Sodium intake reduction efforts in Lebanon

Mohamad M. Almedawar^{1,2}, Lara Nasreddine^{2,3}, Ammar Olabi^{2,3}, Haya Hamade^{2,4}, Elie Awad⁵, Imad Toufeili^{2,3}, Samir Arnaout^{1,2}, Hussain A. Isma'eel^{1,2,6}

¹Division of Cardiology, Department of Internal Medicine, ²Vascular Medicine Program; ³Department of Nutrition & Food Sciences, ⁴Department of Pediatrics and Adolescent Medicine, American University of Beirut, Beirut, Lebanon; ⁵Lebanese University, Beirut, Lebanon; ⁶Visiting Clinical Scholar, Department of Cardiovascular Medicine, Cleveland Clinic Foundation, Cleveland, Ohio, USA

Correspondence to: Hussain Isma'eel. Division of Cardiology, Department of Internal Medicine, 11072020 Riad el Solh, Beirut, Lebanon. Email: hi09@aub.edu.lb.

Abstract: Sodium intake reduction efforts in Lebanon are quite recent and have just started to take effect on the national level. Starting out from an academic institution, the Lebanese Action on Sodium and Health (LASH) campaign was established to counter the increasing prevalence of hypertension and associated adverse health effects. The campaign's strategy was based on four pillars: research, health communication, advocacy, and monitoring. The LASH group set out with determining: baseline sodium intake of the population, main sources of sodium intake, and the knowledge, attitudes, and behaviors (KAB) of the population as a situation analysis that prompts for action. This gave LASH tangible evidence of the magnitude of the problem and the need for the government, the food industry, and the consumers, to be mobilized to take part in devising a solution. Currently, Lebanon is at a stage of technically working to reduce the sodium content in the major sources of sodium, namely local bread and bread-like products. The next steps will include implementation of a plan for monitoring industry compliance, while studying other food targets, including dairy products and processed meat. Meanwhile, the health communication plan is ongoing and the Salt Awareness Week is celebrated every year with media appearances of LASH researchers to raise the issue to the public eye.

Keywords: Sodium chloride; dietary; salt intake reduction; Lebanon; public health; prevention; dietary intervention

Submitted Mar 08, 2015. Accepted for publication Apr 27, 2015. doi: 10.3978/j.issn.2223-3652.2015.04.09 View this article at: http://dx.doi.org/10.3978/j.issn.2223-3652.2015.04.09

Introduction

Cardiovascular diseases (CVDs) represent the majority of all-cause mortality in Lebanon (60%) in persons aged 50 years and older, who represent 22% of the Lebanese population (approximately 4.467 million) (1,2). CVD, mainly stroke, resulted in 2,072 deaths in 2002 and represent 10% of total deaths according to WHO 2011 estimates (3). Hypertension is a major underlying risk factor for CVD with a prevalence of 29% (4).

Several studies have estimated the morbidity and mortality attributable to excessive salt intake worldwide. Mozaffarian *et al.* [2014] showed that excessive dietary sodium intake was responsible for 1.65 million CVD deaths worldwide in 2010. The overwhelming majority of the deaths (84%) occurred in low- and middle-income countries (5). From a preventive point of view, He *et al.* showed that 35,000 annual stroke and ischemic heart disease deaths could be prevented in the UK alone, and 2.5 million cases worldwide, if the salt intake was reduced to a maximum of 6 g/person/day (6). In Lebanon, no studies are published about the contribution of excess salt intake to morbidity and mortality; however, based on the globally collected evidence we chose to adhere the WHO recommendations to work on reducing sodium intake (7).

