

'SAFE' PILLS: SUPPLEMENTS – BELIEFS AND REASONS

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Summary

In recent years, there has been increased consumption of dietary supplements in industrialised nations. General confusion about the topic is driven by persisting mixed and controversial messages in academic and public domains, together with tougher European-wide regulations coming into effect in 2010, partly for increased consumer protection, partly for harmonising laws across European member states. Despite this, supplement markets are forecast to grow. This paper investigates supplement awareness, beliefs, and attitudes of people living around London and other European cities. While also exploring beliefs and attitudes towards GPs and medical professionals, the survey provided some insight into the prevalence of concurrent use of multiple supplement and pharmaceutical preparations.

Introduction

What are 'Supplements'?

Dietary or 'food' supplements can contain food-derived compounds, either from natural or synthetic origin, or a combination of both. They are sold separately to regular food supply as tablets, capsules, liquid or powders. Vitamin and mineral supplement (VMS) products may contain concentrated high-potency forms of vitamins and minerals. Other supplements can contain isolated or a mix of many other varieties of natural and/or synthetic compounds derived from foods, plants and other sources (Figure 1). As there are no regulated standards of definition, clear distinctions between certain supplement categories often become blurred and products can vary widely in composition and characteristics¹. 'Specialty formulas' can contain compounds of many different categories, often marketed to address more specific health goals 'synergistically' (e.g. skin, hair and nail or bone and joint formulas), making dosage and application more consumer friendly.

Figure 1: Examples of Compounds Found in 'Supplements'

- **Vitamins:** e.g. water-soluble vitamin C, B vitamins (B1, B2, B3, B5, B6), C, fat-soluble vitamins A, D, E
- **Minerals:** e.g. magnesium, calcium, zinc, iron
- **'Foods':** or part of food compounds - e.g. fish oils, probiotics, amino acids
- **Plants:** botanical compounds or extracts – e.g. Echinacea, St John's Wort, Milk thistle
- **Other:** or 'specialty' compounds - e.g. glucosamine, chondroitin

Nutrients are Essential for Life: But Doesn't a 'Normal' Diet Provide Everything We Need?

Vitamins and minerals are essential for all body processes. In nature, they are tightly enclosed within the 'food matrix', together with tens of thousands of other chemical compounds. Evolution has enabled us to take advantage of this mix of chemicals. With help of an adequate working digestive

system we can utilise these nutrients that are needed for all metabolic functions. Normally, these compounds are only needed in minute amounts (=‘micro’-nutrients), as opposed to our needs for ‘macro’-nutrients (e.g. proteins, fats and carbohydrates).

Consuming insufficient amounts of dietary nutrients to satisfy our individual body’s needs, a trend seen in both developing and industrialised countries, can over time lead to nutrient deficiencies and disease. But likewise, overconsumption, perhaps through excess use or inappropriate forms of concentrated compounds (e.g. in supplements), can prove harmful. It is generally difficult to consume an excess of ‘micro’-nutrients from a ‘normal’ (and unfortified) diet alone.

The past 50 years have seen continuing changes to our environment, lifestyles, farming and food manufacturing methods, and functional food quality has decreased dramatically²⁻⁴. Food consumption may have increased in industrialised and ‘fast food’ nations, but poor dietary choices coupled with increasing availability of nutritionally poor quality foods have made it challenging to satisfy underlying nutrient needs for the modern individual living in a fast-paced, environmentally challenged society. Together with decreasing levels of physical activity, increasing levels of obesity and other chronic degenerative problems have become major concerns worldwide, especially in the industrialised nations. Not micronutrient excess but micronutrient deficiencies (also called ‘Type B’-Malnutrition) are becoming an increasingly important contributor to obesity prevalence, being part of and related to a range of other chronic and degenerative conditions of metabolic disorders.⁵

In the UK, recent government surveys have confirmed the prevalence of various micronutrient deficiencies in ‘healthy’ populations consuming a ‘normal’ diet, particularly in low income groups.⁶

Various UK government initiatives are aiming to address the need to raise public health awareness, e.g. by encouraging the public to consume more fruits and vegetables (e.g. ‘5-A-Day’ targets since 2000), to smoke less (NHS smoking cessation programs; UK smoking ban since 2007 for all enclosed public places) and to be more physically active (NHS Change for Life initiative, 2009).

