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Original Article

Current Practices in Hashimoto's Thyroiditis: Differences in Attitudes Between Pediatric and Adult Endocrinologists in Türkiye: A National Survey

Yesiltepe Mutlu G et al. Survey: How to Manage Hashimoto's Thyroiditis?

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What is already known on this topic?
Hashimoto's thyroiditis (HT) is a common thyroid disease among adults, and its incidence in children increases over time. There are many studies published in the literature on diagnosis, follow-up, thyroid hormone replacement and supportive treatment methods with challenging results at some points. The lack of a consensus guideline on the diagnosis and management of HT may lead to different attitudes among endocrinologists.

What this study adds?
The attitudes and tendencies of pediatric and adult endocrinologists regarding the diagnosis and treatment of HT are not clear in the literature. This study reveals similarities and differences in the attitudes of pediatric and adult endocrinologists and highlights issues that remain unclear to these specialists, which may lead to further investigations.

Abstract
Introduction: This study aimed to assess the clinical practices and attitudes towards Hashimoto's thyroiditis (HT) among pediatric (PEs) and adult endocrinologists (AEs).
Methods: The members of Turkish Society for Pediatric Endocrinology and Diabetes (n=502) and the Society of Endocrinology and Metabolism of Türkiye (n=910) were invited to participate in an online survey.
Results: Of the respondents (n=168), 72.6%(n=122) were PEs and 27.3%(n=46) were AEs. The response rate was 24% among PEs, 5% among AEs. The mean age was 42.7 years. The use of "only TPO-ab" was preferred more frequently in AEs (28.3%) than in PEs (4.1%) (p=0.002). The rate of informing patient/parents at the time of diagnosis that HT lasts a lifetime was 91.3% among AEs and 62.3% among PEs (p=0.001). The rate of beginning treatment in euthyroid cases with goiter was significantly higher in PEs (26.2%) compared to AEs (4.3%) (p=0.017). Among AEs, 71.7% stated that they would never stop treatment, while among PEs, 33.6% did (p<0.001). Also, 44% of PEs stated that they would try to discontinue treatment in euthyroid at the end of puberty. The rate of those who were undecided about selenium supplementation was higher among PEs (41%) than among AEs (21.7%) (p=0.007). Although none of the PEs recommended gluten restriction, 7.5% of the AEs indicated that they would recommend gluten-free diet even without Celiac disease (p=0.015).
Conclusion: There are significant differences encompassing aspects of diagnosis, treatment and nutritional supplementation in HT between PEs and AEs.
Keywords: Adult endocrinology, attitude in management, Hashimoto's thyroiditis, Pediatric endocrinology, questionnaire, The Society of Endocrinology and Metabolism of Turkey, survey, Turkish Society for Pediatric Endocrinology and Diabetes

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Introduction

Hashimoto's thyroiditis (HT), also known as autoimmune thyroiditis or chronic lymphocytic thyroiditis, remains the most common thyroid disease group in the general population. In recent years, while the reported prevalence of HT in childhood is 1.2%, the prevalence in adults has been reported as 7.5% (1, 2). While it is the most common thyroid gland disease in both children and adults, there are no published treatment guidelines on the management of patients with HT. There is no consensus among clinicians on which autoantibodies should be evaluated for diagnosis, whether subclinical hypothyroidism (SH) cases need levothyroxine (LT4) treatment, and how long the treatment period should be in cases where treatment is initiated.

While serum thyroid peroxidase antibodies (TPO-ab) are present in approximately 95% of patients, thyroglobulin antibodies (Tg-ab) are present in 60-80%, therefore the opinion is that the measurement of Tg-ab alone may be less reliable for diagnosis, is getting accepted more commonly (3,4). However, as far as we know, there is no data in the literature on the extent to which clinicians request these antibodies. There are differing opinions on both the diagnosis and treatment of hypothyroidism. While it has been suggested that treatment should be lifelong, long-term follow-up of pediatric cases has shown that 30-50% of individuals with hypothyroidism become euthyroid during follow-up, indicating that lifelong LT4 treatment may not be necessary (5-8). There is no clear answer regarding when to discontinue the treatment. The presence of goiter is an important factor in starting and continuing treatment for patients with HT. The debate about hormone replacement in HT cases with SH is ongoing. However, LT4 replacement is generally not recommended in euthyroid HT cases.