Public health efforts in Lebanon

To plan and implement sodium intake reduction in Lebanon, a group of researchers and public health specialists

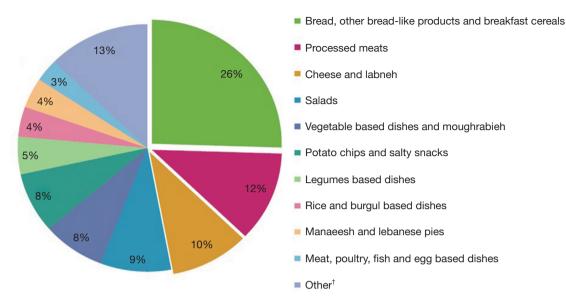


Figure 1 Major food group contributors to sodium intake in Lebanon. †, Other category includes pizza and pasta based dishes, processed poultry, sweets, kishk, tahini and falafel based dishes, gravies sauces and butter, soups, potato based dishes, and milk based products.

convened, with the support of World Action on Salt and Health (WASH), under what became the LASH. The strategic plan of the campaign was based on four pillars, namely research, health communications, advocacy, and monitoring. After a situations analysis, the group recognized that the basic data to launch a public health initiative was not present. Therefore, it was agreed to launch a research arm and simultaneously prepare the ground for the public health initiative. However, at the outset, it was realized that research had to address some local challenges to get the buy-in of key stakeholders within the sector of the food industry to be targeted. Research was centered on: (I) how much sodium does the Lebanese population consume; (II) what are the major sources of intake; (III) what is the baseline knowledge, attitudes and beliefs of the population; and (IV) which tools for monitoring of sodium intake can practically be used in our setting. An overview of this will be presented in the sections that follow.

Research

Sodium consumption in the Lebanese population

In a systematic analysis, Powles *et al.* (2013) estimated the current daily dietary sodium intake in the Lebanese population to be 3.13 g per person per day (8). Based on a nationally representative survey conducted in 2008/2009 on Lebanese adults (n=2,543), the average sodium intake among Lebanese adults aged 20 years and above was estimated at 2.9 g/day, with intakes being significantly higher in males (3.4 g/day) compared to females (2.4 g/day). In total, nearly 60% of the adult Lebanese population was found to exceed the WHO maximum intake level of 2 g/day (9). This was based on dietary diary data and not on 24-hr urine sodium measures.

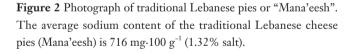
Major sources of sodium intake

Processed foods are the main dietary source of sodium in the Lebanese diet, led by bread and bread-like products (26%), processed meat (12%), and dairy products (9%) (*Figure 1*) (9). These percentages can be explained when looking at the average consumption of bread (136.8 g/p/day), bread-like products such as the traditional pies or "Mana'eesh" (32.1 g/p/day) (*Figure 2*), and dairy products such as cheese (49.5 g/p/day) and strained yogurt or "Labneh" (27.8 g/p/day) in Lebanon. A similar profile of sodium sources (processed foods) was observed in Canada and other developed countries (10), indicating a shift in the Lebanese diet from a Mediterranean to a Western cuisine.

To further dissect the problem, samples of the main breads consumed in Lebanon (white and brown Arabic/ pita, white and brown French baguette, Markouk and Tannour breads) were collected from the main bakeries in Lebanon (n=48) (*Figures 3-6*) and analyzed using the AACC these products.

method 40-71 (American Association of Cereal Chemist) at the department of Nutrition and Food Sciences, AUB. The average sodium content of the white Arabic/pita bread, the most consumed bread type in the country (11), was 519 mg·100 g⁻¹ (1.32% salt). The mean sodium level was 579 mg·100 g⁻¹ (1.47% salt) for brown Arabic/ pita bread, 821 mg·100 g⁻¹ (2.1% salt) for brown French baguette, 866 mg·100 g⁻¹ (2.2% salt) for white French baguette, 866 mg·100 g⁻¹ (2.2% salt) for Tannour bread and 1,111 mg·100 g⁻¹ (2.83% salt) for Markouk bread. Sodium was not detected in the zero-salt labeled bread and was found at a mean level of 127 mg·100 g⁻¹ (0.32% salt) in the low-salt-labeled versions of Arabic/pita bread. This indicated credibility of the claims on sodium contents of