Beliefs, Attitudes, and Behaviours of Supplement Users

Media reports can have a significant impact on consumer awareness and understanding of supplements. Supplement use tends to be biased towards older, more affluent consumers and those living in Greater London⁷. Often, supplements are regarded as a ‘health insurance’ or even to ‘compensate’ for an individual’s dietary and lifestyle choices, especially for ‘heavy’ users⁸. However, a recent Food Standards Agency (FSA) survey found that knowledge of what consumers are taking and their potential beneficial or adverse effects is limited.⁷

Despite popular use of supplements, the majority of supplement users do not tell their medical doctors or health professionals about their supplementation, and GPs don’t tend to inquire^{9,10}. Sufferers of chronic conditions, who are on regular prescription drugs, are even more likely to use concurrent supplementation.^{11,12}

Major contributing factors to these problems are a public perception that these products are inherently safe, and the lack of knowledge and time to discuss the products in the medical profession.¹³⁻¹⁶

Public Confusion is driven by Persisting Contradictory Claims in Media and Academic Domains

Media information (newspapers, magazines, TV, radio, internet) largely drives consumer information. Functional foods, ‘health’ and supplement markets have seen phenomenal growth, particularly over the recent decades. Supplements are now increasingly advertised and widely available from supermarkets, high-street ‘health’ stores, pharmacies, independent distributors, and over the internet (with international and largely unregulated distribution).

Global supplement sales are estimated to reach nearly 200 billion in 2010, nearly tripling from 2005¹⁷. In the UK, annual supplement sales reached £364 m in 2007 and it is estimated that at least 40% of

the population consume vitamin and mineral supplement products⁸. There are an estimated 25,000 different supplement products in the UK and 2/3 of UK sales come from non-VMS products.¹⁸

Despite the prevalent use, there is little rigorous scientific information to guide consumers. The public use of supplements, e.g. general health maintenance, or a nutritional therapists' recommendation for short-term high-dose supplementation for individual therapeutic nutrition intervention protocols, has received some medical and media criticism in the past. This general public confusion about supplements is largely driven by persisting contradictory, controversial and mixed messages in academic¹⁹ and public media domains, **see tables A and B**. (View tables online)

There has been growing awareness of the potential role of nutrition and the use of supplements in increasing total nutrient intakes for improving health, chronic disease amelioration and prevention^{5,20-22}. However, conflicting evidence in academic literature suggests potential risk associated with excessive intakes, finding no evidence of benefit and in certain circumstances even risk of increased mortality rates.^{11,23,24}

Pocobelli *et al.* had attributed limited efficacy to unmeasured healthy behaviours, considered more common in supplement users²⁵. Ongoing observational studies have shown that supplement usage positively correlates with intake of fruits and vegetables, physical activity and certain regular medication usage, such as non-steroidal anti-inflammatory drugs²⁶. These factors are also considered major confounding variables in supplement-efficacy research.

Industry advocates have criticised limited financial resources available for supplement research, arguing that "natural" products cannot be patented unlike pharmaceutical drugs, which provides little motivation for big pharmaceutical companies to fund larger and well designed studies. Furthermore, negative studies were often criticised for using synthetically derived compounds applied in isolation. When reviewing academic research this is often not clearly disclosed as many scientists still believe that 'form' [natural vs. synthetic] is irrelevant. However, synthetic compounds are inherently different from 'naturally' derived compounds, in physical properties, activity, bioavailability and side-effects/toxicity²⁷⁻²⁹ (see Figure 2 below).

Figure 2: Natural vs. Synthetic

'Natural' compounds derived from foods are generally considered safer and much more usable ('bioavailable') for the human body, being highly diverse compounds whose biological and physiochemical actions are highly specific/ selective^{27,28,29}. However, many if not most supplement products contain 'synthetically' derived compounds. Products can carry the 'natural' or 'food source, - grown, or - based' label, if they have been derived from cultured yeast, algae, bacteria or other foods – however, synthetic nutrients are often used during these processes (e.g. 'FoodState'). Other companies may use organic wholefood concentrates and add glandular animal source concentrates or medicinal herb concentrates to their products. This makes it challenging to identify true 'organic' and wholefood sources and whether certain combinations are safe, particularly when individuals are on multiple combinatory pharmaceutical medication. In order to remove public confusion, recent 'voluntary' standard ideas like the '**Naturally Occurring Standard' (NOS)**', (Clement *et al.*, 2009) have been introduced; however, only a handful of manufacturers yet have this certification.

Clement B, Treadway S, Gabbay S (2009), The Naturally Occurring Standard [online]. [Accessed 15th March 2010]. Available from: <http://www.nosg.org/pdf/NOSResearchPaper.pdf>

This currently creates a contradiction in itself, as many supplements today are in fact synthetically created in the laboratory, often linked to pharmaceutical companies.

Despite contradictory messages the supplement market is forecast to grow at single to double-digits year on year^{8,30}.

European Legislation Changes in 2010: A Result of Regulatory Issues and Safety Concerns

The above issues have contributed to growing public safety concerns, particularly from the medical profession, driven by limited scientific evidence for efficacy, reports of adverse effects, drug-nutrient-interactions, and reported deaths. This put pressure on government regulators, who in the past have been accused of inappropriately regulating many publicly available health and supplement products, in regards to ingredients, dosages, manufacturing processes and unsubstantiated label claims.

