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REVIEW ARTICLE

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Impact of low iodine diets on ablation success in differentiated thyroid cancer: A mixed-methods systematic review and meta-analysis

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Abstract

Background: Debate remains regarding whether to recommend a low iodine diet (LID) before radioactive-iodine treatment and its duration and stringency. This mixed-methods review aimed to determine if iodine status affects treatment success, the most effective diet to reduce iodine status, and how LID impacts wellbeing.

Methods: Five electronic databases were searched until February 2021. An effectiveness synthesis (quantitative studies) and views synthesis (qualitative, survey, and experience-based evidence) were conducted individually and then integrated. Quality assessment was undertaken.

Results: Fifty-six quantitative and three qualitative studies were identified. There was greater ablation success for those with an iodine status of <50 mcg/L (or mcg/gCr) compared with ≥250 (odds ratio [OR] = 2.63, 95% confidence interval [CI], 1.18–5.86, *n* = 283, GRADE certainty of evidence very low). One study compared <50 mcg/L (or mcg/gCr) to 100–199 and showed similar rates of ablation success (OR = 1.59, 95% CI, 0.48–6.15, *n* = 113; moderate risk of bias). People following a stricter LID before ablation had similar rates of success to a less-strict diet (OR = 0.67, 95% CI, 0.26–1.73, *n* = 256, GRADE certainty of evidence very low). A stricter LID reduced iodine status more than a less strict (SMD = −0.40, 95% CI, −0.56 to −0.24, *n* = 816), and reduction was seen after 1 and 2 weeks. The main challenges were a negative impact on psychological health, over restriction, confusion, and difficulty for sub-groups.

Conclusions: Although a LID of 1–2 weeks reduces iodine status, it remains unclear whether iodine status affects treatment success as only a few low-quality studies have examined this. LIDs are challenging for patients. Higher-quality studies are needed to confirm whether a LID is necessary.

KEYWORDS
differentiated thyroid cancer, iodine status, low iodine diets, meta-analysis, mixed-methods systematic review

1 | INTRODUCTION

Differentiated thyroid cancer (DTC) is usually treated with total thyroidectomy, followed by radioactive-iodine treatment (RAIT) with ^{131}I to destroy any residual thyroid tissue or cancerous tissue left postsurgery (ablation). After ablation, radio-iodine can also be used to treat residual, recurrent or metastatic disease (therapy).[1] Thyroid-stimulating hormone should be raised to facilitate uptake of ^{131}I. It has been suggested that high iodine status may interfere with RAIT efficacy as nonradioactive iodine competes with ^{131}I for uptake by the thyroid.[2] Furthermore, depleting plasma iodide concentrations may increase the expression of the sodium–iodine symporter gene, increasing the amount of radioactive-iodine uptake in remnant thyroid tissue or DTC cells.[3] Many international guidelines on the management of thyroid cancer suggest reducing iodine status before RAIT using low iodine diets (LID).[1,4,5] However, the available evidence for benefit of low iodine status on the efficacy of RAIT for DTC is weak.[6,7] This has led to inconsistencies both within and between countries regarding recommendations for LID duration and target urinary iodine concentration. In 2015, the Italian Society of Endocrinology recommended that a LID before RAIT was not necessary in countries with mild to moderate iodine deficiency,[8] and was updated in 2018 to suggest avoiding preserved fish, sushi, and seaweed for 1–2 weeks before RAIT.[9] The iodine status of the UK falls into this mild to moderate bracket[10] but British Thyroid Association guidelines state that patients should be advised to follow a LID for 1–2 weeks before RAIT.[1] A recent survey of practice found that different treatment centres in the UK gave varying LID advice.[11]

Debate, therefore, remains not only as to whether to recommend a LID or not, but also the duration and stringency. Previous reviews[6,7] were limited in their searches (e.g., excluded non-English articles, restricted databases), analysis, and descriptions of study quality and additional studies may have been published since the last review in 2016. Furthermore, the impact of the LID on wellbeing has not previously been systematically reviewed. Short-term dietary interventions such as the LID may at first seem achievable but are burdensome.[12–14]

The aim of this review was to conduct the first mixed-method synthesis in people with DTC receiving RAIT after total thyroidectomy to yield maximum breadth and depth of understanding by addressing the following questions:

Effectiveness synthesis

1. What is the effect of iodine status or LID on ablation and therapy success?
2. What is the effect of iodine status on recurrence of thyroid cancer or cancer-related mortality?
3. What is the effect of LID advice on iodine status before RAIT or whole-body scan?
4. Are there any complications or adverse effects from consuming a LID?

Views synthesis

5. What are the facilitators and barriers of consuming a LID?

2 | METHODS

A protocol for this review was registered with the International Prospective Register of Systematic Reviews (PROSPERO ID: CRD42020152261).

2.1 | Eligibility criteria

The eligibility criteria were developed in line with the mixed-methods search tool SPIDER.[15] *Sample*: Individuals of any age with clinically diagnosed DTC. Those with a diagnosis of benign thyroid disease or anaplastic or medullary thyroid cancer were excluded. *Phenomenon of interest*: Iodine status or impact of advice to lower dietary iodine or iodine status in relation to the treatment of DTC. A distinction is made in the British Thyroid Association Guidelines between RAIT to destroy any residual thyroid tissue or cancerous tissue left postsurgery (ablation) and radio-iodine to treat residual, recurrent, or metastatic disease (therapy).[1] Studies examining iodine status/LID on ablation and/or therapy success were included. Studies examining LID advice before I^{131}or I^{123} whole-body scans (WBS) in DTC were included. *Design*: Systematic mixed-method review and synthesis. No date or language restrictions were imposed and relevant non-English texts were translated. *Evaluation*: Studies that evaluated the clinical effectiveness and considered the experiences, barriers, and facilitators of a LID in relation to RAIT for DTC were included. *Research type*: Both qualitative and quantitative study designs were included. Type of quantitative study: Randomised controlled trials (RCTs) and nonrandomized studies of interventions (NRSI) which included comparative nonrandomized studies (i.e., cohort studies, case–control studies, cross-sectional, and case series). Guidelines and expert opinions were excluded. Deviations from the protocol are documented in (Supporting Information File SF1).

2.2 | Search strategy

Five databases were searched from inception to February 2021: Embase and MEDLINE (via OVID), Web of Science, Cochrane Central Register of Controlled Trials (CENTRAL) via Cochrane Library, and CINAHL (via EBSCOhost). The search strategy for Medline is available in SF2. Reference lists of all included articles were hand-searched for additional studies alongside relevant systematic reviews, *OpenGrey* and the first 10 pages of google scholar. The ClinicalTrials.gov website was also searched to identify any ongoing trials.

2.3 | Study selection

Two reviewers independently examined all titles and abstracts (GH and CE). Full-text papers were obtained for all studies for further examination. Any disagreement between reviewers was resolved by discussion with a predetermined investigator (RP).

2.4 | Data extraction

A data extraction form was designed and piloted. Two reviewers independently extracted data and the results were compared. When extracting qualitative data an inclusive approach was taken to minimize the risk of missing findings of value to the synthesis.[16] All reported texts and quotations were examined. This data took the form of first-order constructs (quotes from participants in primary qualitative studies, and author summaries of quotes) and second-order constructs (interpretations of the primary study).[17] In addition, we gathered experience-based evidence (informal reports of patient experiences) from discussion sections of included quantitative studies.[18] For multiple publications, data from the reference that provided the most comprehensive information has been used. When information was missing, where possible, we contacted the study authors directly (SF3).

2.5 | Quality assessment

Potential sources of bias were assessed independently, with group discussion to reach consensus. The ROB 2.0 Tool[19] was used to assess the risk of bias (RoB) of RCTs, and the ROBINS-I tool was used to assess the RoB for NRSI.[20] We did not assess the RoB for abstracts (because of their limited data), NRSI with only one group, or cross-sectional and case series (because of their limited ability to determine causal inference).[21,22] Single-arm studies are considered to have very high RoB. To assess the quality in qualitative studies, the Critical Appraisal Skills Programme (CASP) Qualitative Research Checklist was used.[23] The quality of survey studies in psychology (Q-SSP) checklist provided guidance for the quality of surveys.[24] Overall quality of evidence for our main outcome, ablation success, was assessed using Grades of Recommendation, Assessment, Development, and Evaluation (GRADE).[25]

2.6 | Analysis

We took a results-based convergent synthesis approach where the effectiveness synthesis (including quantitative studies) and views synthesis (including qualitative, survey, and experience-based evidence) were individually synthesized. Following this, the two strands were integrated.[26]

2.7 | Effectiveness synthesis

We did not combine data from RCTs with data from observational studies.[27] Random-effects meta-analyses were used to calculate pooled estimates for each question. For the outcome of ablation success, we calculated odds ratios (OR) and 95% confidence intervals (CIs). For iodine status, we calculated mean differences (MD) and 95% CIs based on the means and standard deviations (SD). As some studies presented urinary iodine using different methods (either mcg/L or mcg/gCr), we used Hedge's g to calculate standardized mean differences (SMD). If the data required were not available, we back-calculated from the data presented, where possible e.g., group numbers from percentages, SD from standard errors or using the quantile estimation method.[28] Fixed-effects models were performed as a sensitivity analysis (SF4a). For dichotomous data, the Mantel–Haenszel method was used to calculate risk ratios and 95% CI for both random and fixed effects meta-analyses. For continuous data, the inverse-variance method was used to calculate pooled MD and 95% CI for both random and fixed effects meta-analyses. Based on previous reviews,[6,7] we predicted that the available evidence examining the effect of iodine status or LID on ablation and therapy success would be sparse and so, as suggested by Scherer and Saldanha,[29] an a priori decision was made to include abstracts where full papers were not available. However, as RoB cannot be assessed for abstracts, a sensitivity analysis was performed with and without the abstract results.[30] Stata 16 was used for all analyses.[31]

The World Health Organization defines moderate urine iodine deficiency for adults as <50 mcg/L, mild iodine deficiency as 50–99 mcg/L, adequate iodine nutrition as 100–199 mcg/L, 200–299 mcg/L as above requirements, and ≥300 mcg/L as excessive. We examined the effect of iodine status on ablation success by comparing (a) deficient (<50 mcg/L or mcg/gCr) versus above requirements/excess (≥200) (which may reflect high-iodine consuming countries such as Korea) and (b) deficient (<50 mcg/L or mcg/gCr) versus adequate (100–199) (which may reflect lower-iodine consuming countries such as the UK).

2.8 | Views synthesis

In line with thematic synthesis[32] two reviewers (GH and AS) established an initial coding framework to capture barriers and facilitators of a LID. "Line-by-line" coding was carried out independently using Nvivo 12-pro software.[33] Individual coding was compared: returning to the original studies to check to understand. Similar codes were grouped and condensed until a smaller number of subthemes were developed from which broader themes were generated. Two additional investigators with clinical and nutritional expertise were consulted to further develop the subthemes and broader themes (CE and CA).

2.9 | Mixed synthesis

The effectiveness and views synthesis were combined and narratively synthesised[34] to examine the effect of advice to lower dietary iodine on iodine status.

3 | RESULTS

Title and abstract of 1109 articles were screened, of which 90 were subsequently screened as full text. We identified 59 studies (reported in 67 articles) for inclusion: 56 quantitative and three qualitative studies. A flowchart of included studies and reasons for exclusions are summarised in SF5/6. Table 1 summarizes the study characteristics.

The results are presented in three main sections: first, the effectiveness synthesis (Questions 1–4), second, the views synthesis (Question 5), and lastly, the mixed synthesis (Question 3).

3.1 | Effectiveness synthesis

3.1.1 | Question 1. Effect of iodine status and LID on ablation and therapy success

Response to treatment was determined from diagnostic WBS alone or diagnostic WBS combined with thyroglobulin results, sometimes with the inclusion of a cut-off for thyroglobulin antibodies (SF7,8). The findings below (Questions 1a–1d) are in relation to RAIT before ablation (to destroy any residual thyroid tissue or cancerous tissue left postsurgery). There were no studies that reported examining the effect of iodine status or LID in relation to RAIT before therapy (to treat residual, recurrent, or metastatic disease).

3.1.1.1 | *1a. Deficient (<50 mcg/L or mcg/gCr) versus above requirements/excess (≥200)*

Two studies[35,36] reported iodine status at these levels (SF7). One study used cutoffs of 200–250 and ≥250 mcg/L (or mcg/gCr)[36] and another used a cutoff of ≥250 mcg/L (or mcg/gCr).[35] To examine whether excess iodine affected ablation success we used the cutoff of ≥250 mcg/L, as this had been used in both studies. There was greater ablation success for those with an iodine status of <50 mcg/L (or mcg/gCr) compared with those with an iodine status of ≥250 (OR = 2.63, 95% CI, 1.18–5.86 n = 283) (Figure 1A). RoB of these studies was moderate (SF9a); GRADE certainty of evidence was very low (SF9g).

3.1.1.2 | *1b. Deficient (<50 mcg/L (or mcg/gcr) versus adequate (100–199)*

One study reported data for this comparison.[36] They showed similar levels of ablation success of those with a deficient iodine status and those with an adequate iodine status (88% compared to 82% OR = 1.59, 95% CI, 0.48 to 6.15, N = 113; moderate RoB).

