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Are illness perceptions, beliefs about medicines and Type D personality associated with medication adherence among thyroid cancer survivors? A study from the population-based PROFILES registry

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\textbf{ABSTRACT}

\textbf{Objective:} To examine self-reported medication adherence and its association with illness perceptions, beliefs about medication and personality among thyroid cancer survivors.

\textbf{Methods:} Individuals diagnosed with thyroid cancer between 1990 and 2008, as registered in the Eindhoven Cancer Registry, received our survey; 86\% (n = 306) responded.

\textbf{Results:} Many patients reported that they never forgot taking their medicines (n = 168; 56\%), never altered the dose (n = 258; 88\%), never stopped taking them (n = 291; 99\%), never decided to miss a dose (n = 284; 97\%) and never took less than instructed (n = 286; 97\%). Fifty-two percent were classified as nonadherent; of which 14% intentional nonadherent only, 70% were nonintentional nonadherent only and 16% were both intentional and nonintentional nonadherent. Nonadherers were younger, more highly educated, more often employed, had a lower stage at diagnosis, and less often reported \textsuperscript{2} comorbid conditions than adherers. Furthermore, their illness affected them more emotionally and they more often reported that their life would be impossible without their medicine. Logistic regression models showed that higher age, lower education and lower perceived necessity of medication was associated with better adherence while beliefs about medication, illness perceptions, and personality were not associated with adherence.

\textbf{Conclusions:} Despite lifelong dependence on supplement therapy, 52\% of thyroid cancer survivors were nonadherent.

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Medication adherence; illness perception; personality; thyroid cancer; oncology

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Background

The World Health Organization defines adherence as the extent to which the person’s behavior (e.g. taking medication) corresponds with the recommendations given by a health care provider (Sabaté & World Health Organization, 2003). A patient is, therefore, nonadherent if doses are missed, extra doses are taken, or doses are taken in the wrong quantity or at the wrong time (Ruddy, Mayer, & Partridge, 2009). Research has shown that poor adherence is expected in approximately 50% of adults (Vermeire, Hearnshaw, Van Royen, & Denekens, 2001). This is a missed opportunity for health improvement, and health resources are not being used to their maximum potential. Nonadherence can be divided into intentional and nonintentional nonadherence. While the consequences of both intentional and nonintentional adherence are comparable, this difference can be important when developing interventions for nonadherence.

Factors which influence medication adherence are interrelated and can be divided into patient-related factors (e.g. perception and beliefs about medication), therapy-related factors (e.g. side effects), disease-related factors (e.g. comorbid conditions), healthcare system factors (e.g. inadequate information on treatment) and social and economic factors (e.g. age and costs) (Verbrugghe, Verhaeghe, Lauwaert, Beeckman, & Van Hecke, 2013). In this particular study, we decided to focus on patient-related factors since they are most suitable to target in interventions. Among others, illness perceptions are a patient-related factor that are associated with adherence according to an extended version of Leventhal’s self-regulatory model (Horne, Weinman, & Hankins, 1999). This model suggests that health behavior is influenced strongly by certain perceptions about one’s illness. These perceptions regarding the nature, duration, causes, consequences and potential for cure or control of the disease regulate individual coping strategies. In other words, illness perceptions are thought to influence whether or not a patient is adherent to taking the prescribed medication.

Another patient-related factor which influences medication adherence is the beliefs that patients hold about their medicines (Horne et al., 2013). These beliefs can comprise the necessity of their medicines not only its potential for effectiveness but also concerns about the possible adverse consequences of the medication. Based upon these beliefs patients may decide not to continue the prescribed medication, if they perceive the necessity or the chances of success to be low, or the costs (e.g. possible side-effects) to be high. This is in agreement with the Health Beliefs Model (Janz & Becker, 1984) which states that a patient will take a health-related action if he or she believes that a negative health condition can be avoided, if he or she has a positive expectation that the action will avoid this negative health condition, and believes that he or she can successfully perform the action. This model was based upon four constructs representing the perceived threat and net benefits: perceived susceptibility, perceived severity, perceived benefits and perceived barriers.