According to the US poison control centre there were an estimated 3,100 major adverse events and 150 deaths from supplements reported in the US in the last 10 years. In comparison, there were 190,000 major adverse events and 14,000 deaths from pharmaceutical drugs reported in that same period, see Figure 3 below, and also **Table C**. (view online)

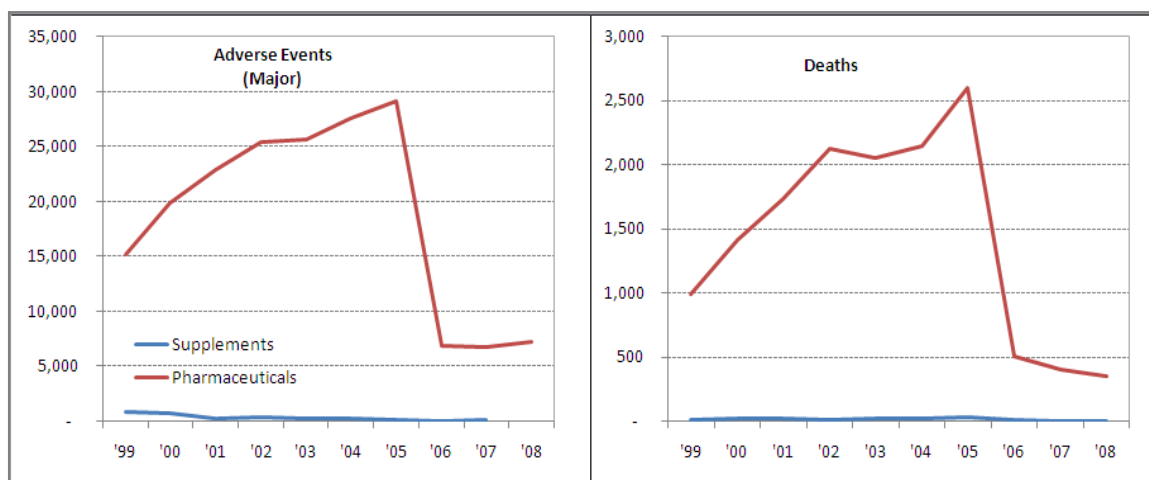


Figure 3. Numbers of Reported Major Adverse Events and Deaths from Reported Exposures to Pharmaceutical drugs and Dietary Supplements, 1999-2008*

* This data is compiled from Annual Reports between 1999-2008 available from the American Association of Poison Control Centre (AAPCC), National Poison Data System (NPDS). Supplements include all reported minerals, vitamin and specialty supplements (including amino acids, homeopathic and herbal remedies). For more information go to www.aapcc.org.

Comparing this to foods, the US Centers for Disease Control and Prevention (CDC) estimate that 76 million Americans get sick, including 300,000 hospitalisations and 5,000 deaths from food-borne illnesses each year. This would equate to nearly a million hospitalisations and 50,000 deaths over a 10 year-period (www.cdc.gov/DataStatistics/).

It appears that in most instances, dietary supplements and herbal medicines are relatively harmless when used appropriately, however, unnecessary or reckless use of these products can lead to problems¹³. However, what is more challenging to assess, is the proportion of events that are not reported or those that could have been caused due to concurrent use of different products, including herbal and pharmaceutical preparations. Botanicals and nutritional supplements, like other biological agents, act at multiple sites in the body. This can produce many effects, some of which may not be detectable on routine clinical or toxicology testing.⁹

Despite knowledge that certain products, particularly botanicals, can interfere with drug metabolism ('drug-nutrient interactions'), research examining the prevalence and overall effect of users mixing various types of supplements of different quality, dosage and potency, also in combination with regular pharmaceutical prescription drugs over longer periods of time, is lacking.

New EU legislation will come into effect in 2010, partly to harmonise laws across the EU facilitating trade and movement of goods or services between the member states, and partly to provide high-

levels of consumer protection. The key EU laws are the Food Supplements Directive (FSD) and Nutrition and Health Claims Regulation (NHCR), passed originally in 2002 and 2006 respectively. On 1st January 2010 it became illegal to sell forms of vitamins and minerals that are not on the FSD's "Positive List", which is far from an exhaustive list of safe and effective 'forms' of vitamins and minerals. During the next stage of the new regulation, 'maximum permitted levels' (MPLs) of micronutrients (for supplements and food fortification) will be set, which has been heavily criticised by the Alliance for Natural Health (ANH) questioning the scientific validity of current risk assessment analysis methods³¹. ANH is concerned that these MPLs are too low for a nutrient to have any therapeutic effects. For instance they claim that beta-carotene normally found in just one large carrot or selenium found in 1-2 Brazil nuts may exceed these MPLs. Furthermore, it is feared that compounds containing nutrients above the set MPLs could be soon considered drugs and fall under medicinal law.