Another category of high salt foods includes white brined cheeses and strained yogurt (Labneh) which are heavily



consumed in the Arab Region. In a previous study (12), samples of regular and reduced-fat varieties of four white brined cheeses (Akkawi, Halloumi, Double Crème and Braided) and Labneh, produced from cow's milk, were analyzed for sodium content. The concentration of sodium was highest in the cheeses with large differences in sodium levels being noted between different brands of the same type of cheese. Double Crème had the lowest sodium content among brined cheeses with a range of 736-1,258 mg·100 g⁻¹, followed by Halloumi cheese with 652-1,320 mg·100 g⁻¹, mereas Braided cheeses exhibited the highest and most variable sodium levels with a range of 2,080-6,250 mg·100 g⁻¹. The range of sodium levels of Labneh was 73-278 mg·100 g⁻¹.

Baseline knowledge, attitudes and beliefs of the Lebanese population

Recently published results of a survey by Nasreddine *et al.* [2014] about knowledge, attitudes, and behaviors (KAB) of Lebanese consumers regarding dietary sodium intake demonstrated a poor knowledge of the effects of sodium on health and its sources in the diet. This reflected in unfavorable attitudes and behaviors of the consumers towards reducing their daily sodium dietary intake. Although 78% of the participants linked high dietary sodium intake to poor health, almost half did not know it leads to stroke and heart attacks. Moreover, only 23% correctly recognized processed foods as the main source of dietary sodium. More importantly, only 32% correctly indicated the recommended upper daily intake limit. Furthermore, less than half of the participants (45%) were



Figure 3 Photograph of white Arabic/pita. The average sodium content of the white Arabic/pita bread is 519 mg-100 g⁻¹ (1.32% salt).



Figure 4 Photograph of Markouk bread. The average sodium content of the Markouk bread is $1,111 \text{ mg} \cdot 100 \text{ g}^{-1}$ (2.83% salt).



Figure 5 Photograph of Tannour bread. The average sodium content of the Tannour bread is 866 mg \cdot 100 g⁻¹ (2.2% salt).

concerned about the level of sodium in their diet and even less (38%) looked at sodium labels before purchasing food products. However, checking the labels did not seem to translate to a change in the decision of buying the high sodium product because only 44% of the later subgroup admitted it affected their decision. This could be partly explained by the finding that 56% stated that food labels on sodium are not comprehensible. Despite the deficiencies observed, around half of the participants perceived themselves as actively reducing their daily intake of sodium.

Intriguingly, women had better knowledge than men on many levels and consequently a more favorable overall attitude and behavior. This finding emphasizes the rationale



Figure 6 Photograph of white and brown French baguette. The average sodium content of the white and brown French baguette is 821 mg \cdot 100 g⁻¹ (2.1% salt) and 866 mg \cdot 100 g⁻¹ (2.2% salt), respectively.

for targeting women in health awareness campaigns as the data shows they have better baseline knowledge, and are a key element in the entire family's dietary intake, given their traditional role in grocery shopping and preparing meals in Lebanon (13). In comparison, a high cardiovascular risk population surveyed with the same questionnaire demonstrated great variability in terms of KAB. *Figure* 7 summarizes the main differences between the general population and the high-risk sample.

Tools for monitoring of sodium intake used in the Lebanese setting

Even though several methods have been proposed for the dietary assessment of sodium (24-hour urinary sodium excretion; 24-hour dietary recalls; food records), the validity, accuracy and/or applicability of several of these methods have been often criticized in the literature (14). The accurate assessment of sodium intake amongst free-living persons remains a difficult and labor-intensive process (14). The lack of adequate tools to evaluate sodium intake is still a problem in clinical practice as well as in research settings and this is particularly true for Lebanon (14). The 24-hour urine sodium excretion is recognized as the "goldstandard" for the assessment of dietary sodium intake (15). However, measurement of 24-hour urine sodium excretion is cumbersome and inconvenient (16) and is associated with low response rates. Among those subjects who agree to participate in such studies, many perform the collection incorrectly, with under-collection and thus underestimation of actual sodium intake being a common observation (16).