An additional patient-related factor that might also play a significant role in medication adherence is Type D personality (e.g. the tendency to experience negative emotions and to be socially inhibited) (Denollet, 2005). Previous studies among patients with obstructive sleep apnea syndrome (Brostrom et al., 2007; Dieltjens et al., 2013), myocardial infarction (Williams, O’Connor, Grubb, & O’Carroll, 2011) and heart failure (Wu & Moser, 2014) have shown that poor adherence to prescribed treatments (self-reported
and objectively assessed) was associated with a Type D personality. In young adults with asthma (Axelsson, 2013; van de Ven, Witteman, & Tiggelman, 2013) and in patients with acute coronary syndrome (Molloy et al., 2012), it was mainly the negative affectivity (NA) component of Type D personality that predicted medication adherence. Among those with high NA, it is believed that this lower adherence could be explained by more concerns about side-effects of medication (van de Ven, et al., 2013), greater concerns in general (Denollet, 2005), experiencing many daily stressors, and providing more negative answers to questionnaires due to their focus on the negative aspects of life. Also, social inhibition (SI) could be of influence regarding adherence in cases when medication must be taken regularly in social situations, or when regular communication with a healthcare provider is necessary. Numerous studies have shown that having a Type D personality is associated with worse health outcomes in medical and general populations, above and beyond clinical characteristics (Denollet, Schiffer, & Spek, 2010; Mols & Denollet, 2010a, 2010b). Besides a number of biological mechanisms that could explain poor health outcomes among those with a Type D personality, poor medication adherence could also provide part of the explanation.

For many chronic conditions, medication adherence is of utmost importance. For instance, thyroid cancer is the most common endocrine malignancy and its incidence has increased considerably in recent years, both in the United States and in most European countries (Davies & Welch, 2006; Ferlay et al., 2010). Treatment of thyroid cancer usually consists of surgery (e.g. (near-) total thyroidectomy with or without lymphadenectomy) followed by radioiodine (iodine-131) treatment to ablate the remaining thyroid tissue. When the whole thyroid is removed, lifelong dependence on supplement therapy with thyroid hormone (e.g. levothyroxine), and regimens suppressing thyroid stimulating hormone (TSH) production in the first years, are necessary to replace the function of the removed thyroid gland (Pacini, Castagna, Brilli, Pentheroudakis, & ESMO Guidelines Working Group, 2010). However, the therapeutic response to levothyroxine can be unsatisfactory as studies have shown that more than a third of patients treated with levothyroxine remain biochemically under- or over-treated (Hannemann et al., 2010; Okosieme, Belludi, Spittle, Kadiyala, & Richards, 2011). There are various reasons for this inadequate thyroid hormone replacement, including poor patient adherence, but also factors such as inappropriate dosage or concurrent use of medications that interfere with L-T4 absorption (Morris, 2009). Given the considerable morbidity associated with under- or over-treatment, adherence to the prescribed dosage is very important for thyroid cancer patients to reduce the risk of recurrence (Biondi & Cooper, 2008).

While adherence is important for self-management of thyroid cancer patients, adherence rates are currently unknown and it is unclear whether the aforementioned patient-related factors (e.g. illness perceptions, beliefs about medication and Type D personality) are associated with medication adherence in this patient population. The main aim of this secondary analysis, was, therefore, to study self-reported medication adherence rates and to examine the role of illness perceptions, beliefs about medication and Type D personality on adherence among thyroid cancer survivors. We hypothesize that in addition to sociodemographic and clinical factors, more positive illness perceptions, more negative medication beliefs, and Type D personality will be (independently) associated with nonadherence.
Methods

Setting and participants

The Eindhoven Cancer Registry compiles data of all individuals newly diagnosed with cancer in the southern part of the Netherlands; an area with 10 hospitals serving 2.3 million inhabitants (Janssen-Heijnen, Louwman, van de Poll-Franse, & Coebergh, 2005). All patients diagnosed with thyroid cancer between 1990 and 2008 (e.g. between 2 and 20 years after diagnosis) identified from this registry were eligible for participation ($n = 568$). Those with an unverified addresses ($n = 90$), with cognitive impairment or who were too unwell, at time of the study ($n = 31$) or those who died prior to the start of study (according to the Eindhoven Cancer Registry, hospital records and the Central Bureau for Genealogy; $n = 6$) were excluded. One hospital declined to participate ($n = 86$). The remaining 355 patients were invited to participate.

Data collection

Details of the data collection for this study have been reported elsewhere (Husson, Nieuwlaat, et al., 2013). In summary, survivors were informed of the study via a letter from their (ex-)attending specialist in November 2010, after which the data collection started. By completing the questionnaire, either online or on paper, patients consented to participate and agreed to the linkage of their questionnaire data to their disease history in the Eindhoven Cancer Registry. Patients were reassured that nonparticipation had no consequences for their follow-up care or treatment. This study was approved by the certified Medical Ethics Committee of the Maxima Medical Centre, Veldhoven, the Netherlands.