Particularly in the UK, this has contributed to growing uncertainty over future public availability, quantity and quality of certain supplement products that are currently available (Figure 4). The legislation changes will have inherent implications for the health industry as well as availability of appropriate consumer and patient information in this area.

Figure 4: Industry Concerns over New EU Legislation Changes

According to director David Adams, of the UK's Health Food Manufacturers' Association (HFMA), the biggest threat is the suggested MPLs and that all claims for non-Vitamin and Mineral Supplement products 'will' be banned. The HFMA estimates that the UK industry could suffer £100 million sales losses, with more than 4,000 job losses and more than 700 independent health stores closing. This could lead to competition from imports of higher potency supplements, e.g. from Guernsey and Jersey (currently £20 million sales) or other countries that remain outside UK and EU medicines and food legislative regimes, contributing to unregulated supply.

Methods

Data from adult respondents were collected through online survey self-assessment with the help of email snow-balling methods to achieve maximum numbers of respondents. A website was created for this purpose, which provided further information on the project, researcher and university affiliations. To help control the inherent bias that this method could present, researcher-assisted street surveys were also conducted. Participants were given 2-page questionnaires with 22 questions (plus sub-questions) concerning their attitudes and beliefs around supplements and their supplement and medication usage over the last 12 months prior to being surveyed. Data was correlated to frequency of supplement use and compared across various demographic and lifestyle factors.

Results

Motivated by the issues raised in the previous sections, the project was driven by the following key research questions:

Key Research Questions

1. *What are people's current beliefs and attitudes about supplements and their usage?*
2. *What are people's perceptions about the general safety and benefits of supplements?*
3. *How do people gain knowledge about supplements?*

4. *How many and what kind of users mix different products concurrently, including herbal and pharmaceutical preparations?*
5. *Do regular supplement users inform their doctors (GPs) of their supplementation regime, particularly those on regular prescription drugs - and could this pose a safety concern?*

In total, 246 participants responded to the survey; 60% online and 40% from street surveys. 83% participants were from the UK, 15% from European countries, 2% from outside Europe. 80% of participants took some form of supplement within the past 12 months.

Table D (view online)

The main results shown focus predominantly on UK participants, which presented higher statistical relevance (n=203), than those of other European countries (n=36) or elsewhere (n=7). Results were correlated to frequency of supplement use (regular=1x/day or more, occasional=ad-hoc as needed, irregular= 1x/week or more, but tends to forget).

Attitudes and Beliefs about Supplementation

UK participants generally believed that supplements are useful when sick and for supplementing the diet (Figure 5), while also appearing more open to supplement use if evidence and knowledge about supplements were adequate.

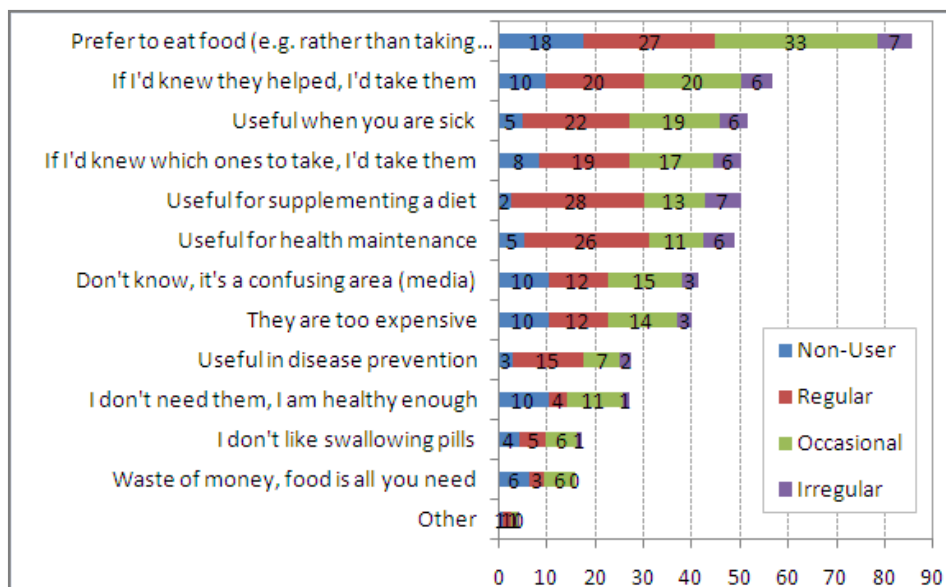


Figure 5. UK Respondents Beliefs About Supplements by Frequency of Supplement Use* (n=203, percent)

* Data represents percent of UK participants that agreed with the respective statements. Percentages may not equal 100% because of multiple answers and rounding.

General uncertainty existed about statements surrounding usefulness ‘in disease prevention’ and affordability.