3.1.1.3 | *1c. LID advice versus no LID advice*

Markovic et al.,[37] reported that following a LID had similar ablation success to those on a regular diet (less strict LID vs. regular diet: OR = 0.76, 95% CI, 0.26–2.24; stricter LID versus regular diet: OR = 0.88, 95% CI, 0.36–2.12 [calculated using author-reported percentages]). RoB for this study was not assessed as the results were reported in an abstract.

3.1.1.4 | *1d. Less-strict LID versus stricter LID*

Three studies[38–40] and two abstracts[37,41] reported data on the effect of a strict versus less-strict LID on ablation success (SF8). People advised to follow a strict diet to reduce iodine before ablation had similar rates of ablation success to those offered a less strict diet (OR = 0.67, 95% CI, 0.26–1.73, n = 256) (Figure 1B). The inclusion of two abstracts[37,41] in a sensitivity analysis showed no important changes to the findings (SF4b). RoB of these studies was serious (SF9b), and GRADE quality of evidence was very low (SF9g).

3.1.2 | Question 2: Effect of iodine status on recurrence of thyroid cancer or cancer-related mortality

No studies examined the impact of a LID on mortality rates. Two abstracts[42,43] reported the impact of the LID on long-term recurrence of DTC, both suggested that higher UIC before RAIT may be associated with disease recurrence. Li et al.[42] reported a 21.9% absolute risk increase in disease recurrence per 50 mcg/g increase of UI/Cr (p = .02) at 18 months postablation. Tobey et al.[43] analysed progression-free survival for patients with iodine status (mcg/24 h) <50, 50–99, 100–250, and >250 during a median follow-up of 45 months (IQR 17.5–78). Those with iodine status >250 had a higher risk of progression (hazard ratio [HR] 22.5, CI 3–170.9, p = .03) but results were attenuated when using a multivariate model (p = .05, effect size not given).

3.1.3 | Question 3: Effect of advice to lower dietary iodine on iodine status

Studies were divided by question type and design; studies compared the effect of a LID on iodine status to a normal diet (SF10), a stricter LID (SF11), or diets of different durations (SF12). Some compared two groups receiving different LID. Others assessed iodine status before and after the LID for the same set of participants (i.e., without a contemporaneous comparison group). Most evidence is from single-arm studies.

3.1.3.1 | *Effect of a LID compared with a normal diet on iodine status*

Studies comparing two groups: Participants following a 1-week LID reduced their iodine status compared to those who ate their normal diet (SMD = −1.89, 95% CI −2.63 to −1.16, n = 40)[2] (Figure 2A). RoB for this study was serious (SF9c).

Single-arm studies: Iodine status was measured before and after a LID in 18 studies (SF10). Seven did not provide data suitable for analysis.[38,44–49] Gosling et al.[50] reported a reduction in iodine status after <1 week LID (SMD = −3.18, 95% CI, −4.17 to −1.65, n = 7).

TABLE 1 Characteristics of included studies

Study (year), [abstract/translated], design, country	Total *n* (*n* withdrawals/excluded); *n* analysed; group: *n*	Age: mean years ± *SD* (if not otherwise stated)/female: *N* (%)	Type of DTC: *n* (%); stage	Diet and groups: Group description(s)	Diet and groups: Advised iodine intake (mcg/d)	Diet and groups: LID duration; before ablation/DxWBS/therapy	Diet and groups: Providers	Reported outcomes: Impact of LID/IS on ablation success	Reported outcomes: Impact of LID on UIS	Reported outcomes: AE/Rec/Mort	Reported outcomes: F&B/EBE
Randomized controlled trials											
Sohaimi (2019), Malaysia	110 (6 excluded: default in therapy); 104 analysed 1: Non-specified LID: 49 2: Strict LID: 55	43.2 ± 13.6; range: 9–77 F: 95 (91.3%)	PTC: 84 (80.8%) FTC: 20 (19.2%); Stage I/II: 77 (74%) Stage III/Iva: 13 (13%) Stage IVc: 14 (13%)	**1.** Written instruction of foods allowed/not allowed **2.** Written instruction of foods allowed/not allowed. 7-day sample menu.	**1.** NR **2.** <50	Both 1 wk; DxWBS or ablation	**1.** NR **2.** Nurses or dietitian	X	✓	X/X/X	X/X
Nonrandomized controlled studies											
Nonrandomized controlled trials											
Gosling (1975), [abstract], Netherlands	15 1. LID: 7 2. LID + ethacrynic acid: 8	NR; F: 4 (57%) in LID group	FTC; Metastatic	**1.** LID **2.** LID + ethacrynic acid (3 doses/d of 50 mg)	20–30 g[a]	4 or 9d (unclear); NR	NR	X	✓	X/X/X	X/X
Jagersma (2016), [abstract], Netherlands	27 1. Control: 15 (9 followed LID) 2. Counselling: 12 (7 followed LID)	1. 49 ± 18 2. 53 ± 15 F: 1. 8 (53%) 2. 7 (58%)	NR; NR	**1.** Control: received standard written instructions **2.** Counselling: received structured individualized dietary counseling: 7 followed LID	NR	NR but at least 7 days; NR	NR	X	✓	X/X/X	X/X
Ju (2016), South Korea	92 (78 provided urine samples) 1. Simple guide: 49 2. Intensive education: 43	44.2 ± 11.6 F: 73 (76%)	PTC: 89 (97%) FTC: 3 (3%); Ex: 61 (66.2%) LNI: 46 (50%)	**1.** 3-page handout on LID with no detailed explanation **2.** As group 1 + intensive education program (for a fee): 2.5-h group workshop that included 30 min of LID education.	1 + 2 <100	2 weeks before and until WBS (3 days after ablation)	Nurse and dietitian	X	✓	X/X/X	X/X
Lee (2016a), [abstract], Crossover, Korea	139	NR: NR	PTC; NR	One group underwent 2 diets **1.** Seaweed restriction only **2.** Conventional LID	NR	1. 1 wk (DxWBS) 2. 2 wks (ablation)	NR	X	✓	X/X/X	X/X

TABLE 1 (Continued)

Study (year), [abstract/ translated], design, country	Total *n* (*n* withdrawals/ excluded); *n* analysed; group: *n*	Age: mean years ± *SD* (if not otherwise stated)/female: *N* (%)	Type of DTC: *n* (%); stage	Diet and groups: Group description(s)	Advised iodine intake (mcg/d)	LID duration; before ablation/ DxWBS/therapy	Providers	Reported outcomes: Impact of LID/IS on ablation success	Impact of LID on UIS	AE/Rec/Mort	F&B/EBE
Lee (2016b), [abstract], Crossover Korea	72	NR; F: 53 (74%)	PTC; NR	One group underwent 2 diets. 1. Simplified LID (presumed seaweed restriction only) 2. Stringent LID	NR	1. 8d, 10d; DxWBS 2. 2 wks; therapy	NR	X	✓	X/X/X	X/X
Lim (2015), Korea	108 (7 excluded non-adherence to LID: Restricted iodine diet (RID): 2; LID: 5); 101 analysed 1. RID: 54/56 2. LID: 47/52	52 (23–73) F: 88 (87%)	NR; Stage I/II: 38 (38%) Stage III/Iva: 63 (62%)	1. RID: Diet guidelines (approved, restricted foods); meal plans 2. LID: Stricter diet guidelines (approved, restricted foods) compared to RID; meal plans	1. 50–100 2. < 50	4 wks; ablation	Nutrition co-ordinators	X	✓	X/X/X	X/X
Padovani (2015), Brazil	306 (181 excluded due to noncompliance with LID); 125 analysed 1. 15d: 79/153 2. 30d: 46/153	*N* = 306 Median (range): 37 (20–65) F: 208 (68%)	N = 306 PTC: 235 (77%) FTC: 71 (23%); NR	Instructed to follow a RID and provided with information on allowed/restricted foods: 1. 15days 2. 30 days	<50	1. 15d 2. 30d; DxWBS or therapy	NR	X	✓	X/X/X	X/✓
Roh (2006), South Korea	27 1. Less stringent LID: 14 2. Stringent LID: 13	43.5 ± 10.8; range: 22–60 F: 26 (96%)	PTC (100%); No metastasis	1. Longer timeframe but less information and support on LID 2. Shorter timeframe but more information and support on LID (e.g., specific customized diets)	NR	1. 2 wks 2. 1 wk; ablation	1. NR (not a dietitian) 2. 2. Dietitian	X	✓	X/X/X	X/X
Suzuki (2012), [abstract], Japan	45 1. Self-managed LID: 38 2. Self-managed LID + pre-packaged diet: 7	NR; NR	NR; NR	1. Self-managed LID: explanatory leaflet and advice of healthcare professional 2. Self-managed LID + pre-packaged diet: explanatory leaflet and advice of healthcare professional and a retort pouch diet for last 4d including day of ablation	NR	2 wks; NR	Doctor or dietitian	X	✓	X/X/X	X/X

(Continues)

TABLE 1 (Continued)

				Diet and groups				Reported outcomes			
Study (year), [abstract/ translated], design, country	Total *n* (*n* withdrawals/ excluded); *n* analysed; group: *n*	Age: mean years ± *SD* (if not otherwise stated)/female: *N* (%)	Type of DTC: *n* (%); stage	Group description(s)	Advised iodine intake (mcg/d)	LID duration; before ablation/ DxWBS/therapy	Providers	Impact of LID/IS on ablation success	Impact of LID on UIS	AE/Rec/Mort	F&B/EBE
Tomoda (2005), Japan	252 1. 1 wk restricted iodine diet: 210 2. 1 wk self-managed LID: 15 3. 2 wk self-managed LID: 17	1: 47.1 ± 16; F: 179 (85%) 2: 44.6 ± 15; F: 10 (67%) 3: 47.8 ± 16; F: 14 (82%)	Presumed DTC; NR	For all 3 diets ppts sent home with a simple, 1-page list of dietary recommendations. Foods to avoid for group 1 were less restrictive compared to groups 2 and 3 (who had the same list).	NR	1: 1 wk 2: 1 wk 3: 2 wks; DxWBS	**1.** 1: NR (explained) **2.** 2 + 3: explained then self-managed	X	✓	X/X/X	X/X
Waxman (2000), [abstract], USA	89 1. Unrestricted-avoid high iodine food: 41 2. Rigorous LID: 48	NR; NR	NR; NR	**1.** Unrestricted diet: avoid high iodine containing foods such as kelp or mineral supplements. **2.** Rigorous LID	NR	1. NR; 2. 2 wks; ablation	Dietitian	✓	X	X/X/X	X/X
Single arm prospective studies											
Jin (2010), [abstract], Korea	221	46 (22–79); F:167 (76%)	Presumed DTC; NR	One group educated on a stringent LID	NR	2 wks; NR	Specialized nutritionist	X	✓	X/X/X	X/X
Lakshmanan (1988), USA	5 (providing 45 urine samples) **1.** Usual diet (5ppts gave 3 samples each = 15 samples) **2.** LID (5ppts gave 6 samples each = 30 samples)	30-50 F: 4 (80%)	Assumed DTC because of I-131 scan; NR	One group: instructed by dietitian and a set of written instructions was given to each ppt detailing the foods high in iodine to avoid.	~50	4 wks; NR	Dietitian	X	✓	X/X/X	X/X
Nakada (2016), [abstract], Japan	40	NR; NR	PTC; pT3/pT4, or pN1a/pN1b	One group advised a LID.	NR	7d before to 3d after ablation	Dietitian	X	✓	X/X/X	✓/X
Nakada (2017) [Abstract], PC, Japan	56	27 to 77 F: 36 (64%)	PTC; NR	NR	<100 mcg/d	7 days before to 3 days after RAIT	NR	X	X	✓/X/X	X/X
Nakada (2020), [abstract], Japan	38	61.2 ± 14.2 F: 68%	PTC; Stage II/III	One group advised a LID. Measurements taken	< 100	2 wks (UIS at 1 wk); ablation	Dietitian	X	✓	X/X/X	X/X

TABLE 1 (Continued)