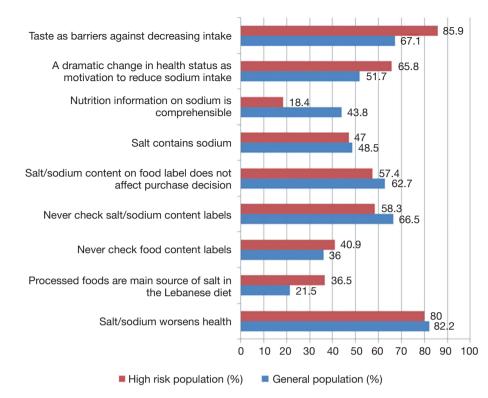


Figure 7 Comparison of knowledge, attitude, and behavior between general and high-risk Lebanese populations.

A pilot-study conducted in Lebanon showed that, in a sample of 90 adults, approximately 40% of the collected 24-hour urine samples were incomplete, thus highlighting the difficulty of adopting this approach in population-based studies. It has therefore been suggested that a preferable method, from the perspective of feasibility and convenience, would be the assessment of sodium excretion from spot urine samples. This would require measurement of the spot urine sodium concentration along with a measure of the state of concentration or dilution of the urine, such as the urine creatinine concentration (16). Despite the concerns raised regarding the validity of this approach, many studies showed that sodium intake estimates derived from spot urine collection strongly correlate with those derived from 24-hour sodium excretion (16-18). An ongoing study in Lebanon is aiming at investigating the validity of spot urine samples in estimating sodium intake amongst adults.

Dietary assessment methods [24-hour dietary recalls, diet records, food frequency questionnaires (FFQs)] may also be utilized for the assessment of sodium intake, particularly when conducting large-scale population studies, which usually require quick, simple and reliable methods for the estimation of dietary intakes. In this context, the 3-day food record approach is considered as one of the best dietary assessment tools. However, its use is limited by the burden placed on the study participants and by the risk of the individual changing his/her dietary habits during the study period (19,20). Previous dietary pilot-studies conducted amongst Lebanese adults documented poor compliance and significant under-reporting when adopting the threeday dietary records, compared to the 24-hour dietary recall approach. The latter has in fact also been adopted in studies assessing dietary sodium intake. Although the 24 -hour dietary recall, when undertaken through a detailed interview, provides detailed information on all food and beverages consumed by the individual, it is considered less accurate when compared with 24-hour urinary collection, resulting most often in an underestimate of salt and sodium intake (21) (WHO, 2013). The limitations of the 24-hour recall approach may be partially overcome when the recall is repeated on multiple days (22). Finally, the use of the FFQ, which allows for the assessment of the usual patterns of food intake over an extended period of time (14,23), has also been proposed for the assessment of dietary sodium intake (24). FFQs rely on recall from 'generic' memory, which may be more easily recalled than 'episodic' memory,

but because of the importance of cultural sensitivity, all FFQs require some adjustments and validation when used for a select cultural group (25). An ongoing study in Lebanon aims at investigating the validity of repeated 24 hour recalls and a short FFQ for the assessment of sodium intake amongst Lebanese adults, with the validation being performed against 24-hour urine sodium excretion. It is important to note that one of the biggest challenges for the assessment of sodium intakes based on dietary assessment tools is the availability of up-to-date, culture-specific salt and/or sodium food composition tables. As region- and country-specific differences may exist in the levels of salt used in various foods, and particularly traditional types of foods, the use of international food composition databases may be a limiting factor to the data generated by dietary assessment methods.