There are also different opinions about nutrition, supplements, and additional treatment methods for adult and pediatric cases of HT. Recently, certain nutritional recommendations have gained popularity for preventing HT in individuals predisposed to autoimmunity and treating individuals with HT. Some studies, which form the basis of these recommendations, have shown that the frequency of HT increases in regions where iodine prophylaxis is performed (9,10). Indeed, the role of iodine in triggering thyroid autoimmunity is strongly supported by animal models (11). As a result of these studies, the need for iodine restriction in HT patients has become a topic of discussion, and some experts have even raised concerns about the potential harms of iodine prophylaxis in HT patients and individuals at risk for HT (12).

Another recent and debatable recommendation for individuals with HT is a gluten-free diet. Some experts advocate this based on the close relationship between celiac disease and autoimmune thyroid diseases and numerous studies which suggest that people with HT may benefit from a gluten-free diet even in the absence of celiac disease (13). Similarly, selenium supplementation in HT has recently become a hot topic and the subject of numerous studies. Seleno-proteins play a crucial role in thyroid hormone deiodination, and selenium deficiency may be considered a predisposing factor for HT as a dietary environmental element (14). However, the results of studies investigating the effect of selenium supplementation in HT cases are contradictory, and there is no compelling evidence supporting selenium supplementation in individuals without selenium deficiency (13).

Many studies on this topic have focused on adults, and there is a lack of agreement among endocrinologists. There have been very few studies involving children. The absence of a unified guideline for diagnosing and managing HT may result in differing approaches among endocrinologists. This study aims to assess the clinical practices and attitudes towards the diagnosis, treatment, and follow-up of HT among pediatric endocrinologists (PEs) and compare them with those of adult endocrinologists (AEs).

Methods

The questionnaire was developed by six pediatric endocrinologists who are members of the Thyroid Working Group of the Turkish Society for Pediatric Endocrinology and Diabetes (TSPED). A web-based survey was constructed with Google Forms (Google, Mountain View, CA). The questionnaire was e-mailed to 502 members of the TSPED and 910 members of the Society of Endocrinology and Metabolism of Türkiye. An initial e-mail including an electronic link to the questionnaire was sent, followed by 2 reminders. The inclusion criteria were: (i) having practiced in Türkiye (ii) being a pediatric and adult endocrinology fellow or attending physician (iii) being voluntary to fill out the survey. The study protocol was approved by the local ethics committee (Protocol No 4449). The questionnaire consisted of a total of 41 questions. These included 8 questions evaluating the demographic characteristics and 33 multiple-choice questions about the attitude on diagnosis, follow-up, treatment, nutrition and nutritional supplements. The entire survey is available as an online supplement (supplementary 1). The resulting data were analyzed using the IBM-SPSS 28 program. Mann-Whitney U test was used to compare frequencies (percentages) between continuous variables with non-normal distribution. Chi-Square test was used to compare categorical variables with non-normal distribution. The Bonferroni correction was used for post hoc analysis. A p-value less than 0.05 was considered statistically significant.

Results

Survey respondents

A total of 168 participants completed the questionnaire. Of the respondents 72.6% (n=122) were PEs, and 27.3% (n=46) were AEs. The response rate to the survey was 24% among PEs (n=502) and 5% among AEs (n=910). Of the participants, 72% (n=121) were female. The mean age was 42.7 years. The mean experience time was longer in AE than in PE (mean: 10 years, 13.8 vs. 8.7, p=0.005). There was a significant difference between AEs and PEs regarding their titles, the proportion of professors was higher among AEs than PEs. The main clinical practice centers were the Ministry of Health Training and Research Hospitals (45.9%) in the PEs group and state university hospitals (32.6%) in the AEs group (p<0.001). The characteristics of the respondents are summarized in Table 1.