Study (year), [abstract/translated], design, country	Total *n* (*n* withdrawals/excluded); *n* analysed; group: *n*	Age: mean years ± *SD* (if not otherwise stated)/female: *N* (%)	Type of DTC: *n* (%); stage	Diet and groups: Group description(s)	Diet and groups: Advised iodine intake (mcg/d)	Diet and groups: LID duration; before ablation/DxWBS/therapy	Diet and groups: Providers	Reported outcomes: Impact of LID/IS on ablation success	Reported outcomes: Impact of LID on UIS	Reported outcomes: AE/Rec/Mort	Reported outcomes: F&B/EBE
Tobey (2018), [abstract], USA	71	42 (median; IQR 32.5, 54.5); NR	NR; intermediate/high risk	One group advised a LID.	NR	2 wks; therapy	X	X	X	X/✓/X	X/X
Cohort studies											
Bertolazzi (2010) [abstract], PC, Italy	186 **1.** THW + LID: 80 **2.** rhTSH + LID: 106	48; F: 128 (69%)	NR; NR	**1.** THW (TSH > 40 uU/ml) and LID **2.** rhTSH (TSH > 100 uU/ml) and LID	NR	2 wks; DxWBS	NR	X	✓	X	X/X
Choi (2008), [translated], PC, South Korea	67 (16 excluded: missing urine samples); 51 analysed **1.** Exposed to contrast agent: 39 **2.** Not exposed: 12	47.8 ± 11.1 F: 40 (78%)	PTC: 50 (98%) FTC: 1 (2%); Stage I/II: 33 (65%) Stage III/IVA: 15 (29%) Metastatic: 1 (2%)	One group: stringent LID. Three leaflets: allowed and restricted food; iodine in Korean commercial food; example of LID	NR (described as stringent)	2 wks; ablation	Nutritionist/dietitian	X	✓	X/X/X	X/X
Cuenca (2008), [translated], HC, Spain	371 **1.** General LID: 150 **2.** Strict LID: 221	47.9 ± 15.2 F: 254 (68%)	PTC: 299 (81%) FTC: 72 (19%); NR	**1.** General LID recommendations **2.** Strict LID: specific information about authorized and prohibited foods	NR	2 wks; DxWBS	NR	X	✓	X/X/X	X/X
Dayrit (2015), [Abstract], PC	59 (50 not reported since these are preliminary results); 9 analysed	39 ± 11 (23–56) F:7	NR	NR	NR	NR	NR	X	X	✓/X/X	X/X
Dobrenic (2011), PC, Croatia	16	Median (range): 55 (43–69) F: 11 (69%)	PTC: 10 (63%) FTC: 6 (37%); Recurrence in 7 (44%): Metastatic: 6 LNI: 1	One group advised to adhere to LID. Sent home with a list of dietary recommendations	NR	2 wks; therapy (*n* = 2) DxWBS (*n* = 14)	Self-managed	X	✓	X/X/X	X/X
Dobrenic (2017), [abstract] PC, Croatia	77	NR; NR	NR; Biochemically persistent	One group: 2 wk LID initially; ppts who did not achieve "moderate" iodine deficiency after 2 wks advised to follow LID for a further wk (3 wk LID)	NR	2–3 wks; therapy	Self-managed	X	✓	X/X/X	X/X

(Continues)

TABLE 1 (Continued)

				Diet and groups				Reported outcomes			
Study (year), [abstract/ translated], design, country	Total *n* (*n* withdrawals/ excluded); *n* analysed; group: *n*	Age: mean years ± *SD* (if not otherwise stated)/female: *N* (%)	Type of DTC: *n* (%); stage	Group description(s)	Advised iodine intake (mcg/d)	LID duration; before ablation/ DxWBS/therapy	Providers	Impact of LID/IS on ablation success	Impact of LID on UIS	AE/Rec/Mort	F&B/EBE
Ito (2018), PC, Japan	45 (8 used both protocols); 37 analysed 1. Self-managed LID: 25 2. Strict LID: 12	56 (median), 22–76 (range) F: 23 (51%)	PTC; LNI	1. Self-managed LID: Provided with a list of foods which should be avoided 2. Strict LID: Provided ready-made packaged LID	1. NR 2. < 30	2 wks; ablation	Radiologist or nutritionist	✓	✓	X/X/X	X/X
Jang (2011), [abstract] HC, Korea	299	NR; NR	PTC; Ex: 13% LNI: 60%	No information on what diet (if any) they had followed as this was a retrospective review to look at associations between UIE and ablation success.	NR	NR; ablation	NR	✓	X	X/X/X	X/X
Kang (2018), PC, South Korea	100 (5 in group 1 and 1 in group 2 did not collect urine samples); 94 analysed 1. Thyroxine withdrawal: 45 2. rhTSH: 49	1. 43.2 ± 9.8 2. 41.6 ± 8.3 F: 86 (91%)	PTC: 87 (92%) FTC: 5 (5%) Other: (2%); Stage I: 60 (64%) Stage III/Iva: 34 (36%)	1. Thyroxine withdrawal 2. rhTSH Both groups given same information on allowed and restricted foods.	[b] I/Cr ratio < 100 (mcg/ gCr)	2 wks; ablation	NR	X	✓	X/X/X	X/X
Kim (2011), PC, South Korea	20 (1 excluded non-adherence to LID); 19 analysed	39.7 ± 10.5 F: 13 (68%)	PTC: 18 (95%) FTC: 1 (5%); Stage I: 14 (74%) Stage III: 5 (26%)	One group: Educated for 2hrs before start of LID. Ppts could ask questions to HCP during LID.	[b] <66mcg/ gCr or 150mc-g/L	2 wks; NR	Specially trained HCP	X	✓	X/X/X	X/X
Kim (2017), HC, South Korea	326	49.3 ± 12.3 F: 248 55.8 ± 15.9 F:11	NR	NR	NR	23.9 ± 2.8 days	NR	X	X	✓/X/X	X/X
Lee (2014), PC, South Korea	202 (7 excluded: non-adherence to LID); 195 analysed	44 ± 11.08 F: 149 (76%)	PTC; T1-3N0M0: 49 (25%) T1-3N1M0: 146 (75%)	One group: Educated for 90-minutes on LID. Hotline to answer questions on LID.	<50	2 wks; ablation	Specially trained HCP	✓	✓	X/X/X	X/✓
Lee (2014), HC, South Korea	2241 (12 excluded due to missing data); 2229 analysed	47.0 ± 11.0 F: 1701 (76.3%)	PTC: 97%; Lung metastasis: 1.0%	NR	NR	2 wks	NR	X	X	✓/X/X	X/X

TABLE 1 (Continued)

Study (year), [abstract/translated], design, country	Total *n* (*n* withdrawals/excluded); *n* analysed; group: *n*	Age: mean years ± *SD* (if not otherwise stated)/female: *N* (%)	Type of DTC: *n* (%); stage	Diet and groups: Group description(s)	Advised iodine intake (mcg/d)	LID duration; before ablation/DxWBS/therapy	Providers	Reported outcomes: Impact of LID/IS on ablation success	Impact of LID on UIS	AE/Rec/Mort	F&B/EBE
Li (2017), [abstract], HC, USA	207	49 F: 72%	NR: NR	One group advised a LID.	NR	2 wks; ablation	NR	X	X	X/✓/X	X/X
Maxon (1983), PC, USA	40 1. Usual diet: 21 2. LID: 19	NR; NR	NR; Residual disease: 9 Metastasis: 10	1. Regular diet 2. LID: detailed diet sheets (listing permitted foods with serving sizes), alternate foods, dietary pattern and sample menu.	50	1 wk; DxWBS	Dietician	X	✓	✓/X/X	X/✓
Markovic (2015), [abstract], HC, Croatia	135 1. Regular diet: 34 2. Advice only: 30 3. Written strict LID: 71	Median (range): 54 (19–79) F: 107 (79%)	DTC (100%); Stage 1	1. Regular diet 2. LID advice only 3. Written instructions, strict LID	NR	NR; ablation	NR	✓	X	X/X/X	X/X
Morris (2001), HC, USA	140 1. Regular diet (RD): 50 (+ 7 healthy controls) 2. LID: 44 (7/44 thyroid cancer gave UI measurement) 3. 3. Control: 39 (all healthy)	NR; NR	NR; LNI: 27 Metastasis: 3	1. Advised not to eat iodinated foods (salt, multivitamins and seafood). 2. Copy of LID diet in pre-ablation instructions mailed/given in person	NR	10–14 days; ablation	NR	✓	✓	X/X/X	X/✓
Nakano (2020), [abstract], HC, Japan	24	NR; NR	PTC	One group advised a self-managed LID	NR	1 wk; ablation	NR	✓	✓	X/X/X	X/X
Park (2004), HC and PC, USA	45 (PC, all had rhTSH) 1. 1 wk LID: 21 2. 2 wk LID: 24 (Of these, previously prepared with THW and followed 2wk LID: 15)	NR; F: PC: 80%; H: --	NR; Residual and recurrent	LID explained at visit. Ppts sent home with a simple 1-pg list of dietary recommendations to limit iodine intake.	<50	1. 1 wk 2. 2 wks; DxWBS	NR (not a dietitian)	X	✓	X/X/X	X/X

(Continues)

TABLE 1 (Continued)

Study (year), [abstract/translated], design, country	Total *n* (*n* withdrawals/excluded); *n* analysed; group: *n*	Age: mean years ± *SD* (if not otherwise stated)/female: *N* (%)	Type of DTC: *n* (%); stage	Diet and groups: Group description(s)	Diet and groups: Advised iodine intake (mcg/d)	Diet and groups: LID duration; before ablation/DxWBS/therapy	Diet and groups: Providers	Reported outcomes: Impact of LID/IS on ablation success	Reported outcomes: Impact of LID on UIS	Reported outcomes: AE/Rec/Mort	Reported outcomes: F&B/EBE
Pluijmen (2003), HC, Netherlands	120 1. Controls: 61 2. LID: 59	43 ± 15; F: 94 (78%)	PTC: 101 (84%) FTC: 19 (16%); LNI: 32	1. Controls: no diet 2. LID: written instructions; assisted by dietitian.	NR	4 days; ablation	Dietitian	✓	X	X/X/X	X/X
Passero (2002), [abstract], HC, USA	59	NR; NR	NR; NR	One group advised a LID	<50	NR; ablation	NR	✓	X	X/X/X	X/X
Sohn (2013), HC, South Korea	295	45.8 ± 9.5 F: 246 (83.4%)	PTC; Ex: 250 (85%) LNI: 179 (61%)	One group advised a LID. Advised on foods and drugs that were allowed/not allowed. Given a 3-day sample menu tailored for Korean people and contact details for dietary questions.	NR	2 wks; ablation	Dietitian	✓	X	X/X/X	X/X
Sun (2015), [abstract] HC, China	95 1. Moderate-severe LID: 30 2. Mild iodine deficient: 26 3. Adequate iodine: 39	NR; NR	PTC; Intermediate risk	1. 2–4wks of moderate to severe LID 2. 2–4 weeks of mild LID 3. 2–4 weeks of adequate LID	NR	2–4 wks; ablation	NR	✓	X	X/X/X	X/X
Tala Jury (2010), HC, Italy	201 1. THW: 125 2. rhTSH: 76	44.0 ± 15.2 F: 164 (81.6%)	PTC: 182 (90.5%) FTC: 19 (9.5%); T1-T3N0M0: 144 (72%) T1-T3N1M0: 57 (28%)	Specific LID not recommended; advised not to take any iodine containing drug or iodine-supplementing preparation.	NR	4 wks; ablation	NR	✓	✓	X/X/X	X/X
Tamura (2016), [translated], HC and survey, Japan	39 (1 urine sample not collected before conducting LID); 38	57.0 ± 2.3 F: 24 (61.5%)	PCT (100%); pT3 or pT4a	One group received: handbook for the LID (food prohibited; allowed in limited amounts; allowed freely); a LID menu for 2wks; individualised advice (consultations 15–30 min long)	<100	10 d (1 wk before; 3 days after); ablation, DxWBS	Nutritionists/dietitians	X	✓	✓/X/X	✓/X
Yoo (2012), HC, South Korea	161 1. Less strict LID: 71 2. Very strict LID: 90	47.8 ± 11.2 F: 133 (82.6%)	NR; Capsular invasion: 109 (68%) Ex: 58 (36%)	1. Guidelines including restricted and allowed items. 2. Further food items were restricted.	NR	1 and 2: 2 wks (at least); ablation	Nuclear medicine physicians	✓	X	X/X/X	✓/X

TABLE 1 (Continued)

Study (year), [abstract/translated], design, country	Total *n* (*n* withdrawals/excluded); *n* analysed; group: *n*	Age: mean years ± *SD* (if not otherwise stated)/female: *N* (%)	Type of DTC: *n* (%); stage	Diet and groups: Group description(s)	Diet and groups: Advised iodine intake (mcg/d)	Diet and groups: LID duration; before ablation/DxWBS/therapy	Diet and groups: Providers	Reported outcomes: Impact of LID/IS on ablation success	Reported outcomes: Impact of LID on UIS	Reported outcomes: AE/Rec/Mort	Reported outcomes: F&B/EBE
Case reports/case series											
Al Asiri (2012) Saudi Arabia	1	62: F	PTC	NR	NR	3 wks	NR	X	X	✓/X/X	X/X
Al Nozha (2011), Saudi Arabia	1	66: F	PTC	NR	NR	4 wks	Dietitian	X	X	✓/X/X	X/X
Hinds (2008), USA	1	21: F	PTC; LNI	LID	NR	4 wks; DxWBS	Endocrinologist	X	✓	X/X/X	X/X
Ju (2015), South Korea	3	P1: 53: F P2: 48: F P3: 59: F	PTC; Stage II or III	Education program: 2.5-h group workshop that included 30 min of LID education.	< 100	2 wks; ablation	MDT including dietitian	X	✓	X/X/X	X/X
Kim (2014), South Korea	2	P1: 70: F P2: 68: F	PTC	NR	NR	2 wks	NR	X	X	✓/X/X	X/X
Krishnamurthy (2007), USA	2	P1: 70: M P2: 81: F	PTC	P1: NR P2: Booklet produced by ThyCa.org containing LID advice	NR	P1: 2 wks P2: NR	NR	X	X	✓/X/X	X/X
Maruca (1984), USA	3 (4 cases, 1 ppt counted twice)	P1: 66: F P2: 31: F P3: 33: F	NR: Metastasis	Whilst in hospital ppts put on a controlled iodine-depletion regimen	<25	5d; therapy	Nutritionist	X	✓	X/X/X	X/X
Nozu (2011), Japan	1	77: F	PTC	NR	NR	2 wks	NR	X	X	✓/X/X	X/X
Shakir (2008), USA	5	P1: 87: F P2: 66: F P3: 77: F P4: 68: M P5: 71: F	P1: FTC P2: PTC P3: PTC P4: PTC P5: FTC	NR	NR	P1: 10d/5wks P2: 6 wks P3: 1 wk P4: 10 d P5: 2 wks	NR	X	X	✓/X/X	X/X
Roopnarinesingh (2011), [abstract], case study, USA.	1	81, F	PTC	NR	NR	2 wks	NR	X	X	✓/X/X	X/X