Regular users were more likely to agree that supplements were useful for ‘supplementing a diet’, ‘health maintenance’ and ‘in disease prevention’. Non-users predominantly believed they were healthy enough and did not need them, that supplements were too expensive, and found it a confusing area. However, 20% of UK non-users indicated that they would take them, if they knew which ones to take.

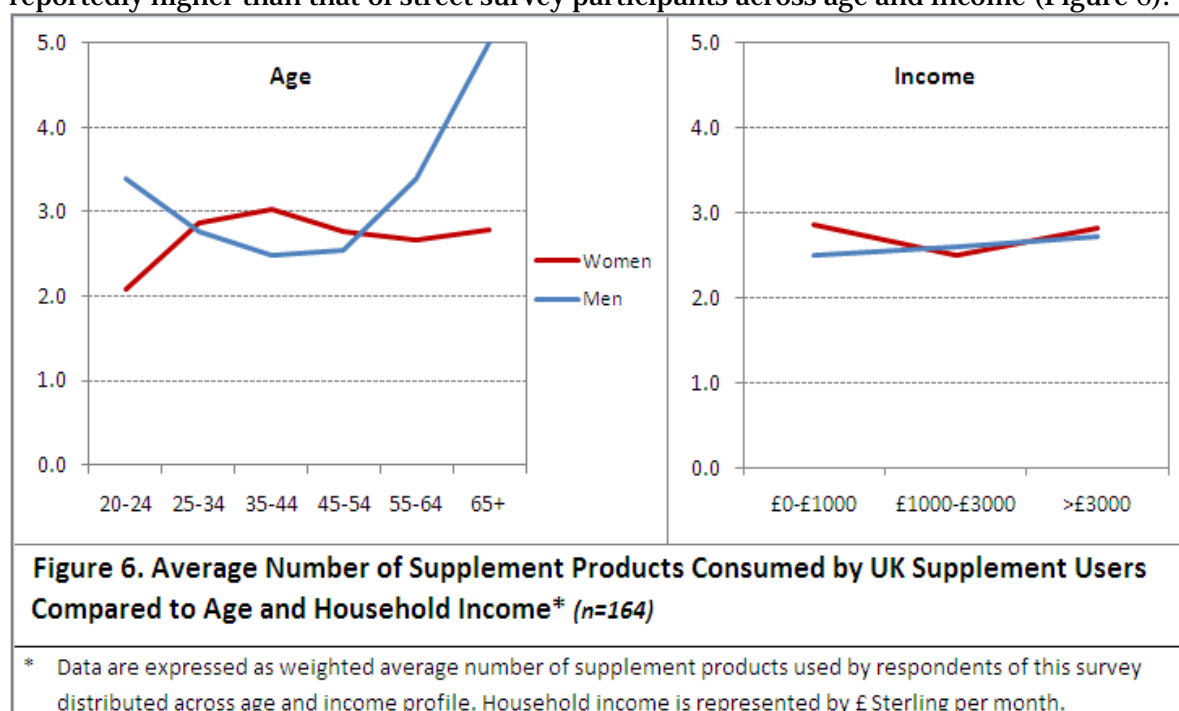
A difference was found between online vs. street participants. Online participants believed supplements to be more useful during sickness, for supplementing a diet and in health maintenance. Street participants indicated lack of knowledge and confusion surrounding supplements and their usage.

Reasons for Supplementation Usage

Generally, supplements were taken for specific health goals or conditions (70%, e.g. boosting immunity, bone/joint or skin health), or else for general health maintenance (54%), or for when sick or run down (43%). More street than online respondents indicated medical conditions (14% vs. 5%). Those that reported diagnosed medical conditions were also more likely to be regular supplement users. Regular users were more likely to justify supplementation for general health maintenance and for compensatory purposes due to their current dietary and lifestyle choices. Occasional/ad-hoc users were more likely to report using supplements for when they are run down, sick or wanted to avoid hangovers.

Trends in Supplementation Usage

Average number of consumed supplement products was higher in women, particularly during childbearing age, rising after 30, while usage for men seemed to peak in early adulthood and later during maturity (Figure 6). For online participants, consumption of supplement products was reportedly higher than that of street survey participants across age and income (Figure 6).



Information and Knowledge Sources

Product labels and health shop information were rated higher than GP or health professional recommendations, however, street respondents appeared more likely to gain information from GP/medical professionals. Despite an overall 42% finding current media messages confusing (Figure 4), 86% formed their knowledge about supplement through media and friends.

Safety and Efficacy Perceptions

- 48% of UK participants believed that supplements can be both safe and unsafe (e.g. side effects) with 38% believing they are inherently safe.
- 52% of users were uncertain about actual benefits and efficacy of supplement products they were taking.
- Regular users were overall more likely to believe that supplements were safe and helped them achieve their health goals.