Attitude regarding the diagnosis, follow-up and treatment

As a diagnostic tool, the most preferred thyroid autoantibody test option in both PEs (86.1%) and AEs groups (58.7%) was “the combination of TPO-ab and Tg-ab”. However, the use of “only TPO-ab” was preferred more frequently in AEs (28.3%) than in PEs (4.1%) (p<0.001). The rate of request for thyroid ultrasound at the time of diagnosis was not significantly different between PEs (94.2%) and AEs (82.6%) (p=0.061). However, the frequency of the respondents who request thyroid ultrasound at the follow-up was higher among PEs than AEs (95.9% vs 76.1%, p<0.001). There was no significant difference between PEs and AEs in terms of the frequency of outpatient visits, the use of fT3 levels alongside TSH and fT4 levels (p=0.35), the ranges at which autoantibody levels are regarded as positive (p=0.08). Among AEs, 91.3% informed the patient/parents at the time of diagnosis that HT lasts a lifetime, which was significantly more frequent than PEs (62.3%) (p<0.001). There was no significant difference between PEs and AEs in providing information about the possibility of changes in thyroid function status (p=0.562).

In cases of SH without goiter, both PEs and AEs mostly stated they would start LT4 treatment when TSH levels were above 10 IU/L (p=0.287). However, the rate of beginning treatment in euthyroid cases with goiter was significantly higher in PEs (26.2%) compared to AEs (4.3%) (p=0.017). There were no significant differences in terms of experience period, age and title between the PEs (n:32) who indicated that they would start treatment in this condition and those who would not (n:85) (p>0.05). Among AEs, 71.7% stated that they would never stop treatment, which was significantly higher than the rate among PEs (33.6%) (p<0.001). Among the PEs, no significant difference was noted between those who stated that they would never stop the treatment (n=41) and those who stated that they would stop the treatment at a certain time (n=81) in terms of experience period, age, and title (p>0.05). Additionally, 44% of PEs stated that they would try to discontinue treatment in euthyroid cases when puberty was completed. The attitudes of PEs and AEs regarding the diagnosis, follow-up and treatment are summarized in Table 2.

Attitude regarding nutritional modifications and supplements

There were no significant differences between PEs and AEs in terms of indications for performing urinary iodine analysis, recommending or eliminating iodized salt in the diet (p=0.434). The rate of those who were undecided about selenium supplementation was higher among PEs (41%) than among AEs (21.7%) (p=0.02). Additionally, the rate of those who indicated that they were undecided on selenium supplementation was higher among PEs compared to AEs (41% vs. 21.7%). Although none of the PEs recommended gluten restriction, 7.5% of the AEs indicated that they would recommend gluten-free diet even without Celiac disease (p=0.015) (The attitudes regarding nutritional modifications and supplements were given at table 3).

Discussion

The findings of this study reveal that there is no consensus among clinicians regarding HT management in Türkiye and that there are significant differences in HT management between PEs and AEs. These differences encompass aspects of diagnosis, treatment initiation and continuation, and nutritional supplementation, reflecting variations in clinical practices.

A notable difference in the diagnostic approach is the preference for thyroid autoantibody testing. PEs overwhelmingly prefer a combination of TPO-ab and Tg-ab, whereas a significant portion of AEs is content with TPO-ab alone. This might suggest a more cautious approach among PE, who perhaps seek a comprehensive antibody profile for better diagnostic accuracy. Although both antibodies have been shown to be positive at rates up to 20-25% in the normal population, there is a known relationship between anti-TPO positivity and TSH levels (15). Despite differing recommendations in various sources regarding the testing for anti-TPO and/or anti-TG antibodies, there are no definite recommendations for measuring thyrotropin receptor antibodies (TRAb or TSHR-Ab) levels (15-17). The prevalence and functional significance of TSHR-blocking autoantibodies (TBAb) in autoimmune hypothyroidism have been investigated less than TSHR-stimulating antibodies, but it is known that there is a low rate of TBAb positivity in HT cases (18). Interestingly, in our study, the rate of those who requested TRAb in addition to the other two antibodies for the diagnosis of HT was approximately 10% among PE and 13% among AEs, which is not significant. The increasing evidence showing that TBAb is important in the diagnosis and management of autoimmune thyroiditis cases, facilitated by recently developed laboratory techniques (19), may be the reason behind this approach.