Data collection was performed within PROFILES, which is a registry for the study of the physical and psychosocial impact of cancer and its treatment from a dynamic, growing population-based cohort of cancer patients. Data from PROFILES studies is available for noncommercial scientific research, subject to study question, privacy and confidentiality restrictions and registration (www.profilesregistry.nl).

Study measures

Socio-demographic and clinical characteristics

The socio-demographic and clinical characteristics of survivors were available from the Eindhoven Cancer Registry, which routinely collects data including date of diagnosis, tumor grade (‘UICC: TNM Atlas Illustrated Guide to the TNM/pTNM Classification of Malignant Tumors’, 1992), clinical stage (‘UICC: TNM Atlas Illustrated Guide to the TNM/pTNM Classification of Malignant Tumors’, 1992) and primary treatment. Comorbidity was assessed using the adapted Self-administered Comorbidity Questionnaire (SCQ) (Sangha, Stucki, Liang, Fossel, & Katz, 2003). Questions on marital status and educational level were added to the questionnaire.
**Medication adherence**

The 5-item self-reported Medication Adherence Report Scale (MARS) was used to assess adherence to medication prescribed after initial cancer treatment (Horne & Weinman, 1999). The MARS contains one item that reflects unintentional nonadherence (‘I forgot to take my medicines’) and four items that largely reflect different forms of intentional nonadherence (e.g. altering the dose, deciding to miss a dose, taking less medication than instructed, and deciding not to take medication for a while). The questions are answered on a 5-point Likert scale ranging from always to never. Participants were classified as adherent if they obtained the maximum score of 5 for the unintentional and 20 on the intentional nonadherence scale. Nonadherence was defined as a score of lower than the maximum of 5 for unintentional and lower than the maximum of 20 for intentional nonadherence, indicating any degree of nonadherence (de Vries et al., 2014). For sensitivity analyses, we created four groups: ‘always adherent’; ‘intentional nonadherent only’ (score <5 on unintentional item and score of 20 on intentional scale); ‘unintentional nonadherent only’ (score of 5 on unintentional item and score <20 on intentional scale); ‘both unintentional and intentional nonadherent’ (score <5 on unintentional item and score <20 on intentional scale). In order to be able to classify those missing more than one item on the 4-item intentional nonadherence scale or a missing on the 1-item unintentional nonadherence scale were excluded from the analysis. The MARS has been used in various countries and patient populations but, to our knowledge, not yet among cancer patients.

**Illness perceptions**

Illness perceptions (i.e. cancer) were assessed using the Dutch version of the eight-item Brief Illness Perception Questionnaire (B-IPQ) (Broadbent, Petrie, Main, & Weinman, 2006; de Raaij, Schroder, Maissan, Pool, & Wittink, 2012). The B-IPQ uses a single-item scale approach to assess perceptions on a continuous linear 0–10 point scale. Five items assess cognitive illness perceptions: (1) How much does your illness affect your life (consequences); (2) How long do you think your illness will continue (timeline); (3) How much control do you feel you have over your illness (personal control); (4) How much do you think your treatment can help your illness (treatment control); and (5) How much do you experience symptoms from your illness (identity). Two items assess emotional representations: (6) How concerned are you about your illness (concern) and (7) How much does your illness affect you emotionally (emotional representation). One item assesses comprehension of illness: (8) How well do you understand your illness (coherence). We chose not to use a total BIPQ score since we believe that the single items give more insight. Although the BIPQ contained questions on ‘illness’ instead of cancer, it was clear to patients that by illness, we meant cancer since patients were explicitly asked by their oncologist to participate in a study on thyroid cancer.

**Beliefs about medicines**

The Beliefs about Medicines Questionnaire (BMQ) was designed to assess personal beliefs about medicines and consists of two parts, BMQ-Specific and BMQ-general (Horne, et al., 1999). It has been used among numerous populations including Dutch
cancer patients (Boons et al., 2017). For this study, only the BMQ-specific part was used, which assesses patients’ beliefs about the prescribed medication (prescribed after primary cancer treatment) for their personal use. BMQ-specific contains two 5-item subscales (‘necessity’ and ‘concern’). These subscales assess the patients’ beliefs about the necessity of their medicines (e.g. without my medicines I would become very ill), and their concerns about possible adverse consequences of these medicines (e.g. my medicines disrupt my life). The answers to these 10 questions are scored on a 5-point Likert scale ranging from strongly disagree to strongly agree. We did not make any changes to this validated questionnaire and, therefore, it did not refer specifically to thyroid cancer. However, it was very clear to patients that they were part of a thyroid cancer study.