(Continues)

TABLE 1 (Continued)

Study (year), [abstract/ translated], design, country	Total *n* (*n* withdrawals/ excluded); *n* analysed; group: *n*	Age: mean years ± *SD* (if not otherwise stated)/female: *N* (%)	Type of DTC: *n* (%); stage	Diet and groups: Group description(s)	Diet and groups: Advised iodine intake (mcg/d)	Diet and groups: LID duration; before ablation/ DxWBS/therapy	Diet and groups: Providers	Reported outcomes: Impact of LID/IS on ablation success	Reported outcomes: Impact of LID on UIS	Reported outcomes: AE/Rec/Mort	Reported outcomes: F&B/EBE
Surveys											
England (2020), Survey (including freetext box), UK	56 (completed by personnel at 47 treatment centres; no patients surveyed)	NA	NA	Described current practice regarding the LID.	NA	NA	NA	X	X	X/X/X	✓/X
Moon (2012), survey, South Korea	121 patients surveyed (4 incomplete surveys excluded); 117 analysed	41.5 (24–66); F: 117 (100%)	Assumed DTC; NR	Survey assessed: Dietary life and cooking skills; knowledge of LID; self-efficacy; personal and environmental barriers	NA	NA;2-4 wks before therapy	NR	X	X	X/X/X	✓/X
Qualitative studies											
Herbert (2020), interviews, UK	28	51 (24–80) F: 19 (68%)	NR; NR	Ppts recruited from three centres which offered different advice: Site 1 advised a LID for 2 wks before treatment, and 48 h after; Site 2 advised a LID for 1 wk before treatment; and Site 3 did not advise a LID.				X	X	X/X/X	✓/X
Lee (2016), interviews, Korea	5	28-58; F: 4 (80%)	NR; Stage 1: 1; Stage 3: 3; Stage 4: 1	Iodine restricted diet beginning 2 wks before RAI therapy. Ppts were going through the last two weeks of hormone withdrawal before high-dose radiation therapy (100-150mCi) to remove any remaining thyroid tissue.				X	X	X/X/X	✓/X
Stajduhar (2000), focus groups/ interview/ field notes, Canada	27	38 (18–80) F: 22 (81%)	NR; NR	NA				X	X	X/X/X	✓/X

Abbreviations: AE, adverse effects; d, days; DTC, Differentiated Thyroid Cancer; DxWBS, Diagnostic Whole-Body Scan; EBE, Experience based evidence; Ex, extrathyroidal invasion; F, female; F&B, facilitators and barriers; FTC, follicular thyroid cancer; HCP, healthcare professional; HC, historical cohort study; I/Cr, iodine/creatine; IQR, interquartile range; LID, low iodine diet; LNI, lymph node involvement; mcg, micrograms; mcg/gCr, urinary iodine-to-creatinine ratio; mCi, millicurie; mort, mortality; Na, serum sodium; NA, not applicable; NR, not reported; pN1a, Cancer has spread to the lymph nodes around the thyroid; pN1b, Cancer has spread beyond the central compartment; pT3, The tumour is larger than 4 cm, but the tumour does not extend beyond the thyroid gland; pT4, The tumour is any size and has extended beyond the thyroid; PC, prospective cohort study; ppts, participants; PTC, papillary thyroid cancer; RAI, radioactive iodine; RAIT, radioactive-iodine treatment; rhTSH, recombinant human thyroid-stimulating hormone; Rec, recurrence; SD, standard deviation; THW, thyroid hormone withdrawal; TSH, thyroid-stimulating hormone; UIC, urine iodine concentration; UIE, urine iodine excretion; UIS, urinary iodine status; WBS, whole-body scan; wk(s), weeks; yr(s), years; --: Uninterpretable.

[a]Expected misprint; probably, mcg/d.

[b]Not iodine intake: advised UIC or I/Cr ratio.

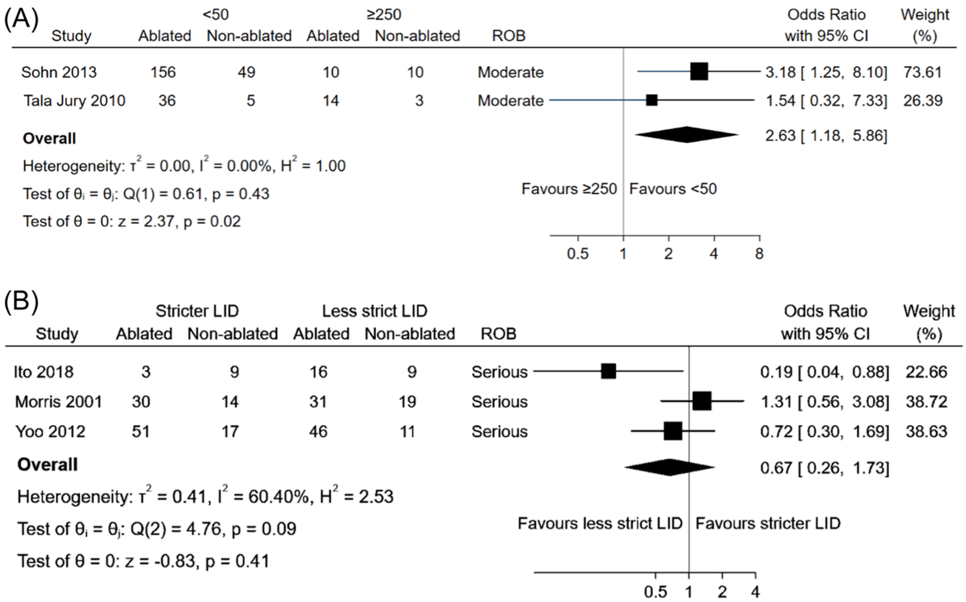

FIGURE 1 (A) Forest plot of odds ratio and 95% CI of pooled studies comparing an iodine status <50 mcg/L (or mcg/gCr) to ≥250 on ablation success. (B) Forest plot of odds ratio and 95% CI of pooled studies comparing a stricter LID to a less-strict LID on ablation success. CI, confidence interval; LID, low iodine diet

Studies in which participants followed a LID for 1-week had reduced iodine status compared to before starting the diet (SMD = −1.28, 95% CI, −2.26 to −0.31, n = 185).[51–54] Studies in which participants followed a LID for 2-weeks had reduced iodine status compared to before starting the diet (SMD = −1.30, 95% CI, −2.18 to −0.43, n = 392) (Figure 2A).[39,51,55–58] Single-arm studies have reduced capacity to provide robust evidence on causal inference and thus there is very low certainty in these data.

3.1.3.2 | *Effect of stricter LID compared with less-strict LID on iodine status*

Six studies compared iodine status of those on stricter LID compared to a less-strict diet (where stricter refers to the group with more dietary guidelines/education) (SF11).[53,58–62] One RCT reported participants following a stricter LID had similar iodine status compared to those following a less-strict LID (SMD = −0.14, 95% CI, −0.52 to 0.25, n = 104) (Figure 2B).[53] The RoB judgement was "some concerns" (SF9d). Five observational studies reported that those following a stricter LID had lower iodine status compared with those following a less-strict LID (SMD = −0.40, 95% CI, −0.56 to −0.24, n = 816). All five studies were judged to be at serious RoB (SF9c).[58–62] Sensitivity analysis excluding Ju et al.,[58] who measured iodine status using intake (3-day diet records) rather than UIC showed no important changes to the findings (SF4c).

3.1.3.3 | *Effect of duration of LID on iodine status*

The most common comparisons of diet duration on iodine status were 1 versus 2 weeks and 2 versus 4 weeks. One single-arm study[63] compared 2 and 3-week LID and reported p > .05 for the difference in iodine status (data not reported) (SF12).

3.1.3.3.1 | *1-week versus 2-week LID.*

Studies comparing two groups: Participants on a 2-week LID had lower iodine status compared with those on a 1-week LID (SMD = −0.99, 95% CI, −1.46 to −0.53, n = 77) (Figure 2C).[62,64] ROB in both studies was serious (SF9c).

Single-arm studies: Participants who followed a 2-week LID had lower iodine status compared with those on a 1-week LID (SMD = −0.27, 95% CI, −0.46 to −0.08, n = 214) (Figure 2C).[51,65] There was very low certainty in this evidence.

3.1.3.3.2 | *2 weeks versus 4-week LID.*

Studies comparing two groups: Participants on a 4-week LID had similar iodine status as those on a 2-week diet (SMD = −0.06, 95% CI, −0.43 to 0.30, n = 125) (Figure 2C).[3] RoB for this study was serious (SF9c).

Single-arm studies: Participants following a 2-week LID had similar iodine status compared to those following a 4-week diet (SMD = 0.11, 95%CI, −0.17 to 0.38, n = 101) (Figure 2C).[60] There was very low certainty in this evidence.

3.1.4 | Question 4: Are there any complications or adverse effects from consuming a LID?

Thirteen studies reported adverse effects from consuming a LID.[2,54,66–76] Maxon et al.,[2] noted that no-one following the LID experienced side effects such as diarrhoea or nausea. Tamura et al.,[54] provided a single statement, reporting no signs of hyponatremia after the LID. Seven case studies/case series described hyponatremia in 12 patients with DTC.[66–71,76] Four cohorts studies[72–75] examined hyponatremia shortly before or after ablation and reported a total of 62 cases of hyponatremia: Eight as severe.

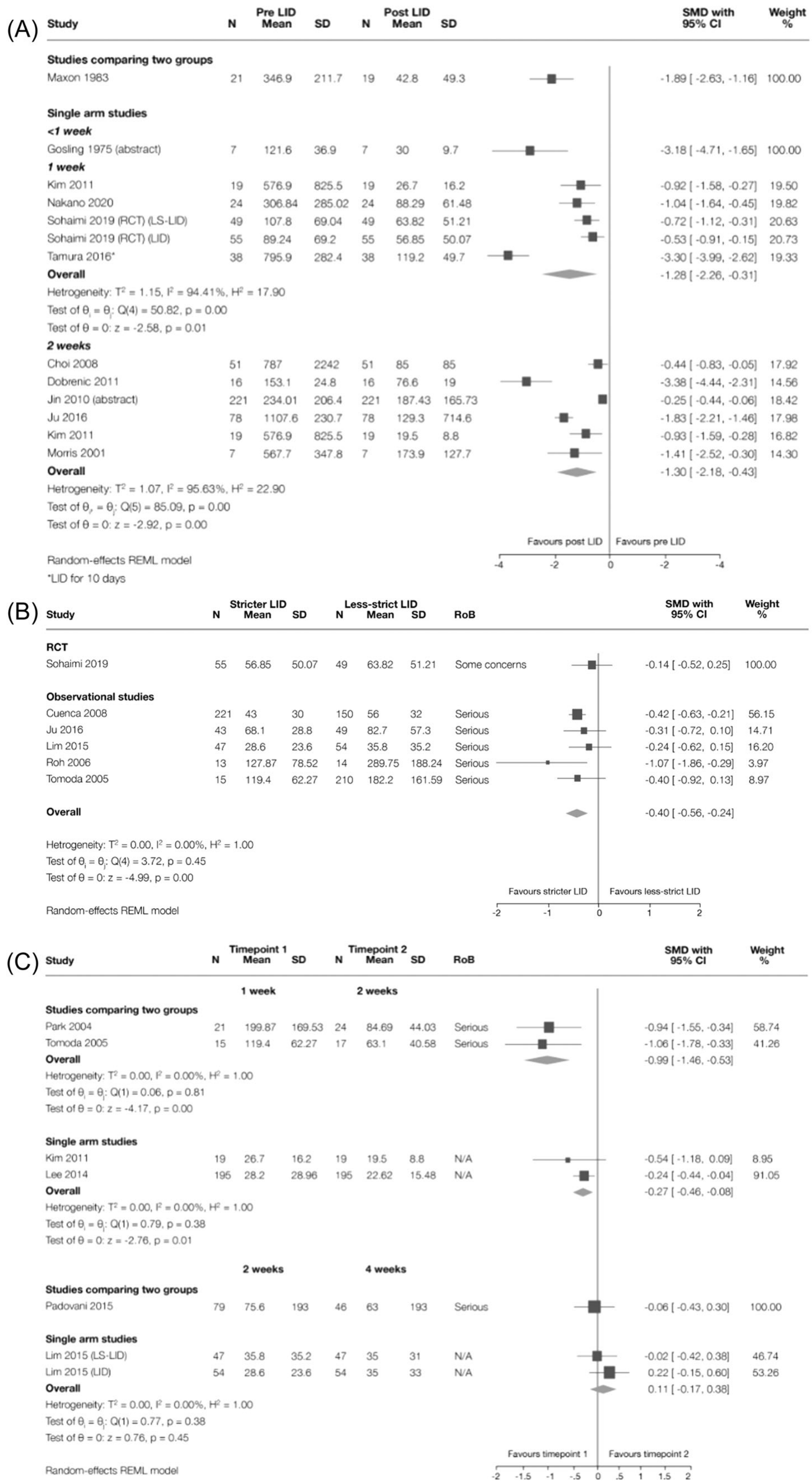

FIGURE 2 (See caption on next page)

3.2 | Views synthesis

The facilitators, barriers, and challenges experienced by patients consuming a LID were reported in three qualitative studies[13,14,77] and three surveys.[11,54,78] Results from quantitative studies[40,45,79] and experience-based evidence reported in four studies[2,39,47,65] strengthened the evidence base.