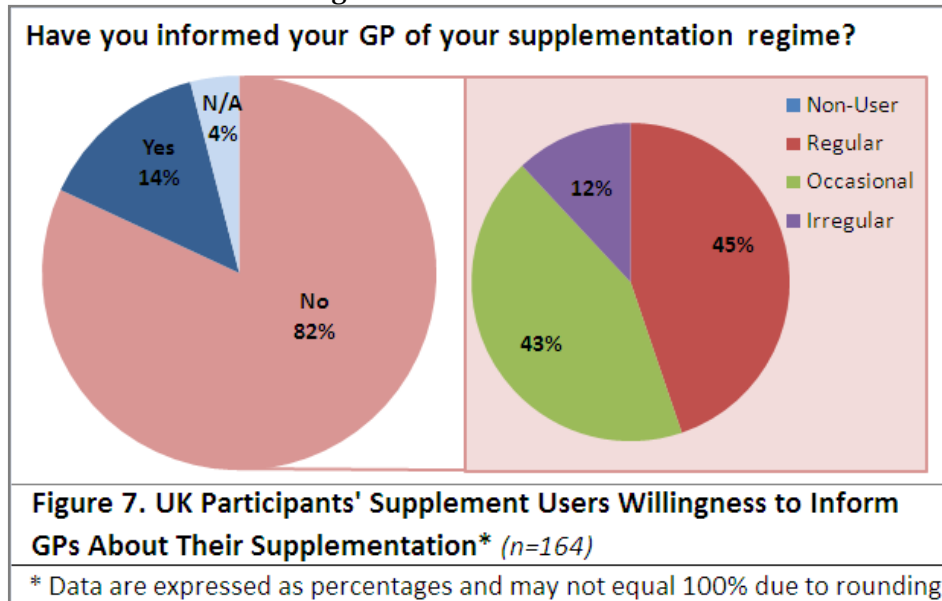
Uncertainty was driven largely by occasional users, however, 11% of regular users were unsure if supplements helped them (indicating: helped 'sometimes', 'don't know', or 'no difference').

Positive Correlations to Other Factors

Fruit and vegetable consumption, physical activity, household income and medication use was positively correlated to supplement use.

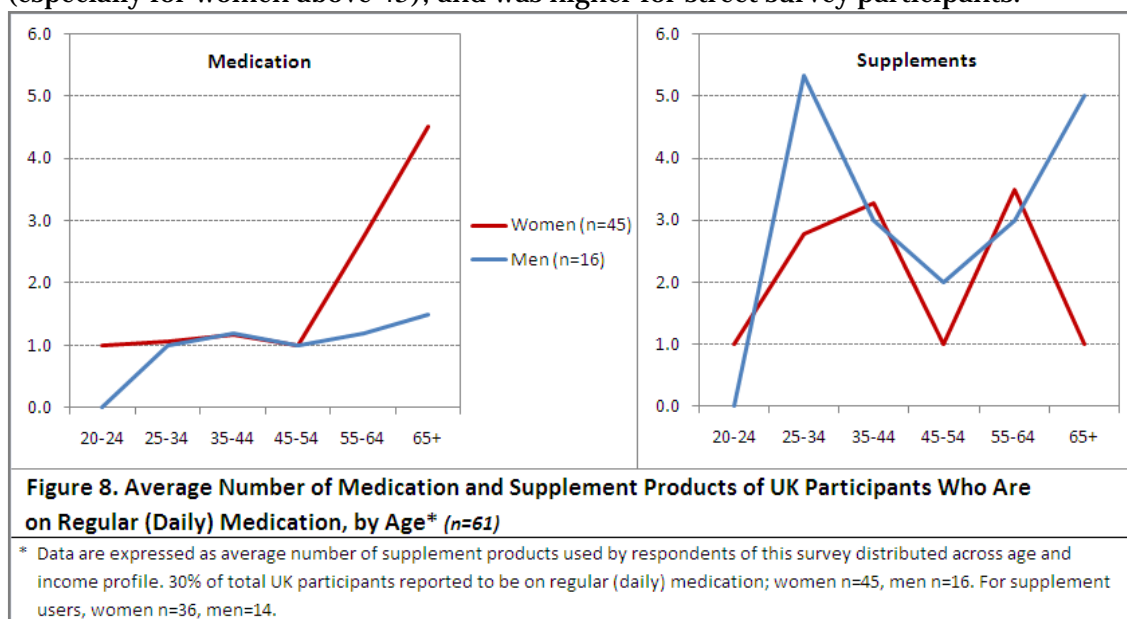
Concurrent Supplement or Medication Usage and Users' Willingness to Inform Medical or Health Professionals of Supplement Usage