**Negative affectivity, social inhibition and Type D personality**

NA, SI and the Type D personality construct were assessed with the Dutch 14-item Type D Personality Scale (DS14) (Denollet, 2005). The items are answered on a 5-point scale ranging from 0 (false) to 4 (true). To compare the separate and combined effects of high and low trait levels, the standard cut-off score of ≥10 on the NA and SI subscales of the DS14 (Denollet, 2005) was used to classify patients in 4 personality groups: both NA ≤ 9 and SI ≤ 9 (NA-/SI-; the ‘reference’ group), NA ≤ 9, but SI ≥ 10 (NA-/SI+; the ‘SI only’ group), NA ≥ 10 but SI ≤ 9 (NA+/SI-; the ‘NA only’ group), and NA ≥ 10 and SI ≥ 10 (NA+/SI+; the ‘Type D’ group).

**Statistical analyses**

All statistical analyses were performed using SPSS version 19.0 (Statistical Package for Social Sciences, Chicago, IL, USA) and *p* values <.05 were considered statistically significant unless stated otherwise.

Demographic and clinical data of respondents, nonrespondents and patients with unverifiable addresses were compared using chi-square statistics for categorical variables and analysis of variance (ANOVA) for continuous variables.

Independent *t*-tests and chi-square tests were used to compare the nonadherent and always adherent thyroid cancer survivors with respect to socio-demographic and clinical variables, the illness perception items, BMQ subscales and the categorized Type D personality scores. Sensitivity analyses were performed for the four groups: ‘always adherent’; ‘intentional nonadherent only’; ‘unintentional nonadherent only’; ‘both unintentional and intentional nonadherent’.

Four multivariate logistic regression models (Bonferroni corrected; *p* = .017) were conducted to identify independent associations (corrected for predetermined sociodemographic and clinical factors) between illness perceptions, medication beliefs (BMQ) and Type D personality (independent variables) with dichotomized medication adherence (outcome with adherence as reference category). The models were composed as follows: (1) demographics + clinical variables + illness perception; (2) demographics + clinical variables + medication beliefs; (3) demographics + clinical variables + Type D personality; (4) Complete model. Patients with missing items concerning the selected variables were excluded from the analyses.
Results

**Respondents, nonrespondents and patients with unverifiable addresses**

Eighty-six percent ($n = 306$) of the 355 thyroid cancer survivors returned a completed questionnaire. When comparing respondents, nonrespondents and those with unverifiable addresses, no differences between these three groups were found with respect to sex, type of thyroid cancer, disease stage or primary treatment (Husson, Haak, et al., 2013). However, patients with an unverified address were younger in comparison to nonrespondents and respondents (mean 52, 56 and 54 years respectively; $p = .04$).

**Sociodemographic and clinical characteristics**

Univariate analyses showed that adherent patients were older, more often had two or more comorbid conditions, and had a low educational level, while nonadherent patients were more often employed and were more often diagnosed with stage I disease compared to their counterparts (Table 1). No differences between these groups were found for time since diagnosis, sex, marital status, type of thyroid cancer and primary treatment. Sensitivity analyses comparing those ‘always adherent’, ‘intentional nonadherent only’, ‘unintentional nonadherent only’ and those ‘both unintentional and intentional nonadherent’ showed similar differences except for comorbid conditions (data not shown).

**Medication adherence**

A large proportion of patients indicated that they never forgot to take their medicines ($n = 168; 56\%$), never altered the dose of their medication ($n = 258; 88\%$), never stopped taking their medicines for a while ($n = 291; 99\%$), never decided to miss out a dose ($n = 284; 97\%$) and never took less than instructed ($n = 286; 97\%$). Complete MARS data was available for 294 patients, of which 48.3% were classified as being adherent and 51.7% were classified as nonadherent (Table 1). Of the nonadherent patients, 14% were classified as intentional nonadherent only and 70% were classified as nonintentional nonadherent only and 16% as both intentional and nonintentional nonadherent.

No significant differences were found between the adherent and the nonadherent group with respect to the individual BMQ items assessing their beliefs about the prescribed medicines except for item 3 (‘My life would be impossible without my medicines’; Figure 1). No significant differences were found between the two groups on the B-I PQ items, except for emotional representation ($3.1$ vs. $3.7$ for adherent and nonadherent respectively; $p < .05$), and the 4 personality groups. Sensitivity analyses showed no differences between those being ‘always adherent’, ‘intentional nonadherent only’, ‘unintentional nonadherent only’ and those ‘both unintentional and intentional nonadherent’ with respect to the individual BMQ items, the two BMQ scales, the BIPQ items and the four personality groups.