3.2.1 | Question 5: What are the facilitators and barriers of consuming a LID?

The themes, subthemes, and supportive evidence for this synthesis are shown in Table 2 (full extractions SF13). Six themes formed the overarching synthesis: self-perception, changes to health, dietary adaptation, behavioural strategies, information provision, and environment. Across these themes seven facilitating factors were identified: the diet having an understandable rationale; providing an opportunity for an individual to have an active role in their treatment; experiencing other health benefits whilst on the diet; it being easier relative to other cancer journeys; substituting high for low iodine products; having clear advice, and positive and effective reinforcement. Five barriers/challenges were identified: negative impact on psychological and physical health; dealing with other treatment and medication side effects; greater difficulty for subgroups, for example, those experiencing existing dietary restriction; over restriction; and confusion. Three of the subthemes (reduction in energy intake; information seeking; preparing low iodine meals) could be considered as facilitating factors for some but barriers/challenges for others.

The CASP quality appraisal tool and Q-SSP indicated some uncertainties surrounding the quality of one of the qualitative studies[77] and one of the surveys[54] (SF9e,f). The relative contributions of these studies to the analytic themes and intervention recommendations based on these were explored in relation to their evaluated quality. For example, careful consideration was given when interpreting the findings of Lee et al[77] so as not to attribute reported difficulties to the LID when it could have been due to hormone imbalances resulting from THW.

3.3 | Mixed synthesis

A mixed synthesis of the "effectiveness and views" was undertaken to explore Question 3 further by examining if variation in iodine status resulted from different types of LID interventions in terms of the levels of investment from the educator, and participant empowerment to follow the diet. First, the themes from the views synthesis were translated into recommendations for interventions (Table 2, final column). A matrix was created to illustrate recommendations reflected in the effectiveness studies that had explored the impact of a LID on iodine status (Table 3). Studies expected to have sufficient information on intervention design (full-text RCTs, NRSI, and prospective studies) were included ($n = 16$). Iodine status was plotted against the level of overall intervention investment for the educator/participant empowerment to follow the diet (high, medium, low) for 15 studies (Ito et al.,[38] did not report iodine measurements). The average mean iodine status was lowest for the high educator investment/patient empowerment group (medians (mcg/gCr or mcg/d or mcg/l): high = 42.8, medium = 76.8, low = 76) (SF14).

4 | DISCUSSION

4.1 | Summary of findings

LID before RAIT was developed and widely adopted in the 1980s. Since then, two reviews (in 2010 and 2016) have summarised LIDs in the treatment of DTC.[6,7] Our review updates the evidence on the impact of iodine status/LID on treatment success and is the first mixed-method review in this area.

A key finding of this review is the lack of high-quality evidence examining the effect of iodine status or LID on ablation and therapy success. Guidelines advocate the postponement of RAIT with iodine values exceeding 200 mcg/L.[80] Our review found there was greater ablation success for those with a deficient iodine status (<50 mcg/L or mcg/gCr) compared to above requirements/excessive (≥250). However, the quality of evidence for this comparison is very low as it was based on the results of two studies[35,36] with moderate risk of bias and relatively wide 95% CIs that crossed the line of no effect in one study. Only one study compared a deficient (<50 mcg/L or mcg/gCr) and adequate (100–200) iodine status on ablation success and there was no effect on ablation success.[36] The studies examining LID on ablation success[37–41] are limited in several ways: potential non-adherence to the diet; comparisons of varying stringencies of diet instead of between a control and LID; the inclusion of a small number of patients with metastasis[39]; and a serious risk of bias (e.g., they did not use analysis methods that could control for potential confounders such as staging and administered activity). A previous review suggested that <100 mcg/L (or mcg/gCr) may increase ablation success[6] however this review suggests a more cautionary interpretation of the evidence as there is insufficient high-quality evidence to

FIGURE 2 (A) Forest plot of standardized mean differences (SMD) and 95% confidence interval (CI) of pooled studies comparing the effect of low iodine diet (LID) compared with normal diet on iodine status (B) Forest plot of SMD and 95% CI of pooled studies comparing the effect of stricter LID compared to less-strict LID on iodine status (C) Forest plot of SMD and 95% CI of pooled studies comparing the effect of LID duration on iodine status.

TABLE 2 Facilitators and barriers to consuming a LID.

Themes[a]	Subthemes	Study (year), evidence type (1st or 2nd OC[b])	Supporting evidence	Recommendation for intervention
Self-perception	+ Strong belief: *Understandable rationale/clear coherence*	Herbert (2020) Qualitative (1st oc)	It's easily understandable why you have to go on that diet. Without it, the treatment isn't as effective, so I'd rather the treatment be effective and try and get cured than eat stuff that I'm normally eating.	Education: rationale for LID explained
		Lee (2016) Qualitative (2nd oc)	They understood the importance of the LID treatment enough that they demonstrated a strong will to remain focused on it.	
		Moon (2012) Survey	Perceived barrier related to LID practice: I do not believe that LID is helpful for my treatment (1 strongly disagree – 7 strongly agree): 1.93 ± 1.24.	
	+ Active role in treatment/ sense of control	Herbert (2020) Qualitative (1st oc)	I wanted to make sure that I was really strict, because at the end of the day, that is something that I can kind of control. As long as I have a LID, then I have done everything I can to make sure that the treatment works.	Empowering patients to reduce their iodine intake (to take control in their treatment)
		Lee (2016) Qualitative (1st oc)	I also checked and kept a daily record of what I ate.	
		England (2019) Qualitative (2nd oc)	…clinicians also said that there were people who liked feeling in control of a part of their cancer treatment.	
Changes to health	+ Other health benefits	Herbert (2020) Qualitative (2nd oc)	+…some stated that it helped them to lose weight and feel healthier.	*No recommendation*
		England (2019) Qualitative (2nd oc)	+…clinicians also said that there were people…who experienced other health benefits from thinking about what they were eating.	
	+/− Reduction in energy intake	Herbert (2020) Qualitative (2nd oc)	+…some stated that it helped them to lose weight	Education: food recommendation and clear length and level of restriction
		Ju et al (2016) Quantitative	+/− The mean level of energy intake during the LID period was 1325 kcal, which was 446 kcal lower than the intake during the usual diet (1771 kcal).	
		Maxon (1983) EBE	+/− Participants were informed that the LID did not meet recommended daily calories (i.e., 1400 kcal).	
	- Negative impact on psychological health (guilt over relapses, blame, anxiety, depression boredom, overwhelming, early unsettled feelings) and physical health	Herbert (2020) Qualitative (1st oc)	Then when I went in, I explained that I'd messed up, so they had to look into it. I think they went to see Doctor [Name] then to see if it was okay to continue, which it was at that time.	Ongoing support
		Lee (2016) Qualitative (1st oc)	I had some food I wasn't allowed to eat in the first treatment. I regret and feel sorry for my body because it's due my carelessness that I am going through this second treatment.	
		England (2019) Qualitative (2nd oc)	The diet was identified as being a source of anxiety for some people…	
		Stajduhar (2000), Qualitative (2nd oc)	Yet, little nutritional consultation was offered to assist them in understanding what constituted a low-iodine diet. As a result, many participants did their own research,	

TABLE 2 (Continued)

Themes[a]	Subthemes	Study (year), evidence type (1st or 2nd OC[b])	Supporting evidence	Recommendation for intervention
	(fatigue, hunger, loss of appetite, nutrient content)		yet some continued to be unclear and worried that this might have affected their treatment.	
		Ju et al (2016) Quantitative	The intake levels of most nutrients, were significantly lower during LID compared to the usual diet.	
		Lee (2014) EBE	In our experience, a LID could be a source of anxiety because the patients feel that the variety of foods that could be eaten safely is low.	
		Maxon (1983) EBE	They did complain that the diet was boring.	
		Morris (2001) EBE	Others found it "overwhelming" to maintain the diet while adapting to a new diagnosis of cancer and withdrawing from medications.	
Dietary adaptation	+/− Cancer treatment context *+ Easy compared to other cancer journeys; short time frame.* *- Dealing with other treatment and medication side effects*	Herbert (2020) Qualitative (1st oc)	+ I mean compared to having chemotherapy or radiotherapy, anything like that, if this can sort it out and it means me not on anything else, it's far easier on me and my family than anything else. - ...when you are already experiencing... Your emotions are all over the place because you have just been told you have got cancer. You have just had surgery or whatever and now you have got to take more treatment that you don't know is definitely going to work and then you have got to go and do this [referring to the LID], it is a lot.	Support
		England (2019) Survey	+/− 31 of the 56 clinicians (53%) indicated that they thought people coped very well with the diet	
		Lee (2016) Qualitative (2nd oc)	- As time went on and the hormone deficiency grew more severe while the LID aggravated nutrition deficiencies, patients became more worn out from the physical symptoms they experienced.	
		Morris (2001) EBE	- Others found it "overwhelming" to maintain the diet while adapting to a new diagnosis of cancer and withdrawing from medications.	
	- Greater difficulty for sub-groups:[c] e.g. older people, diabetics, vegetarians, those culturally consuming diets higher in iodine	Lee (2016) Qualitative (1st oc)	It was difficult to refrain from what I wanted to eat. I am going to have kimchi when the treatment is over.	Education: food recommendations adapted for sub-groups
		Herbert (2020) Qualitative (1st oc)	I am vegetarian so I did find the diet very hard.	
		England (2019) Qualitative (2nd oc)	...some groups of people were more likely to find the diet difficult, specifically, people with diabetes, vegans/vegetarians, older people and people from non-British backgrounds	
		Nakada (2016) Quantitative	Practice of LID may be difficult in older patients or patients with higher UIC under routine diet. Since risk of failure of LID increases in such group, it is recommended LID plan for rh-TSH aided remnant tissue ablation should be applied on a patient-to-patient basis taking patients' personal characteristics into consideration.	

(Continues)

TABLE 2 (Continued)

Themes[a]	Subthemes	Study (year), evidence type (1st or 2nd OC[b])	Supporting evidence	Recommendation for intervention
		Moon (2012) Survey	Perceived barrier related to LID practice: I enjoy foods with high iodine content (1 strongly disagree – 7 strongly agree): 4.53 ± 1.48.	
		Ju (2015) EBE	Maintaining the LID is challenging for Korean patients, whose regular diet consists of foods with very high iodine content, such as seaweeds, seafoods, soy sauce, soybean pastes, and salted vegetables such as kimchi.	
	- Unable to moderate: *Over restriction in terms of time on the diet and dietary choices (especially for those on a LID for recurrence).*	Herbert (2020) Qualitative (1st oc)	Sometimes you may eat something that you think, Oh my gosh, that might have had dairy in or iodine. Literally once I find something that hasn't got any iodine or low iodine in, this time I was living on a jacket potato.	Education: clear length and level of restriction
		Lee (2016) Qualitative (1st oc)	Because there isn't much I am allowed to eat, I cannot eat regularly. I would eat only once a day, when I felt like I was starving.	
		England (2019) Qualitative (2nd oc)	...and there were comments that some people were more restrictive than advised and attempted to follow no- iodine diets, rather than reduced iodine.	
		Moon (2012) Survey	Knowledge questionnaire item – "I have to practice LID after radioactive iodine treatment" Almost half (46.2%) thought this statement was true when the answer was false.	
Behavioural strategies	+ Substituting high for low iodine products	Herbert (2020) Qualitative (2nd oc)	Substitutions for milk were discussed by most people particularly because of its importance in tea, coffee and cereal. Participants reported trying non-dairy substitutes for milk such as soya, oat, rice and coconut...Other substitutions included swapping milk for dark chocolate, butter for dairy-free spreads and consuming gluten-free products.	Education and behaviour modification: food recommendation - substitution of high for low iodine products
		Lee (2016) Qualitative (1st oc)	I love sweets! But since I couldn't have them, I had apples and pears instead.	
	+/− Information seeking: Checking products are low in iodine (on ingredients lists/with companies)	Herbert (2020) Qualitative (1st oc)	+ Also, it got me checking the labels on the ingredients a little bit more thoroughly just so I could prep a couple of days before going on the diet and then also during the diet, I'd look and see, "This is okay or not". - Just going to the supermarket, taking so long to check products that haven't got iodine in, that's the only hard part is identifying the products you can't have...	Education: food recommendation – food labelling
		Lee (2016) Qualitative (2nd oc)	+ They were interested in everything about their diets and proactively searched online to get information about the regimen.	
		Stajduhar (2000) Qualitative (2nd oc)	- Yet, little nutritional consultation was offered to assist them in understanding what constituted a low-iodine diet. As a result, many participants did their own research, yet some continued to be unclear and worried that this might have affected their treatment.	
		Moon (2012) Survey	- Perceived barrier related to LID practice: I cannot distinguish foods high in iodine from those low in iodine (1 strongly disagree – 7 strongly agree): 4.79 ± 1.81.	