The information provided about the prognosis at the time of diagnosis also differed significantly between the groups. Almost all AEs (91.3%) informed their patients that the disease would last for life, compared to 62.3% of PEs. Similarly, when LT4 treatment was initiated, a significant proportion of AEs (approximately 72%) stated that they would never attempt to discontinue treatment, whereas this rate was approximately 34% among PEs. There is no consensus in the literature regarding the duration of LT4 treatment in HT patients. However, some studies have shown that hypothyroid pediatric patients with HT can become euthyroid in 30-50% of cases during follow-up, indicating that lifelong treatment may not be necessary for these patients (5-8). Raddetti et al. even suggested that discontinuation of treatment should be attempted in pediatric patients with TSH levels <10 U/L at diagnosis (8). Despite these studies in pediatric patients, to our knowledge, there are no similar studies in adults. Thus, the discrepancy could stem from differing perspectives on the natural history of HT in children versus adults, with AEs possibly anticipating a more chronic course based on their patient population.

When it comes to initiating treatment, both groups show a consensus in starting LT4 therapy in cases of SH when TSH levels exceed 10 IU/L. However, surprisingly, the proportion of those who recommended LT4 therapy to patients with goiter, even if they were euthyroid, was significantly higher among PEs than among AEs. Although some studies have shown that LT4 treatment reduces thyroid volume in both pediatric and adult HT patients with goiter, even if they are euthyroid (20, 21), a more recent randomized controlled trial demonstrated that this reduction in thyroid volume was not permanent (22). No significant difference was found at the end of 36 months when comparing pediatric patients who were euthyroid at baseline and started on LT4 with those who were not. However, the fact that PEs are more likely to initiate treatment in euthyroid cases with goiter in our study underlines a more aggressive attitude towards goiter in children, which may be due to concerns over potential growth effects.

The attitudes of responders on nutritional modifications in HT management were similar regarding iodine restriction. Only 5% of PEs and 17% of AEs recommended iodine restriction. Although some data suggest that iodine can trigger thyroid-related autoimmunity and that the prevalence of HT increases in areas where iodine prophylaxis is used (9-11), studies which show the effect of iodine restriction in the treatment of HT are extremely scarce. To our knowledge, there is no such study in children. Yoon et al. demonstrated that iodine restriction normalized thyroid function in adults with HT (23). However, it should be taken into consideration that the region where the study was conducted was a region with excessive iodine intake. Given that mild to moderate iodine deficiency is still a problem in Türkiye (24,25), it is not surprising that very few of the participants, especially PEs, recommended iodine restriction in HT.

The attitudes towards gluten restriction showed variability between the two groups. For instance, while none of the PEs recommends gluten restriction without Celiac disease, a small percentage of AEs do. This may reflect an emerging, albeit controversial, belief among some AEs that gluten could play a role in thyroid autoimmunity even in the absence of Celiac disease. Indeed Poblocki et al. found that a gluten-free diet decreased TSH levels in patients receiving LT4 treatment (26). However, studies demonstrating a positive effect of a gluten-free diet on thyroid status are extremely limited. Two systematic reviews, which included 3 and 6 studies respectively, showed that a gluten-free diet decreased anti-TPO levels but did not affect TSH levels (27,28). Notably, all of these studies were conducted in adults (26-28). To the best of our knowledge, there are no studies examining the effects of a gluten-free diet on HT in children, which may be related to the fact that none of the PEs recommend this dietary modification.

The recent study also showed a lack of consensus between PEs and AEs regarding selenium supplementation, a popular recommendation in HT management in recent years. Notably, a higher proportion of PEs remain undecided compared to AEs (41% vs. 21.7%). In a 2018 survey, only 20% of European Thyroid Association members believed that selenium supplementation has evidence-based benefits, yet a significant proportion (67%) reported recommending selenium supplementation to their patients (29). Systematic reviews have shown that selenium supplementation, like iodine restriction and gluten-free diet recommendations, has no favorable effect on thyroid functions, although it does decrease the level of thyroid auto-antibodies in HT cases (30,31). Additionally, considering the possible side effects of selenium (e.g., gastric irritation, hair loss, skin rash), there are no evidence-based guidelines on which cases warrant selenium supplementation, whether selenium levels should be evaluated beforehand, and the appropriate doses if supplementation is performed (32). Moreover, it is controversial whether the decrease in antibody levels resulting from these nutritional modifications is clinically significant, and it is clear that more evidence is needed for these recommendations to become widely applicable.