Four separate logistic regression models were used to identify associations of demographic and clinical characteristics, with either (1) illness perceptions, (2) beliefs...
Table 1. Sociodemographic and clinical characteristics of thyroid cancer survivors according to medication adherence.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total</th>
<th>Adherent</th>
<th>Nonadherent</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at time of survey (mean ± SD)</td>
<td>55.9 (14.3)</td>
<td>60.5 (13.4)</td>
<td>51.6 (13.8)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Years since diagnosis (mean ± SD)</td>
<td>9.5 (5.4)</td>
<td>9.4 (3.4)</td>
<td>9.6 (5.5)</td>
<td>0.69</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td>0.31</td>
</tr>
<tr>
<td>Male</td>
<td>74 (25%)</td>
<td>32 (23%)</td>
<td>42 (28%)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>220 (75%)</td>
<td>110 (77%)</td>
<td>110 (72%)</td>
<td></td>
</tr>
<tr>
<td>Type of thyroid cancer</td>
<td></td>
<td></td>
<td></td>
<td>0.95</td>
</tr>
<tr>
<td>Papillary</td>
<td>211 (72%)</td>
<td>103 (73%)</td>
<td>108 (72%)</td>
<td></td>
</tr>
<tr>
<td>Follicular (incl. Hürthle cell)</td>
<td>70 (24%)</td>
<td>33 (23%)</td>
<td>37 (24%)</td>
<td></td>
</tr>
<tr>
<td>Medullary</td>
<td>11 (4%)</td>
<td>5 (4%)</td>
<td>6 (4%)</td>
<td></td>
</tr>
<tr>
<td>Stage at diagnosis</td>
<td></td>
<td></td>
<td></td>
<td>.002</td>
</tr>
<tr>
<td>I</td>
<td>168 (58%)</td>
<td>65 (47%)</td>
<td>103 (69%)</td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>56 (19%)</td>
<td>36 (26%)</td>
<td>20 (13%)</td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>44 (15%)</td>
<td>24 (17%)</td>
<td>20 (13%)</td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>20 (7%)</td>
<td>13 (9%)</td>
<td>7 (5%)</td>
<td></td>
</tr>
<tr>
<td>Primary treatment</td>
<td></td>
<td></td>
<td></td>
<td>n.a.</td>
</tr>
<tr>
<td>Surgery (+ 1³¹I ablation)</td>
<td>292 (99%)</td>
<td>141 (99%)</td>
<td>151 (99%)</td>
<td></td>
</tr>
<tr>
<td>Other (chemotherapy/ 1³¹I therapy/ no treatment)</td>
<td>2 (1%)</td>
<td>1 (1%)</td>
<td>1 (1%)</td>
<td></td>
</tr>
<tr>
<td>Comorbidity</td>
<td></td>
<td></td>
<td></td>
<td>.02</td>
</tr>
<tr>
<td>None</td>
<td>64 (22%)</td>
<td>29 (20%)</td>
<td>35 (23%)</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>66 (22%)</td>
<td>23 (16%)</td>
<td>43 (28%)</td>
<td></td>
</tr>
<tr>
<td>2+</td>
<td>164 (56%)</td>
<td>90 (63%)</td>
<td>74 (49%)</td>
<td></td>
</tr>
<tr>
<td>Marital status</td>
<td></td>
<td></td>
<td></td>
<td>.31</td>
</tr>
<tr>
<td>No partner</td>
<td>63 (21%)</td>
<td>34 (24%)</td>
<td>29 (19%)</td>
<td></td>
</tr>
<tr>
<td>partner</td>
<td>231 (79%)</td>
<td>108 (76%)</td>
<td>123 (81%)</td>
<td></td>
</tr>
<tr>
<td>Education level</td>
<td></td>
<td></td>
<td></td>
<td>.02</td>
</tr>
<tr>
<td>Low</td>
<td>27 (9%)</td>
<td>18 (13%)</td>
<td>9 (6%)</td>
<td></td>
</tr>
<tr>
<td>Medium</td>
<td>186 (64%)</td>
<td>93 (66%)</td>
<td>93 (61%)</td>
<td></td>
</tr>
<tr>
<td>High</td>
<td>80 (27%)</td>
<td>30 (21%)</td>
<td>50 (33%)</td>
<td></td>
</tr>
<tr>
<td>Current occupation</td>
<td></td>
<td></td>
<td></td>
<td>.004</td>
</tr>
<tr>
<td>Employed</td>
<td>153 (53%)</td>
<td>62 (44%)</td>
<td>91 (61%)</td>
<td></td>
</tr>
<tr>
<td>Not working/retired</td>
<td>136</td>
<td>78 (56%)</td>
<td>58 (39%)</td>
<td></td>
</tr>
</tbody>
</table>

aOf the nonadherent patients, 14% were classified as intentional nonadherent only and 70% were classified as nonintentional nonadherent only and 16% as both intentional and nonintentional nonadherent.