TABLE 2 (Continued)

Themes[a]	Subthemes	Study (year), evidence type (1st or 2nd OC[b])	Supporting evidence	Recommendation for intervention
	+/− Preparing low iodine meals	Lee (2016) Qualitative (1st oc)	+ From two weeks before the RAI treatment, I started to freeze what I could eat. I also checked and kept a daily record of what I ate.	Education: food recommendation – food provision
		Herbert (2020) Qualitative (1st and 2nd oc)	- A few participants discussed repeatedly eating the same meal due to a lack of time to prepare and organise a LID meal: "I was back at work, so I just used to have jam sandwiches, usually".	
		Yoo (2012) Quantitative	+ We thought that those who work and thus cannot cook every meal according to the LID might have a lower radioactive iodine ablation success rate, but there was no difference between actively working patients and stay-at-home patients.	
		Moon (2012) Survey	- Item: I am not knowledgeable about how to prepare low-iodine menus (1 strongly disagree – 7 strongly agree): 5.51 ± 1.72.	
		Tamura (2016) Survey	- Response of patients to questionnaire survey. Have you had any difficulties in preparing LID? 60% said yes.	
Information provision	+ Clear advice about the LID *UK LID working group diet sheet and HCP*	Herbert (2020) Qualitative (1st oc)	I used to keep that [referring to the 'diet sheet'] in my bag, so when I went shopping, I could look at the list and then look at what was in it…because I kept forgetting.	Education: clear education/food recommenda-tion/level of restriction
		England (2019) Survey	There was good awareness and usage of the UK LID-WG diet sheet (66% reported using it) and only four centres indicated that they were unaware of it.	
	- Confusion *Lack of clear advice, limited knowledge of acceptable foods. Led to skipping meals, repetition of same meals and feelings of limited food choice.*	Herbert (2020) Qualitative (1st oc)	I did get a bit confused about the whole thing, so I just really limited my diet to a few recipes and I just repeated them over and over again. At the end of it, I was, kind of, getting a bit desperate for food.	
		Lee (2016) Qualitative (1st oc)	I would cook a porridge with rice crust. I skipped lunch at work because I was so concerned with what I was not allowed to eat.	
		Stajduhar (2000) Qualitative (2nd oc)	Participants were concerned about the lack of information about dietary considerations associated with treatment. Participants explained that they must be on a LID six weeks before treatment and approximately 24–48 h posttreatment. Yet, little nutritional consultation was offered to assist them in understanding what constituted a LID.	
		Moon (2012) Survey	The respondents also possessed little knowledge of the foods restricted in LID, such as soybean paste, soy sauce, multi-vitamins, processed meats, milk, and dairy products. The item 'LID is a low-salt diet (false)' presented the lowest percentage of correct answers (12%).	
		England (2019) Survey	For some questionnaire items, different responses were provided by different clinicians from the same centre.	
		Morris (2001) EBE	Since 1997 some patients submitted feedback on the LID. Some suggested the diet was difficult to understand and confusing.	

(Continues)

TABLE 2 (Continued)

Themes[a]	Subthemes	Study (year), evidence type (1st or 2nd OC[b])	Supporting evidence	Recommendation for intervention
		Lee (2014) EBE	In our experience, a LID could be a source of anxiety because the patients feel that the variety of foods that could be eaten safely is low.	
Environment	+ Positive and effective reinforcement *e.g., practical and emotional support and responsive HCP*	Herbert (2020) Qualitative (1st oc)	… my parents, obviously, were here as well, so they've just reminded me not to have milk and stuff.	Ongoing support
		Lee (2016) Qualitative (2nd oc)	…they wanted emotional support to maintain a temperate lifestyle and to remain disciplined.	
		Moon (2012) Survey	Perceived barrier related to LID practice: I do not have someone who will prepare low-iodine menus for myself (1 strongly disagree – 7 strongly agree): 4.86 ± 2.14.	

Abbreviations: +, facilitating factor to consuming a LID; −, challenge/barrier to consuming a LID; EBE, experience-based evidence; HCP, health care professional; kcal, kilocalories; LID, low iodine diet; LID-WG, low iodine diet working group; OC, order construct; UIC, urinary iodine concentration; rhTSH, recombinant human thyroid-stimulating hormone; RAI, radio-active iodine.

[a]The synthesis of both first and second order constructs, into 3rd order constructs (interpretations of the review authors).

[b]1st and 2nd order constructs relevant for qualitative studies: 1st order constructs are those that reflect participants' understandings, as reported in the included studies (usually found in the results); 2nd order constructs are interpretations of participants' understandings made by authors of these studies (usually found in the discussion/conclusion).

[c]Who experience existing dietary restriction for other health or lifestyle reasons.

draw any firm conclusions as to whether iodine status affects ablation success.

Despite insufficient evidence for efficacy, the majority of studies included in our review, assumed a LID to be necessary and examined the effect of varying lengths of time and stringency of iodine restriction on iodine status. A previous review[6] supported a decrease in iodine status after consuming a LID for 1–2 weeks. This review suggests that a greater reduction in iodine status may be seen from a 2-week compared to a 1-week diet. However, this conclusion is based upon a small number of studies[51,62,64,65] with serious or unknown bias. Furthermore, reductions in iodine status <50 (mcg/gCr or mcg/L) were seen in the single-arm studies after 1 week.[51,65] Although the evidence is limited and has a serious or unknown bias, there is little to suggest any benefit to iodine status in consuming a LID for >2 weeks. This supports Morsch et al.'s[81] findings when they compared the effect of a 2- and 3-week LID on iodine status in people having a thyroid evaluation and found no difference between durations. The views synthesis found many challenges to consuming a LID and it is likely that non-adherence to the diet will increase, and patient wellbeing be negatively affected, the greater the duration of iodine restriction.

We found a stricter diet may be more effective in reducing iodine status than a less-strict diet. However varying intensities of LID education meant that the "stricter" and "less strict" categories were not uniform across the studies and there may have been overlaps in the extent to which diets were altered. The mixed-synthesis aimed to deal with this variation by categorizing each study as either having high, medium, or low educator investment/participant empowerment to follow the diet. We observed that those within the high category had a lower iodine status, suggesting a need for detailed LID education and sufficient support to effectively reduce iodine status. However, a balance must be reached in the amount of information provided. Enough should be offered to allow individuals to feel confident and equipped to consume a LID, but with an awareness that this advice is given at a time when patients could be processing large amounts of new medical information (e.g., postsurgical care, changes in medication) and are vulnerable to information overload.[82] If, after considering the evidence, clinicians think that a LID is a necessary part of treatment, a strategy that could be explored is the use of timely LID information through smartphone/tablet apps as these have been shown to improve knowledge and treatment adherence for other interventions, especially with a duration less than a month.[83]

An adverse effect of the LID, as shown in the views synthesis, was the negative impact on psychological health. At best, individuals reported it as boring, confusing, overwhelming, and unsettling; at worst, individuals were anxious and self-blaming if they had consumed food containing iodine, and, most likely in conjunction with a strong belief in the diet, that relapses were attributed to actions whilst on the diet. The opportunity for blame in this patient group is high as recurrence rates are up to 68% in high-risk patients.[80] This review has shown that a LID could add to what has

TABLE 3 Matrix of effectiveness synthesis studies use of intervention recommendations identified in the views synthesis.

			Education														
			Support	Relationship with HCP			Food recommendations										
							Delivery and amount of detail on LID										
Study (year)	Type of LID	Clear length of restriction	Inclusion of family/friends	Number of contact sessions/Format: In or Gr	HCP	Ongoing support (e.g., phone)	Written	Face-to-face (length)	List of foods to avoid/restrict	List of allowed foods	Food labelling/food composition	Meal plan/sample menu	Food provision	Adapted for subgroups	Advised iodine intake (mcg/d)	Overall intervention investmentfor educator and level of ppt empowerment to follow a LID[a]	Post IS mean (SD) (unit)
Choi (2008)	*LID*	2wks	X	1/In	Nu/DN	X	✓	✓ (NR)	✓	✓	✓	✓	X	✓	NR	Medium	85 (85) (24 h; mcg/d)
Dobrenic (2011)	*LID*	2wks	X	1/In	NR	X	✓	NR	✓	✓	X	X	X	X	NR	Low	76.6 (9.0) (spot; mcg/L)
Ito (2018)	*LS- LID*	2wks	X	1/In	Radiol/Nu	X	✓	✓ (NR)	✓	X	X	X	X	X	NR	Low	_ _
	S- LID	2wks	X	NR	NR	X	NR	NR	X	X	X	✓	✓	X	<30	Low	_ _
Ju (2016)	*LS- LID*	2wks and 3 days	X	1/In	Nurse	X	✓	✓ (10–15 min)[b]	✓	✓	X	X	X	X	<100	Low	82.7 (57.3) (3 day diet records; mcg/d)
	S- LID	2wks and 3 days	X	1/In and Gr	DN + other HCP	X	✓	✓ (In: 10–15 min; Gr: 2.5 h)[c]	✓	✓	X	✓	X	X	<100	High	68.1 (28.8) (3 day diet records; mcg/d)
Kang (2018)	*LID*	2wks	X	NR	NR	X	✓	NR	✓	✓	X	X	X	X	<100 (µg/gCr]	Low	THW: 23.8 (19.9) rhTSH: 47.4 (18.4) (spot I/Cr; mcg/gCR)
Kim (2011)	*LID*	2wks	X	Multiple[d]/In	Nurses/DNs	✓	✓	✓ (2 hrs)	✓	✓	X	✓	X	✓	<150	High	19.5 (8.8) (spot I/Cr; mcg/gCr)
Lakshmanan (1988)	*LID*	4wks	X	1/In	DN	X	✓	✓ (NR)	✓	X	✓	X	X	✓	~50	Medium	69 (14) (spot; mcg/gCr)
Lee (2014)	*LID*	2wks	X	Multiple/In	Nurses	✓ (hotline)	✓	✓ (90 min)	✓	✓	X	✓	X	✓	<50	High	22.62 (15.48) (spot UI; mcg/L)

(Continues)

TABLE 3 (Continued)

Study (year)	Type of LID	Clear length of restriction	Education Support: Inclusion of family/ friends	Relationship with HCP: Number of contact sessions/ Format: In or Gr	Relationship with HCP: HCP	Ongoing support (e.g., phone)	Food recommendations: Delivery and amount of detail on LID: Written	Delivery and amount of detail on LID: Face-to-face (length)	List of foods to avoid/ restrict	List of allowed foods	Food labelling/ food composition	Meal plan/ sample menu	Food provision	Adapted for sub-groups	Advised iodine intake (mcg/d)	Overall intervention investmentfor educator and level of ppt empowerment to follow a LID[a]	Post IS mean (SD) (unit)
Lim (2015)	*LS- LID*	2wks	X	1/In	NC	X	✓	✓ (NR)	✓	✓	X	✓	X	✓	<50	Medium	35.8 (35.2) (24 h I/ Cr; mcg/gCr)
	S- LID	2wks	X	1/In	NC	X	✓	✓ (NR)	✓	✓	X	✓	X	✓	50 – 100	Medium	28.6 (23.6) (24 h I/ Cr; mcg/gCr)
Maxon (1983)	*LID*	1wk	X	Multiple[e]/ In	DN	X	✓	✓ (NR)	✓	✓	X	✓	X	✓	<50	High	42.8 (49.3) (24 h I/ Cr; mcg/gCr)
Padovani (2015)	*LID*	15d/30 d	X	1/In	NR	X	✓	NR	✓	✓	X	X	X	X	< 50	Low	2 wks: 76 (NR) 4 wks: 63 (NR) (24 h UI; mcg/L)
Park (2004)	*LID*	1wk/2wks	X	1/In	NR	X	✓	✓ (NR)	✓	X	X	✓	X	X	< 50	Medium	1 wk: 199.87 (169.53) 2wks: 84.69 (44.03)(spot I/ Cr; mcg/gCr)
Roh (2006)	*LS- LID*	2wks	X	1/In	NR (not a DN)	X	✓	NR	✓	X	X	X	X	X	NR	Low	289.75 (188.24) (spot I/Cr; mcg/gCr)
	S-LID	1wk	X	1/In	DN	X	✓	✓ (NR)	✓	✓	X	✓	X	✓	NR	Medium	127.87 ± 78.52 (spot I/Cr; mcg/gCr)
Sohaimi (2019)	*LS-LID*	1wk	X	1/In	NR	X	✓	✓ (NR)	✓	✓	X	X	X	NR	NR	Low	63.82 (51.21) (spot UI; mcg/L)
	S-LID	1wk	X	1/In	DN/nurse	X	✓	✓ (NR)	✓	X	X	✓	X	✓	<50	Medium	56.85 (50.07) (spot UI; mcg/L)

