prevent the disease from becoming chronic. Even though there was no statistically significance regarding pain location and intensity, most of them had bilateral location and strong intensity headaches.

The use of imaging exam was not frequent, and it may be because most children and adolescents have diagnosis of primary headaches, which can be given, in the vast majority of cases, through clinical history (15). According to our data, only 15% of the logistic regression model was able to predict the characteristics that would be associated with headache diagnosis. Taking into account, the characteristics of headaches in childhood have their own particularities, so the main complaints of patients should be considered in order to assess, diagnose, and manage the disease appropriately (15).

Treatment for headaches depends on the patient's clinical presentation. In this sample, it was observed that most of the sample did not use abortive medication, however, those who did, usually took common analgesics. The use of prophylactic medication in adults is recommended when the individual has more than three headache attacks per month, while in children it is recommended when the headache is frequent, such as chronic and disabling headaches (15,26), and the most common class, in our sample, were antivertigo and antidepressants, that corroborate with other studies (12,26).

The main outcome for these patients was discharge from the service, followed by continuing treatment in hospital; adolescents were transferred to the adult service due to their age. This highlights the complexity of headaches





and the need for precise diagnosis for specific and individualized treatments that will promote the goal of improving the patient's clinical condition, which means that the proportion of individuals still undergoing treatment or moving to other services will decrease due to the control and learning of the management of the disease.

Our study has some limitations, this is a retrospective study with data collected from heterogeneous medical records in the childhood population, in which the child may not be able to accurately describe the characteristics of the headache, often depending on the reports of parents and/or guardians, and also because the medical records do not follow a structured questionnaire during the evaluations of these patients and most of the data are qualitative.

However, despite the limitations, this study has strengths such as the sample size that allow the findings to establish a reliable clinical profile of this population diagnosed with headaches, being highly prevalent diseases, and to add relevant data to those already available in the literature. These findings can help to improve the structuring of the evaluation of these patients and, consequently, better-individualized management of headaches in children and adolescents.

## Conclusion

The main clinical characteristics of children and adolescents treated in the tertiary setting showed that females are most affected by headaches. Migraine was the most common diagnosis, with pulsatile pain and episodic frequency. The majority of patients did not use abortive or preventive medications and were discharged from the hospital, while adolescents could be transferred to other services due to their age. The best treatment for these patients should take into account the main complaints, considering the particularities of each type of headache and also the age group, in order to identify and treat the disease properly and avoid chronification and continuity in the tertiary service, referring them to less complex services.

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