This study is not without its limitations. The main limitation is the low response rate for the survey, particularly among AEs. This low response rate may limit the generalizability of the findings to the broader population of endocrinologists in Türkiye. Additionally, the attitudes and practices of non-responders might differ significantly from those who chose to participate, which could skew the study results. Nevertheless, we think that the results of our study are important in terms of showing the current problems and contradictions among clinicians in Türkiye in HT management.

In conclusion, while the management of HT shows significant variation between PEs and AEs in Türkiye, these differences highlight the need for continued research and the development of comprehensive, evidence-based guidelines to harmonize practices and optimize patient outcomes in HT. As nutritional and supplementation practices evolve, robust clinical trials are needed to establish the efficacy and safety of interventions like iodine restriction and selenium supplementation in HT patients. This will help standardize care and ensure all patients receive the most effective and evidence-based treatments.

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Table 1: The characteristics of the respondents

	All the participants (n=168)	**Pediatric endocrinologists (PEs) (n=122)**	**Adult endocrinologists (AEs) (n=46)**	**p value**
~~Mean~~ Median age (year)	41 (8)	41 (8)	42 (10.5)	0.441
Gender Female (%)	121 (72%)	91 (74.6%)	30 (65.2%)	0.25
~~Mean~~ Median experience time in the field (year)	8 (10)	7 (10)	10.5 (15)	**0.005**
Having >5 years of experience time (%)	62	57	73	0.067
Title				**0.03**
Fellow	37 (22%)	31 (25.4%)	6 (13%)	
Consultant	68 (40.5%)	52 (42.6%)	16 (34.8%)	
Asistant professor	8 (4.8%)	7 (5.7%)	1 (2.2%)	
Associated professor	21 (12.5%)	14 (11.5%)	7 (15.2%)	
Professor*	34 (20.2%)	18 (14.8%)	16 (34.8%)	
Clinical practice center				**<0.001**
Ministry of Health training and research hospital	63 (37.5%)	56 (45.9%)	7 (15.2%)	
State university hospital	56 (41.1%)	41 (33.6%)	15 (32.6%)	
State hospital	16 (9.5%)	12 (9.8%)	4 (8.7%)	
Private university hospital	10 (6%)	7 (5.7%)	3 (6.5%)	
Private hospital†	15 (8.9%)	3 (2.5%)	12 (26%)	
Private center	8 (4.8%)	3 (2.5%)	5 (11%)	

* Significant in relation to "Professor", †Significant in relation to "Private Hospital",

Table 2: Attitude regarding the diagnosis, follow-up and treatment

Responses	**All of the participants (n=168)**	**Pediatric endocrinologists (n=122)**	**Adult endocrinologists (n=46)**	**p value**
'As a diagnostic test, I use the following thyroid autoantibodies' TPO-ab+Tg-ab TPO-ab+Tg-ab+TRAB- Only TPO-ab*	132 (78.6%) 18 (10.7%) 18 (10.7%)	105 (86.1%) 12 (9.8%) 5 (4.1%)	27 (58.7%) 6 (13%) 13 (28.3%)	**0.002**
Thyroid autoantibody positivity 'I would consider any value above the reference range as positive.' 'I would consider as positive if it is at least twice the upper limit or higher.' 'I would consider as positive if it is at least 3 times the upper limit or higher.' Other	79 (47%) 48 (28.6%) 26 (15.5%) 15 (8.9%)	50 (41%) 40 (32.8%) 19 (15.6%) 13 (10.6%)	29 (63%) 8 (17.4%) 7 (15.2%) 2 (4.3%)	0.08
Request of T3 and, or free T3 test Yes No Undecided	33 (19.6%) 130 (77.4%) 5 (3%)	22 (18%) 95 (77.9%) 5 (4.1%)	11 (23.9%) 35 (76.1%) 0	0.350
Request of thyroid ultrasound at the time of diagnosis Yes No Only in case of suspicious nodule on physical examination	153 (91.1%) 1 (0.6%) 14 (8.3%)	115 (94.2%) 0 7 (5.8%)	38 (82.6%) 1 (2.2%) 7 (15.2%)	0.061
Request of thyroid ultrasound at the follow-up period # Yes No	152 (90.5%) 16 (9.5%)	117 (95.9%) 5 (4.1%)	35 (76.1%) 11 (23.9%)	**<0.001**
'When I give information about the diagnosis of HT, I also inform that it lasts a lifetime' Agree† Disagree Undecided	118 (70.2%) 28 (16.7%) 22 (13.1%)	76 (62.3%) 25 (20.5%) 21 (17.2%)	42 (91.3%) 3 (6.5%) 1 (2.2%)	**0.001**