bAdapted Self-administered Comorbidity Questionnaire [37].
cEducation: Low (no or primary school); Medium (lower general secondary education or vocational training); High (pre-university education, high vocational training, university). N = number; SD = standard deviation. Fisher’s exact test was performed in cases where cell counts were <5%.

Figure 1. The Beliefs about Medicines Questionnaire (BMQ) items stratified by type of medication adherence.
Table 2. Logistic models of factors associated with medication nonadherence.

<table>
<thead>
<tr>
<th>Model 1 (Demographic and clinical variables + Illness perceptions)</th>
<th>Model 2 (Demographic and clinical variables + Beliefs about medicines)</th>
<th>Model 3 (Demographic and clinical variables + personality)</th>
<th>Model 4 (All variables)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Block 1</strong> (Demographic variables)</td>
<td><strong>Block 2</strong> (Clinical variables)</td>
<td><strong>Block 3</strong> (Illness perceptions)</td>
<td><strong>Block 4</strong> (Beliefs about medicines)</td>
</tr>
<tr>
<td>Age at survey (years)</td>
<td>Tumor type</td>
<td>Consequences</td>
<td>Reference (NA-SI-)</td>
</tr>
<tr>
<td>(0.92–0.98)**</td>
<td>Papillary vs. Follicular</td>
<td>(0.80–1.14)</td>
<td>Not included</td>
</tr>
<tr>
<td>Sex</td>
<td>Papillary vs. Medullary</td>
<td>Timeline</td>
<td>Not included</td>
</tr>
<tr>
<td>0.79 (0.40–1.55)</td>
<td>Disease stage</td>
<td>Personal control</td>
<td>Not included</td>
</tr>
<tr>
<td>Educational level</td>
<td>I vs II</td>
<td>1.00 (0.90–1.11)</td>
<td>Not included</td>
</tr>
<tr>
<td>Low vs. medium</td>
<td>0.92 (0.38–2.23)</td>
<td>Treatment control</td>
<td>Not included</td>
</tr>
<tr>
<td>Low vs. high</td>
<td>0.69 (0.29–1.62)</td>
<td>Identity</td>
<td>Not included</td>
</tr>
<tr>
<td>Marital status</td>
<td>0.87 (0.38–2.00)</td>
<td>Concern</td>
<td>Not included</td>
</tr>
<tr>
<td>Occupational status</td>
<td>0.87 (0.34–2.22)</td>
<td>Emotional representation</td>
<td>Not included</td>
</tr>
<tr>
<td>Low vs. high</td>
<td>1.14 (0.69–3.07)</td>
<td>Coherence</td>
<td>Not included</td>
</tr>
<tr>
<td>Years since diagnosis</td>
<td>1.77 (0.85–3.70)</td>
<td>(0.94–5.21)</td>
<td>Not included</td>
</tr>
<tr>
<td>No vs. 1</td>
<td>2.66 (1.07–6.63)</td>
<td>1.96 (0.87–4.43)</td>
<td>Not included</td>
</tr>
<tr>
<td>0.85 (0.41–1.78)</td>
<td>2.08 (0.91–4.76)</td>
<td>0.93 (0.46–1.89)</td>
<td>Not included</td>
</tr>
<tr>
<td>No vs. 2 or more</td>
<td>0.88 (0.40–1.93)</td>
<td>1.05 (0.51–2.14)</td>
<td>Not included</td>
</tr>
<tr>
<td>Comorbidity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low vs. 1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low vs. 2 or more</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Model 4 (All variables)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*p < .017.
**p < .01.

OR: odds ratio; CI: confidence interval.

Demographic variables: time since diagnosis, age at survey, BMQ-specific and BIPQ.