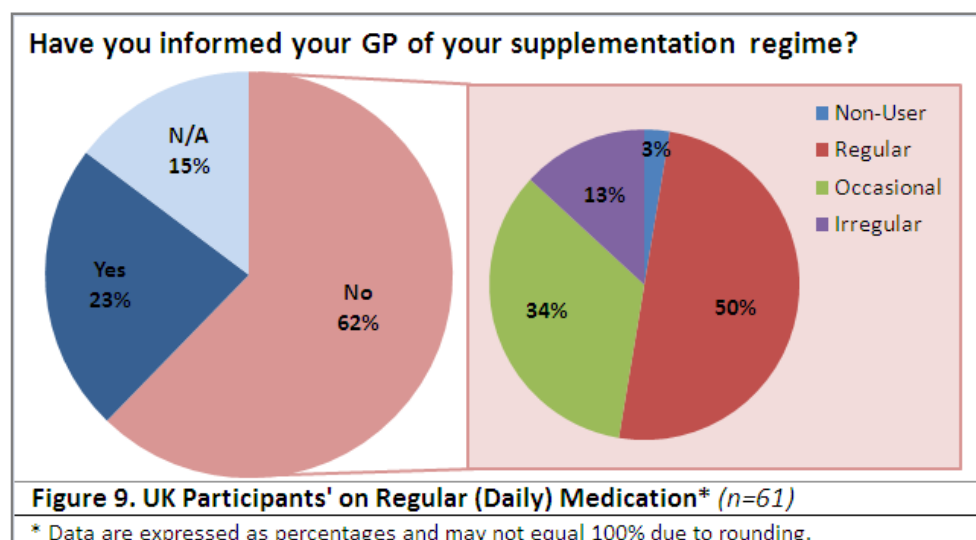
82% of all UK respondents using supplements chose not tell their doctors about supplementation, of which 45% were regular users (Figure 7). These users were more likely not to tell their GPs about their health goals and supplementation regime, partly because they 'didn't think it was important', partly because they 'rarely go to the GP'. They were also more likely to specify associated negative beliefs about their GP's knowledge in this area.



30% of UK participants reported taking regular pharmaceutical medication; they were also more likely to use regular and multiple supplement products (41%), particularly those over 45, while not informing their GPs about it (Figures 8 and 9).

Average number of reported daily prescription drugs consumed appeared to increase with age, (especially for women above 45), and was higher for street survey participants.





Discussion and Conclusions

This survey showed that awareness and beliefs about supplements vary substantially among adults reflecting continued mixed messages in public and academic domains. Despite this and increasing market uncertainty due to European legislation changes, supplement markets are forecast to grow. Supplement usage showed positive correlations to multiple concurrent supplement use, fruit and vegetable consumption, activity levels, and prevalence of regular medication use.

Results echoed previous findings that supplement users found it unnecessary to inform their doctors of their supplement regime. This was also true for those on concurrent medical prescription drugs, being coupled with lack of trust in their GP's knowledge about the topic.^{13,15}

Though problems potentially exist with the methods used, overall findings emphasise the continued need for improved awareness and education around supplements and their usage for the public as well as medical and other healthcare professionals. Understanding motivation, beliefs and attitudes around supplement usage can provide a valuable tool for effective communication and education in this area. Improved and appropriate media coverage is likely to be a key tool in raising awareness as is improving the profile of the nutritional therapy profession.

Independent nutritional therapists and other appropriately trained nutrition health professionals could take a leading role in advising doctors and patients in this area when making evidence-based and evidence-informed recommendations based on clinical practice and scientific data.

More research is needed to provide thorough efficacy analysis of specific types and forms (synthetic vs. 'natural') of supplements used. Exact form, dosage and potency information, also in combination with prescription drugs, could provide better insight into potential adverse or beneficial effects of supplement use over longer periods of time. Future studies should use an integrated (interdisciplinary) approach to link dietary and lifestyle attitudes with subsequent behaviour patterns, including supplement usage, to investigate possible avenues for intervention to encourage more healthful rather than compensatory behaviours.

Considering the continuous deterioration of modern food supplies, low-potency whole food supplements, rather than high-dose synthetic supplements, could play an important role in long-term health maintenance strategies as part of a healthy diet and lifestyle. Recommending high-dose synthetic supplements therapeutically as a treatment strategy, commonly practiced by nutritional therapists, should be based on evidence-'informed' clinical practice, while using appropriate laboratory investigations and keeping abreast of the latest scientific research.

In conclusion, we should however not forget that:

- Health, exercise and fresh 'food' cannot be found in a pill.
- Synthetic compounds, artificially created in a laboratory, are inherently different to 'naturally' extracted compounds - in activity, bioavailability and side-effects/toxicity.

- 'Taking pills', even supplements which are generally regarded as 'safe' (GRAS), cannot compensate for an individual's shortcomings in regards to poor dietary and lifestyle choices.
- An integrated healthcare approach, including therapeutic coaching and nutrition counselling is key in creating sustainable behaviour changes.