TABLE 3 (Continued)

Study (year)	Type of LID	Clear length of restriction	Education Support: Inclusion of family/ friends	Relationship with HCP: Number of contact sessions/ Format: In or Gr	Relationship with HCP: HCP	Relationship with HCP: Ongoing support (e.g., phone)	Food recommendations: Delivery and amount of detail on LID: Written	Delivery and amount of detail on LID: Face-to-face (length)	List of foods to avoid/ restrict	List of allowed foods	Food labelling/ food composition	Meal plan/ sample menu	Food provision	Adapted for sub-groups	Advised iodine intake (mcg/d)	Overall intervention investmentfor educator and level of ppt empowerment to follow a LID[a]	Post IS mean (SD) (unit)
Tamura (2016)	*LID*	1wk and 3d	X	1/In	NU/DNs	X	✓	✓ (15–30 min)	✓	✓	X	✓	X	✓	<100	High	119.2 (49.7) (spot; mcg/gCr)
Tomoda (2005)	*LS- LID*	1wk	X	1/In	NR	X	✓	NR	✓	X	X	X	X	X	NR	Low	182.2 (161.59) (spot I/Cr; mcg/gCr)
	S- LID	1wk/2 wks	X	1/In	NR	X	✓	NR	✓	X	X	X	X	X	NR	Low	1wk:119.4 (62.27) 2wks: 63.1 (40.58) (spot I/Cr; mcg/gCr)

Abbreviations: Cr, creatinine ratio; d, days; DN, dietitian; g, gram; Gr, group; HCP, healthcare professional; hr(s), hour(s); In, individual; I/Cr, iodine/creatine; IS, iodine status; L, litre; LID, low iodine diet; LS, less-strict; mcg, microgram; NC, Nutrition co-ordinators; NU, Nutritionist; NR, not-reported; ppt, participant; Radiol, Radiologist; RAIT, radioactive-iodine treatment; SD, standard deviation; S-LID, stricter low iodine diet; rhTSH, recombinant human TSH; THW, thyroid hormone withdrawal; UI, urinary iodine; wk(s), weeks; --, uninterpretable.

[a]Low: provision of a leaflet; medium: provision of a leaflet + 1 face-to-face contact; high: intensive food recommendations, face-to-face contact >1, ongoing support, possible food provision.

[b]explaining RAIT - minimal time on LID.

[c]30 min on LID.

[d]Compliance regularly checked and reinforced.

[e]Free access.

been reported as an already psychologically distressing time for people with thyroid cancer.[84,85]

4.2 | Strengths and limitations

This review provides a comprehensive description of the evidence base due to a mixed-method approach, thorough database search, inclusive study design criteria and translation of non-English studies. We adhered to strict review methodology that aimed to reduce bias, such as using two authors to screen studies, extract data and assess bias. However, although the search strategy was comprehensive, it is possible that some studies may have been missed.

It is the first review to metaanalyse studies that have investigated a LID on iodine status and ablation success. Although the meta-analyses must be viewed with caution and the differences that exist between these studies understood, we endeavoured to deal with these differences by choice of analysis and conducting appropriate sensitivity analysis. A further strength is the use of appropriately designed tools to assess bias and quality in contrast to previous reviews where quality issues were highlighted but not objectively assessed.

4.3 | Implications for practice and research

Given the uncertainties of whether a LID has any effect on ablation success, and the fact that following a LID diet may pose challenges that cause stress and anxiety at an already difficult time, future studies are needed to definitively determine whether a LID is beneficial before RAIT. Comparisons should be conducted between iodine status and treatment success as this is a more objective measure of exposure and would reduce the bias inherent in a comparison of LID advice alone. Ablation success should be defined using thyroglobulin measurements and neck ultrasound as recommended in the latest international guidance as it offers a more complete assessment than using a response-evaluation WBS alone.[1,4] In addition, correcting for creatinine when examining UIC is needed because it is influenced by many factors such as urinary volume, fluid intake, time of collection, and renal and thyroid function.[86]

People may feel that failure to follow the diet might result in recurrence.[14] However, this review has shown there is only minimal evidence of questionable quality (both abstracts) that examined the long-term recurrence of DTC. As such, we do not yet know the effect of iodine status/LID advice on long-term recurrence of DTC. Mortality rates have also yet to be reported. Future studies may want to consider this long-term follow-up.

If future studies demonstrate that iodine status impacts RAIT success, it is important that LID guidelines in terms of duration and stringency are standardized within locations of similar iodine consumption and cultural dietary factors. Countries where consumption of iodine-rich foods is common such as Korea, Japan, and Canada will require more stringent guidelines compared to those with a lower iodine status such as the UK. A key consideration will also be the delivery of this information.

5 | CONCLUSION

This review suggests that a LID reduces iodine status, but there is not sufficient high-quality evidence to determine the benefits of iodine status/LID on treatment success. It offers healthcare providers an insight into how consuming a LID may affect their patients and, despite being advised as a short-term dietary intervention, highlights the challenges for patients that this diet can present. The lack of a robust evidence base on which healthcare providers can advise their patients regarding the use of a LID before RAIT means that patients may be asked to make unnecessary and disruptive changes to their diet at an already stressful time. The question remains as to whether low iodine status is beneficial to treatment success, and high-quality studies are needed to address this.

AUTHOR CONTRIBUTIONS

Georgia Herbert: Conception of the study, extraction, interpretation, and presentation of data, quality assessment of studies and drafted the initial manuscript. Clare England: Conception of the study, extraction and interpretation of data, and quality assessment. Rachel Perry: Conception of the study, developed and ran the search, extraction and interpretation of data, and assessment of risk of bias. Alex Whitmarsh: Interpretation and presentation of the data. Theresa Moore: Interpretation and presentation of the data, and assessment of the risk of bias. Aidan Searle: Extraction and interpretation of data, and quality assessment. Sneha Chotaliya: Extraction and interpretation of data. Andy Ness: Conception of the study and interpretation of data. Matthew Beasley: Conception of the study and interpretation of data. Charlotte Atkinson: Conception of the study, interpretation of data, and extraction of data. All authors revised the initial draft manuscript critically for important intellectual content and read, commented on, and approved the final version of the manuscript.

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CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

The data that supports the findings of this study are available in the supplementary material of this article.

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REFERENCES

1. Perros P, Boelaert K, Colley S, et al. Guidelines for the management of thyroid cancer. *Clin Endocrinol*. 2014;81:1-122.
2. Maxon HR, Thomas SR, Boehringer A, et al. Low iodine diet in I-131 ablation of thyroid remnants. *Clin Nucl Med*. 1983;8(3):123-126.
3. Padovani RP, Maciel RM, Kasamatsu TS, et al. Assessment of the effect of two distinct restricted iodine diet durations on urinary iodine levels (collected over 24 h or as a single-spot urinary sample) and Na(+)/I(-) symporter expression. *Eur Thyroid J*. 2015;4(2):99-105.
4. Haugen BR, Alexander EK, Bible KC, et al. 2015 American Thyroid Association management guidelines for adult patients with thyroid nodules and differentiated thyroid cancer: the American Thyroid Association Guidelines Task Force on thyroid nodules and differentiated thyroid cancer. *Thyroid*. 2016;26(1):1-133.
5. Ito Y, Onoda N, Okamoto T. The revised clinical practice guidelines on the management of thyroid tumors by the Japan Associations of Endocrine Surgeons: Core questions and recommendations for treatments of thyroid cancer. *Endocr J*. 2020;67(7):669-717.
6. Li JH, He ZH, Bansal V, Hennessey JV. Low iodine diet in differentiated thyroid cancer: a review. *Clin Endocrinol*. 2016;84(1):3-12.
7. Sawka AM, Ibrahim-Zada I, Galacgac P, et al. Dietary iodine restriction in preparation for radioactive iodine treatment or scanning in well-differentiated thyroid cancer: a systematic review. *Thyroid*. 2010;20(10):1129-1138.
8. Pacini F, Brianzoni E, Durante C, et al. Recommendations for post-surgical thyroid ablation in differentiated thyroid cancer: a 2015 position statement of the Italian Society of Endocrinology. *J Endocrinol Invest*. 2016;39:341-347.
9. Pacini F, Basolo F, Bellantone R, et al. Italian consensus on diagnosis and treatment of differentiated thyroid cancer: joint statements of six Italian societies. *J Endocrinol Invest*. 2018;41(7):849-876.
10. Miller R, Spiro A, Stanner S. Micronutrient status and intake in the UK – where might we be in 10 years' time? *Nutr Bull*. 2016;41(1):14-41.
11. England CY, Moss L, Beasley M, Haupt-Schott I, Herbert G, Atkinson C. A survey of UK centres on low iodine diet recommendations prior to radioiodine ablation therapy for differentiated thyroid cancer. *Eur Thyroid J*. 2019;9(3):132-138.
12. Prestwich RJ, Gerrard GE. Low-iodine diet before radioiodine uptake scans or therapy-flawed advice to UK patients. Editorial. *Clin Oncol*. 2005;17(2):73-74.
13. Stajduhar KI, Neithercut J, Chu E, et al. Thyroid cancer: patients' experiences of receiving iodine-131 therapy. *Oncol Nurs Forum*. 2000;27(8):1213-1218.
14. Herbert G, Searle A, England CY, et al. Experiences of low iodine diets in the treatment of differentiated thyroid cancer with radioactive iodine ablation therapy. *Clin Nutr ESPEN*. 2020;39:190-197.
15. Cooke A, Smith D, Booth A. Beyond PICO: the SPIDER tool for qualitative evidence synthesis. *Qual Health Res*. 2012;22(10):1435-1443.
16. Noyes J, Booth A, Flemming K, et al. Cochrane qualitative and implementation methods group guidance series-paper 3: methods for assessing methodological limitations, data extraction and synthesis, and confidence in synthesized qualitative findings. *J Clin Epidemiol*. 2018;97:49-58.
17. Barnett-Page E, Thomas J. Methods for the synthesis of qualitative research: a critical review. journal article. *BMC Med Res Methodol*. 2009;9(1):59.
18. Sutcliffe K, Thomas J, Stokes G, Hinds K, Bangpan M. Intervention Component Analysis (ICA): a pragmatic approach for identifying the critical features of complex interventions. *Syst Rev*. 2015;4(1):140.
19. Sterne JAC, Savović J, Page MJ, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. *BMJ*. 2019;366:l4898.
20. Sterne JA, Hernán MA, Reeves BC, et al. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. *BMJ*. 2016;355:i4919.
21. Tugwell P, Knottnerus JA, McGowan J, Tricco A. Big-5 Quasi-Experimental designs. *J Clin Epidemiol*. 2017;89:1-3.
22. Reeves BC, Wells GA, Waddington H. Quasi-experimental study designs series—paper 5: a checklist for classifying studies evaluating the effects on health interventions—a taxonomy without labels. *J Clin Epidemiol*. 2017;89:30-42.
23. Critical Appraisal Skills Programme. CASP Qualitative Studies Checklist. October 2018. Accessed February 16, 2021.
24. Protogerou C, Hagger MS. A checklist to assess the quality of survey studies in psychology. *Methods in Psychology*. 2020;3:100031.
25. Guyatt GH, Oxman AD, Vist GE, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ*. 2008;336(7650):924-926.
26. Hong QN, Pluye P, Bujold M, Wassef M. Convergent and sequential synthesis designs: implications for conducting and reporting systematic reviews of qualitative and quantitative evidence. *Syst Rev*. 2017;6(1):61.
27. Reeves BC, Deeks JJ, Higgins JPT, et al. Including non-randomized studies on intervention effects. In: Higgins JPT, Thomas JC, Chandler J, et al, eds. *Cochrane Handbook for Systematic Reviews of Interventions version 62 (updated February 2021)*. John Wiley & Sons; 2021.
28. McGrath S, Zhao X, Steele R, Thombs BD, Benedetti A. Estimating the sample mean and standard deviation from commonly reported quantiles in meta-analysis. *Stat Methods Med Res*. 2020;29(9):2520-2537.
29. Scherer RW, Saldanha IJ. How should systematic reviewers handle conference abstracts? A view from the trenches. *Syst Rev*. 2019;8(1):264.
30. Higgins J, Green S. Cochrane handbook for systematic reviews of interventions version 5.1.0 [updated March 2011]. *The Cochrane Collaboration, 2011*. 2011. Available from www.handbook.cochrane.org
31. StataCorp. *Stata Statistical Software: Release 16*. StataCorp LLC; 2019.
32. Thomas J, Harden A. Methods for the thematic synthesis of qualitative research in systematic reviews. *BMC Med Res Methodol*. 2008;8(1):45.
33. NVivo qualitative data analysis software, Version 12 pro. 2018.
34. Noyes J, Booth A, Cargo M, et al. Chapter 21: Qualitative evidence. In: Higgins J, Thomas J, Chandler J, eds. *Cochrane Handbook for Systematic Reviews of Interventions version 62 (updated February 2021)*. John Wiley & Sons; 2021.
35. Sohn SY, Choi JY, Jang HW, et al. Association between excessive urinary iodine excretion and failure of radioactive iodine thyroid ablation in patients with papillary thyroid cancer. *Thyroid*. 2013;23(6):741-747.
36. Tala Jury HP, Castagna MG, Fioravanti C, Cipri C, Brianzoni E, Pacini F. Lack of association between urinary iodine excretion and successful thyroid ablation in thyroid cancer patients. *J Clin Endocrinol Metab*. 2010;95(1):230-237.