Sex = Male (reference) vs. female; Educational status = low (reference) versus medium/high; Marital status = partner (reference) versus no partner; Comorbidity = no comorbidity (reference) versus one or more comorbidities.
about medicines, (3) personality and (4) all variables with medication nonadherence. Model 1, consisting of demographic and clinical variables and illness perceptions, showed that higher age (odds ratio [OR]: 0.95, 95% confidence interval (CI): 0.92–0.98, \( p < .01 \)) was associated with a lower risk for nonadherence (Table 2). In Model 2, we included patients’ beliefs about medication instead of illness perception. This resulted in similar results for age. The BMQ scale ‘necessity’ became significant in this model, whereby a higher perceived necessity of medication resulted in a higher probability of nonadherence (OR: 1.06, 95% CI: 1.01–1.13, \( p = .039 \)), however after Bonferroni correction it was no longer significant. In Model 3, we included personality instead of illness perception which resulted in the similar significant effect for age only (OR: 0.95, 95%CI: 0.92–0.97). Finally, the overall model also showed a similar effect for age (OR: 0.94, 95%CI: 0.91–0.98), education became significant in this model whereby a higher education resulted in lower adherence (OR: 5.75, 95%CI: 1.48–22.30), and the BMQ scale ‘necessity’ became significant again whereby a higher perceived necessity of medication resulted in a higher probability of nonadherence (OR: 1.11, 95% CI: 1.03–1.19, <.01).

**Discussion**

Medication adherence is important among thyroid cancer survivors since lifelong dependence on supplement therapy with thyroid hormone (e.g. levothyroxine), and regimens suppressing thyroid stimulating hormone (TSH) production in the first years, are necessary (Pacini et al., 2010). In this secondary analyses, we hypothesized that thyroid cancer survivors, between 2 and 20 years after diagnosis, would report a lower medication adherence if they had less positive illness perceptions, lower beliefs in the necessity of their medication, greater concerns about taking these medicines, or if they had a Type D personality. However, the results did not confirm our hypotheses. In short, only lower age, higher education and higher necessity of medication were associated with lower self-reported adherence and this effect was modest, while illness perceptions, the other medication beliefs subscales, and Type D personality were not associated with adherence.

Self-reported medication nonadherence was reported relatively frequently among our sample. In total, 52% of patients were categorized as nonadherent, which was intentional in 30% and nonintentional in 70% of patients. In the literature, there are few data on medication adherence among patients with thyroid cancer. However, a study among 74 pediatric thyroid cancer patients showed that 41% reported that they were unable to fully adhere to postoperative medication regimens (Morris et al., 2012), which is quite similar to our study. A survey among patients with primary hypothyroidism reported that 22% of patients admitted to noncompliance with levothyroxine (Crilly, 2004), which is much lower compared to our results.

Analyses showed that those being always adherent in our sample were significantly older, had a lower educational level, and were more often unemployed or retired. Furthermore, they were more frequently diagnosed at a higher disease stage and more often reported \( \geq 2 \) comorbid conditions. Finally, they reported a lower understanding of their illness. It could be hypothesized that this group is more willing to
strictly follow instructions from their doctor while accepting side-effects due to possible under- or overtreatment with levothyroxine. It is also possible that these patients are already taking medication for their co-morbid conditions and, therefore, just add levothyroxine to their daily medication routine. Indeed, recent studies among hypertensive patients and those with asthma suggest that patients’ habit taking for taking medication is more predictive of self-reported and objective adherence than are patients’ perceptions of their illness and its treatment (Alison Phillips, Leventhal, & Leventhal, 2013; Bolman, Arwert, & Vollink, 2011). Conversely, the younger and higher educated patients who have more understanding of their illness, are diagnosed with a lower disease stage, and have less comorbid conditions are possibly more likely to take control over their own health, and therefore, search for more information on their medication and illness. We speculate that they may be less adherent to their treatment since they try to adjust the dosage of levothyroxine themselves in order to reduce possible side-effects.

In our logistic regression models, only lower age, higher education and higher necessity of medication resulted in higher nonadherence. Other studies that attempt to explain nonadherence in thyroid cancer survivors are, to our knowledge, lacking so we cannot compare these results with other studies. New studies that investigate nonadherence in thyroid cancer survivors are necessary. In anticipation of these future studies, we have some hypotheses that might explain our results. As explained above, survivors with a higher age might be more willing to follow the instructions they received from their doctor who they consider to have authority over the treatment of their disease. In contrast, younger and higher educated patients may be more driven to actively search for disease- and treatment-related information themselves and alter their medication dose accordingly to reduce the side effects associated with under/over-treatment. Our results showed that those with a higher perceived necessity of medication reported higher nonadherence. This might sound a bit inconsistent, however, we believe that those who believe in the necessity of their medication might simultaneously feel that they currently do not receive the optimal dose of levothyroxine which might explain their (intentional) nonadherence. Some patients are probably well aware of the influence of their medication on their daily life, and may be more likely to be nonadherent in their attempt to fine-tune their levothyroxine dosage to reduce possible side-effects or improve their quality of life. Others may elevate their doses of levothyroxine due to fear of cancer relapse. This fine-tuning can be a long process since one of our previous studies in this same sample showed that disease-specific symptoms were still present between 2 and 20 years after thyroid cancer diagnosis and these symptoms were negatively associated with health-related quality of life (Husson, Haak, et al., 2013).