'When I give information about the diagnosis of HT to the patients and/or their relatives, I also inform that their thyroid functions may change over time.'				0.562
Agree	165 (98.2%)	119 (97.5%)	46 (100%)	
Disagree	2 (1.2%)	2 (1.6%)	0	
Undecided	1 (0.6%)	1 (0.8%)	0	
The frequency of outpatient visits for HT cases who do not require LT4 treatment				0.051
Every 3 months	16 (9.5%)	14 (11.5%)	2 (4.3%)	
Every 6 months	106 (63.1%)	84 (68.9%)	22 (47.8%)	
Annually	33 (19.7%)	16 (13.1%)	17 (37%)	
Other	13 (7.7%)	8 (6.5%)	5 (10.9%)	
'I start LT4 treatment in a patient with subclinical hypothyroidism without goiter if':				0.287
TSH >10 IU/L	103 (61.3%)	83 (68%)	20 (43.5%)	
TSH >5 IU/L	31 (18.5%)	21 (17%)	10 (21%)	
TSH is above the reference ranges.	34 (20.2%)	18 (15%)	16 (34.8%)	
'I start LT4 treatment in a case of HT with Goiter':				**0.017**
Even if the patient is euthyroid‡	34 (20.2%)	32 (26.2%)	2 (4.3%)	
If TSH >10 IU/L	23 (13.7%)	16 (13.1%)	7 (15.2%)	
If TSH >5 IU/L	74 (44%)	50 (41%)	24 (52.2%)	
If TSH is above the reference ranges	31 (18.5%)	20 (16.4%)	11 (24%)	
Other	6 (3.6%)	4 (3.3%)	2 (4.3%)	
General approach to discontinue thyroid hormone treatment in a patient who is diagnosed with HT and started treatment #.				**<0.001**
'I do not recommend discontinuing treatment'	74 (44%)	41 (33.6%)	33(71.7%)	
'I try to discontinue treatment if the patient is euthyroid in the follow-up at any time'	94 (56%)	81 (66.4%)	13 (28.3%)	

Tg-ab: Thyroglobulin antibody, TPO-ab: thyroid peroxidase antibody, TRAB: Thyroid stimulating hormone receptor antibody, LT4: levothyroxine *Significant in relation to "Only TPO-ab", #Fisher test was used. †Significant in relation to "Agree", ‡Significant in relation to "Even if the patient is euthyroid".

Table 3: Attitude regarding nutritional modifications and supplements

Responses	All of the participants n=168	Pediatric endocrinologists n=122	Adult endocrinologists n=46	p value
Selenium supplementation				**0.007**
It may be given after measuring blood/urinary level and if necessary and,or if the patient has overt/subclinical hypothyroidism.	53 (31.6%)	31 (25.4%)	22 (47.8%)	
I'm undecided*	60 (35.7%)	50 (41%)	10 (21.7%)	
It is completely unnecessary	55 (32.7%)	41 (33.6%)	14 (30.4%)	
Gluten-free diet†				**0.015**
I state that no restrictions are required	83 (49.4%)	65 (53.3%)	18 (39.1%)	
I don't make suggestions unless asked.	73 (43.5%)	54 (44.3%)	19 (41.3%)	
I recommend.	3 (1.8%)	0	3 (6.5%)	
Other	9 (5.4%)	3 (2.4%)	6 (13.1%)	
Iodine restriction				0.434
I state that no restrictions are required	98 (58.3%)	74 (60.7%)	24 (52.2%)	
I don't make suggestions unless asked.	36 (21.5%)	28 (23%)	8(17.4%)	
I recommend.	14 (8.3%)	6 (4.9%)	8 (17.4%)	
I decide based on urine iodide level	20 (11.9%)	14 (11.5%)	6 (13%)	

*Significant in relation with 'undecided'. †For the statistical analysis only 2 groups included ('I recommend' and the others)