Health communication

Once the amount and sources of sodium intake were determined (Figure 1), the public health arm was charged with: (I) developing a workable plan to reduce sodium intake; (II) creating and disseminating educational material for awareness raising; (III) identifying key stakeholders [ministry of health, ministry of industry (MoI), syndicate of bakeries, and others] and (IV) meeting these individuals and getting their buy-in for a plan that would include policy changes with monitoring activities. The efforts of the campaign were acknowledged by the ministries of public health and industry in Lebanon, with a promise of support and intervention on the national level. However, similar to other experiences across the globe, the public health arm was faced with resistance and delays. In our situation, we were particularly affected with the turmoil arising from the repercussions of the Arab Region revolutions. Simply, given the numerous public health challenges from the influx of refugees from neighboring Syria, and local security challenges in Lebanon, sodium reduction fell low on the list of priorities (26). Nonetheless, during the process there were numerous lessons learned that reshaped the group's understanding of the better course to be followed and this will be highlighted in the section below.

Based on the initial situation analysis, a health awareness campaign was planned to address the significant knowledge and behavior gaps in the population. To disseminate knowledge and awareness, LASH members developed educational material including a "low salt shopping guide", low salt posters, and information leaflets, in both English and Arabic. The shopping guide (http://www.aub.edu.lb/ fm/vmp/events-activities/Pages/shopping-guide.aspx) serves as a guidebook for avoiding purchase of high sodium food while choosing lower sodium alternatives, in addition to tips on how to read labels and stay below the maximum allowable daily sodium intake. The posters (http://www.aub. edu.lb/fm/vmp/events-activities/Pages/lash-salt-posters. aspx) aim at raising awareness and driving attention towards the risk of consuming high levels of salt in the Lebanese diet. These posters were designed to correlate with the Lebanese context and utilize connotations specific to the population. Moreover, at the bottom of every poster, a "Fact" statement provides evidence-based salt information, including adverse health effects of high salt diets or hidden sources of salt. As for the information leaflets (http://www. aub.edu.lb/fm/vmp/events-activities/Pages/lash-salt_leaflet. aspx), they were designed to convey concise information regarding sources of sodium in the diet and reading labels. More importantly, the color and format were chosen to allow cheap, high-volume printing and nationwide dissemination.

Advocacy

LASH members participated in a vital workshop held by the World Health Organization Eastern Mediterranean Regional Office (WHO-EMRO) in September 2013 on methods for salt reduction and monitoring of salt content in food. Through the workshop, LASH members placed Lebanon on the regional salt reduction scene and were exposed to the efforts in the region that were successful in reducing dietary intake on the national level such as in Kuwait. The proceedings of the workshop and resulting policy statements were used by LASH as the backbone proposal when contacting key stakeholders and inviting them to the launching of the campaign, which took place during the World Salt Awareness Week, March 2014. Through the launch conference, the group gained the patronage of the Lebanese Ministry of Public Health (MoPH) and obtained contacts within the Lebanese MoI. The conference also generated massive media interest in the topic, which unfortunately did not last long as more eminent security threats shook the country throughout the year. After getting political coverage, a key element for the success of any national effort in Lebanon, LASH turned its gaze towards the industry and its influential lobbyers and policy makers. To that end, LASH had a preliminary meeting with the Director of MoI followed by a workshop in MoI

headquarters to discuss the urgency and technical aspect of reducing salt in processed food products. Mandated by the ministry to take part, industry representatives got involved in the workshop after having refused to do so in past activities. It was agreed upon that pilot salt reductions in bread and other food items including cured meats, pickles, olives, cheese, and nuts, would take place in ministry-selected producers. Moreover, the MoI stressed on developing a plan to have clear and straightforward labeling of food products with simultaneous public training and capacity building to properly read and interpret food labels. The ministry also pledged to make this issue a priority, urging all attendees from the government and industry sectors to assume their responsibilities to have a tangible result in all mentioned food types by the next year.