37. Markovic V, Penic B, Punda A, et al. Adherence to low iodine diet and ablation success rate in patients operated from well differentiated thyroid carcinomas. *Thyroid*. 2015;25(SUPPL. 1):A147. 15th International Thyroid Congress and 85th Annual Meeting of the American Thyroid Association. Lake Buena Vista, FL United States.
38. Ito S, Iwano S, Kato K, Naganawa S. Predictive factors for the outcomes of initial I-131 low-dose ablation therapy to Japanese patients with differentiated thyroid cancer. journal article. *Ann Nucl Med*. 2018;32(6):418-424.
39. Morris LF, Wilder MS, Waxman AD, Braunstein GD. Reevaluation of the impact of a stringent low-iodine diet on ablation rates in radioiodine treatment of thyroid carcinoma. *Thyroid*. 2001;11(8):749-755.
40. Yoo IDKS, Seo YY. The success rate of initial (131)i ablation in differentiated thyroid cancer: comparison between less strict and very strict low iodine diets. *Nucl Med Mol Imaging*. 2012;46(1):34-40.
41. Waxman A. The effect of low-iodine diet on the ability to achieve ablation following high dose I-131 therapy for differentiated thyroid cancer. *JNM*. 2000;41(5):311P.
42. Li JH, He ZH, Hennessey JV. Urinary iodine/creatinine ratio measurements prior to radioactive iodine ablation may predict short-term disease outcomes in patients with differentiated thyroid cancer. *Thyroid*. 2017;27(Suppl 1):A35. Abstract 1573 87th Annual Meeting of the American Thyroid Association. Canada.
43. Tobey AE, Hongxiu L, Auh S, et al. Urine iodine excretion exceeding 250 ug/24h is associated with higher likelihood of progression in intermediate and high-risk thyroid cancer patients treated with radioactive iodine. *Thyroid*. 2018;28(Suppl 1):A40-A41. (Abstract) 88th Annual Meeting of the American Thyroid Association. United States.
44. Maruca J, Santner S, Miller K, Santen RJ. Prolonged iodine clearance with a depletion regimen for thyroid carcinoma: concise communication. *J Nucl Med*. 1984;25(10):1089-1093.
45. Nakada K, Tamura M, Furuta Y, et al. What makes practice of low iodine diet difficult in patients undergoing remnant tissue ablation for thyroid cancer? *J Nucl Med*. 2016;57(suppl 2):102 (Abstract).
46. Nakada K, Tamura M, Kato N, Sakurai M, Furuta Y. Is two weeks low iodine diet superior to one week low iodine diet in decreasing urinary iodine concentration in patients undergoing rhTSH-aided radioiodine ablation for differentiated thyroid cancer? *J Nucl Med*. 2020;61(suppl 1):49 (Abstract).
47. Ju DL, Park YJ, Paik HY, Song Y. The impact of low adherence to the low-iodine diet on the efficacy of the radioactive iodine ablation therapy. *Clin Nutr Res*. 2015;4(4):267-271.
48. Hinds SR, Stack AL, Stocker DJ. Low-iodine diet revisited: importance in nuclear medicine imaging and management. Case Reports. *Clin Nulc Med*. 2008;33(4):247-250.
49. Lakshmanan M, Schaffer A, Robbins J, Reynolds J, Norton J. A simplified low iodine diet in I-131 scanning and therapy of thyroid cancer. *Clin Nulc Med*. 1988;13(12):866-868.
50. Goslings BM. Proceedings: effect of a low iodine diet on 131-I therapy in follicular thyroid carcinomata. *J Endocrinol*. 1975;64(3):p30 (Abstract).
51. Kim HK, Lee SY, Lee JI, et al. Daily urine iodine excretion while consuming a low-iodine diet in preparation for radioactive iodine therapy in a high iodine intake area. *Clin Endocrinol*. 2011;75(6):851-856.
52. Nakano S, Ando T, Fujii K, et al. Is one-week self-managed low iodine diet sufficient for preparation of low dose iodine ablation for papillary thyroid carcinoma in iodine-rich areas? *World J Endocr Surg*. 2020;12(suppl 1):87 (Abstract). <17th Biennial Congress of the Asian Association of Endocrine Surgeons, AsAES 2020. Australia.
53. Sohaimi WF, Abdul Manap M, Kasilingam L, et al. Randomised controlled trial of one week strict low-iodine diet versus one week non-specified low iodine diet in differentiated thyroid carcinoma. *Iran J Nucl Med*. 2019;27(2):99-105.
54. Tamura M, Nakada K, Tsuruhara R, et al. Efficacy of dietitian-instructed low iodine diet for radioiodine remnant tissue ablation for thyroid cancer. *Kaku Igaku*. 2016;53(1):53-60.
55. Choi J, Kim H, Park J, et al. Analysis of urine iodine excretion decrease by two-week stringent low iodine diet for remnant thyroid ablation with radioactive iodine in Korean patients with thyroid cancer; prospective study. *Nucl Med Mol Imaging*. 2008;42:337-346.
56. Dobrenic M, Huic D, Zuvic M, Grosev D, Petrovic R, Samardzic T. Usefulness of low iodine diet in managing patients with differentiated thyroid cancer - initial results. *Radiol Oncol.* 2011;45(3):189-195.
57. Jin CS, Jeong CM. Analysis of urinary iodine excretion after two-week stringent low iodine diet for remnant ablation therapy in patients with thyroid cancer. *J Nucl Med*. 2010;51(2. (Abstract) <Society of Nuclear Medicine and Molecular Imaging Annual Meeting, SNMMI 2010. Salt Lake City, UT United States.
58. Ju DL, Park YJ, Paik H-Y, et al. Dietary evaluation of a low-iodine diet in Korean thyroid cancer patients preparing for radioactive iodine therapy in an iodine-rich region. *Nutr Res Pract*. 2016;10(2):167-174.
59. Ignacio Cuenca J, Ramón Rodríguez J, Guerrero R, et al. Utility of a low-iodide diet in131I whole body scanning of patients with differentiated thyroid cancer. *Endocrinol Nutr*. 2008;55(3):117-122.
60. Lim CY, Kim JY, Yoon MJ, Chang HS, Park CS, Chung WY. Effect of a low iodine diet vs. restricted iodine diet on postsurgical preparation for radioiodine ablation therapy in thyroid carcinoma patients. *Yonsei Med J*. 2015;56(4):1021-1027.
61. Roh J, Kim BI, Ha JS, et al. Comparison of urine iodine/creatinine ratio between patients following stringent and less stringent low iodine diet for radioiodine remnant ablation of thyroid cancer. *Nucl Med Mol Imaging*. 2006;40(6):322-326.
62. Tomoda C, Uruno T, Takamura Y, et al. Reevaluation of stringent low iodine diet in outpatient preparation for radioiodine examination and therapy. *Endocr J*. 2005;52(2):237-240.
63. Dobrenic M. Low iodine diet in patients with differentiated thyroid cancer. *Eur J Nucl Med Mol Imaging*. Vol 44, 2017:S791. (Abstract). <30th Annual Congress of the European Association of Nuclear Medicine, EANM 2017. Austria.
64. Park JT, Hennessey JV. Two-week low iodine diet is necessary for adequate outpatient preparation for radioiodine rhTSH scanning in patients taking levothyroxine. *Thyroid*. 2004;14(1):57-63.
65. Lee M, Lee YK, Jeon TJ, et al. Low iodine diet for one week is sufficient for adequate preparation of high dose radioactive iodine ablation therapy of differentiated thyroid cancer patients in iodine-rich areas. *Thyroid*. 2014;24(8):1289-1296.
66. Asiri M, Tunio M, Riaz K, AlArifi M. Severe symptomatic hyponatremia following low iodine diet for radioactive iodine-131 therapy in patient with papillary thyroid cancer: a case report and review of literature. *Nucl Med Rad Ther*. 2012;6:1.
67. Al Nozha OM, Vautour L, How J. Life-threatening hyponatremia following a low-iodine diet: a case report and review of all reported cases. *Endocr Pract*. 2011;17(5):e113-e117.
68. Kim SK, Yun GY, Kim KH, et al. Severe hyponatremia following radioactive iodine therapy in patients with differentiated thyroid cancer. *Thyroid*. 2014;24(4):773-777. Comment in: Thyroid. 2014 May;24(5):923; PMID: 24428776. https://www.ncbi.nlm.nih.gov/pubmed/24428776
69. Krishnamurthy VR, McDougall IR. Severe hyponatremia: a danger of low-iodine diet. *Thyroid*. 17, 2007:889-892<9.
70. Nozu T, Yoshida Y, Ohira M, Okumura T. Severe hyponatremia in association with I(131) therapy in a patient with metastatic thyroid cancer. *Intern Med*. 2011;50(19):2169-2174.
71. Shakir MK, Krook LS, Schraml FV, Hays JH, Clyde PW. Symptomatic hyponatremia in association with a low-iodine diet and levothyroxine withdrawal prior to I131 in patients with metastatic thyroid carcinoma. Case reports. *Thyroid*. 2008;18(7):787-792.

72. Dayrit JCP, Cunanan EC, Kho SA. The prevalence of hyponatremia in hypothyroid, salt-deprived patients during radioactive 131iodine ablation for well-differentiated thyroid cancer: A cross-sectional study. *Endo Rev*. 2015;36(Suppl 2):(Abstract). <97th Annual Meeting and Expo of the Endocrine Society, ENDO 2015. United States.
73. Kim J, Cho SG, Kang SR, et al. Preparation for radioactive iodine therapy is not a risk factor for the development of hyponatremia in thyroid cancer patients. Evaluation Studies. *Medicine*. 2017;96(5):e6004.
74. Lee JE, Kim SK, Han KH, et al. Risk factors for developing hyponatremia in thyroid cancer patients undergoing radioactive iodine therapy. *PLoS One*. 2014;9(8):e106840.
75. Nakada K, Furuta Y, Tamura M, Sakurai M. Does low iodine cause severe hyponatremia in patients undergoing rh-tsh aided remnant tissue ablation for thyroid cancer? *Thyroid*. 2017;27(Suppl 1):A150-A151. (Abstract) <87th Annual Meeting of the American Thyroid Association. Canada.
76. Roopnarinesingh N, Thomas A. Severe hyponatremia with low iodine diet prior to radioactive iodine-131 ablation therapy. *Endo Rev*. 2011;32(3 Meeting):P3-636. (Abstract) <93rd Annual Meeting and Expo of the Endocrine Society, ENDO 2011. Boston, MA United States(var.pagings).
77. Lee KJ, Chang SO, Jung KY. Experiences with a low-iodine diet: a qualitative study of patients with thyroid cancer receiving radioactive iodine therapy. *Eur J Oncol Nurs*. 2016;23:43-50.
78. Moon J-A, Yoo C-H, Kim MH, et al. Knowledge, self-efficacy, and perceived barriers on the low-iodine diet among thyroid cancer patients preparing for radioactive iodine therapy. *Clin Nutr Res*. 2012;1(1):13-22.
79. Ju DL, Park YJ, Paik HY, et al. Dietary evaluation of a low-iodine diet in Korean thyroid cancer patients preparing for radioactive iodine therapy in an iodine-rich region. *Nut Res Pract*. 2016;10(2):167-174.
80. Luster M, Clarke SE, Dietlein M, et al. Guidelines for radioiodine therapy of differentiated thyroid cancer. *Eur J Nucl Med Mol Imaging*. 2008;35(10):1941-1959.
81. Morsch EP, Vanacor R, Furlanetto TW, Schmid H. Two weeks of a low-iodine diet are equivalent to 3 weeks for lowering urinary iodine and increasing thyroid radioactive iodine uptake. Randomized Controlled Trial. *Thyroid*. 2011;21(1):61-67.
82. Khaleel I, Wimmer BC, Peterson GM, et al. Health information overload among health consumers: A scoping review. *Patient Edu Couns*. 2020;103(1):15-32.
83. Timmers T, Janssen L, Kool RB, Kremer JA. Educating patients by providing timely information using smartphone and tablet apps: systematic review. *J Med Internet Res*. 2020;22(4):e17342.
84. Misra S, Meiyappan S, Heus L, et al. Patients' experiences following local-regional recurrence of thyroid cancer: a qualitative study. Research Support, Non-U.S. Gov't. *J Surg Oncol*. 2013;108(1):47-51.
85. Hedman C, Strang P, Djarv T, Widberg I, Lundgren CI. Anxiety and fear of recurrence despite a good prognosis: an interview study with differentiated thyroid cancer patients. *Thyroid*. 2017;27(11):1417-1423.
86. Vejbjerg P. Estimation of iodine intake from various urinary iodine measurements in population studies. *Thyroid*. 2009;19(11):1281-1286.

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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