In contrast to our hypotheses, illness perceptions, most medication beliefs subscales and Type D personality were not associated with self-reported medication adherence in this population. Perhaps these factors are more important shortly after diagnosis. The thyroid cancer survivors included in this study were diagnosed between 2 and 20 years ago. The relatively long time since the first prescription of the medication could have an influence on self-reported adherence since behavior patterns (e.g. like taking medication) need time to become incorporated into daily life. Illness perceptions,
medication beliefs, and Type D personality might influence these behavior patterns shortly after diagnosis, while longer after diagnosis, other factors like age play a more important role. A study among thyroid cancer patients from diagnosis onwards may, therefore, yield other results. A possible explanation for the fact that we did not find an effect of Type D personality on adherence is the fact that patients with a Type D personality might be more fearful of thyroid cancer then for taking their medication for thyroid cancer and thus may be more willing to adhere to their medicine routine. Fear for cancer might also explain why we did not find an effect of illness perceptions and medication beliefs on adherence. Patients might adhere to their treatment despite their illness perceptions and medication beliefs out of fear. A previous study among breast cancer patients taking endocrine therapy already showed that illness perceptions and medication beliefs are associated with fear of recurrence (Corter, Findlay, Broom, Porter, & Petrie, 2013). Finally, the small sample size of our study might have contributed to our null-findings.

The present study has limitations that should be mentioned since they could possibly explain our null findings as well. First and most importantly, we asked patients about medication adherence after primary treatment for thyroid cancer but we did not ask specifically about adherence to levothyroxine. Medication adherence was assessed with a self-reported questionnaire. This might not be as reliable as an objective measure such as pharmacy records or medication monitoring devices. For example, a recent study on adherence and Type D personality showed a large gap between self-reported adherence and actual adherence. Namely, 47% reported not missing any medication while the objective measure showed that they took less than 80% of their medication (Wu & Moser, 2014). Possible memory-bias associated with the use of a self-reported questionnaire and social desirability might have also influenced our results due to this method of assessment. Namely, 56% \( (n = 168) \) of the patients in our study indicated that they never forgot to take their medicines, which seems quite high. Unfortunately, the patients in our study did not fill out a social desirability scale and, therefore, we were unable to take social desirability into account. The MARS is mainly focused on taking less medication (e.g. deciding to miss a dose, taking less medication than instructed, and deciding not to take medication for a while) while it is very well possible that those with hypothyroidism take more than prescribed. The MARS only partly addresses this by asking about ‘altering the dose’, perhaps future studies could focus more on this aspect. Also, it is a limitation that we do not exactly know what medication patients is using and when patients started using their medication. The amount of time passed since then can influence adherence. In addition, health care system factors could influence medication adherence and we did not control for this. It would also be helpful if future studies would attempt to classify ‘nonadherence’ in a less stringent manner. Given the small sample size of our study, we were not able to perform multivariate analysis for the four adherence groups. Our results should, therefore, be interpreted with caution, as there may be differences between intentional and nonintentional adherent patients. Future research with more participants should try to answer this research question. A final weakness is the cross-sectional design of the study which limits the determination of causal relationships.
Despite the limitations noted, strengths are also identified. The current study is the first study that investigates the role of illness perceptions, beliefs about medication and Type D personality in self-reported medication adherence among thyroid cancer survivors. A broad spectrum of possible factors associated with medication nonadherence was included in our analyses. Another strength is our population-based design and high response rate.

In conclusion, the findings of this study indicate that nonadherence is prevalent among thyroid cancer survivors. To our knowledge, successful interventions to improve adherence to levothyroxine are currently lacking. The reasons for nonadherence should be investigated in greater depth. It is also important to actively inform the patient when altering the medication dosage, on the benefits and importance of levothyroxine treatment, and to discuss compliance.

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Disclosure statement

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