Monitoring

Furthermore, after all the above efforts were undertaken with the different industry and government stakeholders, and given the relative lack of sophistication in the industry and government systems in Lebanon, the adopted approach was modified. The challenge in implementing any maximum bread salt levels at the bakery levels was due to the fact that, unlike Kuwait where a centralized mill distributes flour to all bakeries, the different bakeries get their flour from many different sources and often produce flours with different baking qualities. Accordingly, bakeries frequently end up increasing their bread salt level to make up for any diminution in functionality caused by a lower flour quality. This was highlighted in the discussions and comments aired by bakers during a meeting at the MoI. Accordingly, the following steps were suggested:

- Updating the MoI Lebanese Standards with respect to sodium levels in bread;
- (II) Conveying to bakeries the potential added value of low sodium bread products;
- (III) Asking producers of bread to include nutritional labels on their products;
- (IV) Verifying the compliance of low sodium breads to specific standards (for example, low sodium foods are those containing 120 mg of sodium per 100 gram of product).

It is believed that this approach will create a clear niche category for low sodium bread. Coupling this with nutrition education, sodium level monitoring activities and the added value (higher profit) of this niche category, we estimate that this may: (I) lead to market dynamics that will further expand the low sodium bread category; and (II) build on achieving proper labeling for all bread types for future interventions.

Conclusions

All along, the campaign was logistically, academically, and financially supported by the hosting institution, the American University of Beirut (AUB), and the Vascular Medicine Program at AUB. The collaboration with Consumers International in Lebanon (http:// consumersinternational.org/) after the WHO workshop also helped LASH members gain more insight into the dynamics of approaching government agencies and the industry representatives. To our knowledge, this campaign is one of rare salt reduction campaigns that originated from an academic setting and made it to the national level. This, of course, had its drawbacks in terms of financial capabilities, media coverage, and access to mass distribution of knowledge and research findings to the unaware public. Working with our governmental partners, the WHO, and others, we are continuing to provide a reliable research and knowledge base to make positive health changes on the national level.

Acknowledgements

We would like to express gratitude to all LASH members for their tremendous efforts in driving the campaign forward and continuously donating their time for making it a success (http://www.aub.edu.lb/fm/vmp/research/ Pages/lash-members.aspx). Moreover, we would like to acknowledge Professor Graham MacGregor, founder and chairman of WASH and CASH, for the support in helping us launch the campaign. We would also like to express gratitude to the efforts of students, staff, and faculty members associated with the AUB and its Medical Center, including Maha Hamade, Nihal Ismail, Milad Hadchiti, Rana Alley, Shireen Makarem, Zeina Ghannam, Nay Rahi, Christelle Akl, Layla Carine Tannous, Nathalie Barakat, and Samson Atamian.

Disclosure: The authors declare no conflict of interest.

References

1. Sibai AM, Fletcher A, Hills M, et al. Non-communicable disease mortality rates using the verbal autopsy in a cohort of middle aged and older populations in Beirut during

wartime, 1983-93. J Epidemiol Community Health 2001;55:271-6.

- Central Administration and Statistics Population Statistics, 2009. Available online: http://www.cas.gov.lb/index.php/ demographic-and-social-en/population-en
- WHO. The Atlas of Heart Disease and Stroke, 2011. Available online: http://www.who.int/cardiovascular_ diseases/resources/atlas/en/
- 4. WHO. Noncommunicable diseases country profiles 2014. Available online: http://www.who.int/nmh/countries/en/
- Mozaffarian D, Fahimi S, Singh GM, et al. Global sodium consumption and death from cardiovascular causes. N Engl J Med 2014;371:624-34.
- He FJ, MacGregor GA. Effect of modest salt reduction on blood pressure: a meta-analysis of randomized trials. Implications for public health. J Hum Hypertens 2002;16:761-70.
- World Health Organization. Population sodium reduction strategies. Available online: http://www.who.int/ dietphysicalactivity/reducingsalt/en/
- Powles J, Fahimi S, Micha R, et al. Global, regional and national sodium intakes in 1990 and 2010: a systematic analysis of 24 h urinary sodium excretion and dietary surveys worldwide. BMJ Open 2013;3:e003733.
- 9. Labanese Action on Sodium and Health. Available online: http://www.aub.edu.lb/fm/vmp/research/Pages/lash.aspx
- Health Canada. Canadian Community Health Survey, Cycle 2.2, Nutrition (2004) A Guide to Accessing and Interpreting the Data, 2006. Available online: http://www. hc-sc.gc.ca/fn-an/surveill/nutrition/commun/cchs_guide_ escc-eng.php
- Nasreddine L, Hwalla N, Sibai A, et al. Food consumption patterns in an adult urban population in Beirut, Lebanon. Public Health Nutr 2006;9:194-203.
- Jaoude DA, Olabi A, Najm NE, et al. Chemical composition, mineral content and cholesterol levels of some regular and reduced-fat white brined cheeses and strained yogurt (Labneh). Dairy Sci Technol 2010;90:699-706.
- Nasreddine L, Akl C, Al-Shaar L, et al. Consumer knowledge, attitudes and salt-related behavior in the Middle-East: the case of Lebanon. Nutrients 2014;6:5079-102.
- Bentley B. A review of methods to measure dietary sodium intake. J Cardiovasc Nurs 2006;21:63-7.
- 15. Ji C, Sykes L, Paul C, et al. Systematic review of studies comparing 24-hour and spot urine collections for

estimating population salt intake. Rev Panam Salud Publica 2012;32:307-15.

- Mann SJ, Gerber LM. Estimation of 24-hour sodium excretion from spot urine samples. J Clin Hypertens (Greenwich) 2010;12:174-80.
- 17. Tanaka T, Okamura T, Miura K, et al. A simple method to estimate populational 24-h urinary sodium and potassium excretion using a casual urine specimen. J Hum Hypertens 2002;16:97-103.
- Kawasaki T, Ueno M, Uezono K, et al. Average urinary excretion of sodium in 24 hours can be estimated from a spot-urine specimen. Jpn Circ J 1982;46:948-53.
- Wrieden W, Peace H, Armstrong J, et al. A short review of dietary assessment methods used in National and Scottish Research Studies. Briefing Paper Prepared for: Working Group on Monitoring Scottish Dietary Targets Workshop, September 2003. Available online: http:// www.food.gov.uk/sites/default/files/multimedia/pdfs/ scotdietassessmethods.pdf
- Thompson FE, Subar AF. Dietary assessment methodology. nutrition in the prevention and. Treatment of Disease 2008;2:3-39.
- 22. Biró G, Hulshof KF, Ovesen L, et al. Selection of methodology to assess food intake. Eur J Clin Nutr 2002;56:S25-32.
- 23. Subar AF. Developing dietary assessment tools. J Am Diet Assoc 2004;104:769-70.
- 24. Charlton KE, Steyn K, Levitt NS, et al. Development and validation of a short questionnaire to assess sodium intake. Public Health Nutr 2008;11:83-94.
- Coulston AM, Boushey CJ, Ferruzzi MG. Nutrition in The Prevention and Treatment of Disease, 2nd ed. London: Elsevier-Academic Press, 2008.
- 26. Refaat MM, Mohanna K. Syrian refugees in Lebanon: facts and solutions. Lancet 2013;382:763-4.

Cite this article as: Almedawar MM, Nasreddine L, Olabi A, Hamade H, Awad E, Toufeili I, Arnaout S, Isma'eel HA. Sodium intake reduction efforts in Lebanon. Cardiovasc Diagn Ther 2015;5(3):178-185. doi: 10.3978/j.issn.2223-3652.2015.04.09