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References

1. Yetley EA. (2007) Multivitamin and multimineral dietary supplements: definitions, characterization, bioavailability, and drug interactions. *Am J Clin Nutr.* 85(suppl):269S–276S.
2. Thomas D. (2007) The mineral depletion of foods available to us as a nation (1940-2002)--a review of the 6th Edition of McCance and Widdowson. *Nutr Health.* 19(1-2):21-55.
3. Thomas D. (2003) A study on the mineral depletion of the foods available to us as a nation over the period 1940 to 1991. *Nutr Health.* 17(2):85-115.
4. Fan MS, Zhao FJ, Fairweather-Tait SJ, Poulton PR, Dunham SJ, McGrath SP. (2008) Evidence of decreasing mineral density in wheat grain over the last 160 years. *J Trace Elem Med Biol.* 22(4):315-24.
5. Garcia O, Long K, Rosado J. (2009) Impact of micronutrient deficiencies on obesity. *Nutrition Reviews.* 67(10):559-572.
6. Food Standards Agency (FSA). (2007) Low income diet and nutrition survey 2007, *In: Miller N. NHS and private testing: bridging the knowledge gap. BANT AGM Conference. 6 February 2010, London.* London: BANT (conference paper), p62.
7. Food Standards Agency (FSA). (2008) *Consumer consumption of vitamin and mineral food supplements.* London: GfK NOP Social Research.
8. Mintel. (2007) *Vitamins and Mineral Supplements, Market Intelligence, May 2007.* London: Mintel International Group Ltd.
9. Curtis P, Gaylord S. (2005) Safety Issues in the Interaction of Conventional, Complementary, and Alternative Health Care. *Complementary Health Practice Review.* 10(1):3-31.
10. Halsted CH. (2003) Dietary supplements and functional foods: 2 sides of a coin? *Am J Clin Nutr.* 77(suppl):1001S-1007S.
11. Satia JA, Littman A, Slatore CG, Galanko JA, White E. (2009) Associations of herbal and specialty supplements with lung and colorectal cancer risk in the VITamins and Lifestyle study. *Cancer Epidemiol Biomarkers Prev.* May;18(5):1419-28.
12. Neuhouser ML. (2003) Dietary supplement use by American women: challenges in assessing patterns of use, motives and costs. *J Nutr.* Jun;133(6):1992S-1996S.
13. Phua DH, Zosel A, Heard K. (2009) Dietary supplements and herbal medicine toxicities—when to anticipate them and how to manage them. *Int J Emerg Med.* 2:69–76.
14. Ashar BH, Rice TN, Sisson SD. (2007) Physicians' Understanding of the Regulation of Dietary Supplements. *Arch Intern Med.* May 14;167(9):966-969.
15. Blendon RJ, DesRoches CM, Benson JM, Brodie M, Altman DE. (2001) Americans' Views on the Use and Regulation of Dietary Supplements. *Arch Intern Med.* 161(6):805-810.
16. Rayman M. (1999) New MSc in nutritional medicine launched at Surrey University. *Nutrition Practitioner.* Feb 1(1):6, *In: Neil K. Functional Medicine: Application to Nutritional Therapy. BANT AGM Conference. 6 February 2010, London.* London: BANT (conference paper), p51.

17. Thurston C. (2008) Dietary Supplements: The Latest Trends & Issues. *Neutraceuticals World*. [online]. [Accessed 9 January 2010]. Available from: <http://www.nutraceuticalsworld.com/contents/view/13904/>.
18. Adams D. (2010) *Expert Opinion on European Legislation Changes*. [Email] (Special Projects Director, Health Food Manufacturer's Association (HFMA); Personal communication, 15th February 2010).
19. Tatsioni A, Bonitsis NG, Ioannidis JP. (2007) Persistence of contradicted claims in the literature. *JAMA*. Dec 5;298(21):2517-26.
20. Burnett-Hartman AN, Fitzpatrick AL, Gao K, Jackson SA, Schreiner PJ. (2009) Supplement use contributes to meeting recommended dietary intakes for calcium, magnesium, and vitamin C in four ethnicities of middle-aged and older Americans: the Multi-Ethnic Study of Atherosclerosis. *J Am Diet Assoc*. Mar;109(3):422-429.
21. Wienecke E, Gruenwald J. (2007) Nutritional supplementation: is it necessary for everybody? *Adv Ther*. Sep-Oct;24(5):1126-35.
22. Fletcher RH, Fairfield KM. (2002) Vitamins for chronic disease prevention in adults: clinical applications. *JAMA*. Jun 19;287(23):3127-3129.
23. Murphy SP, White KK, Park SY, Sharma S. (2007) Multivitamin-multimineral supplements' effect on total nutrient intake. *Am J Clin Nutr*. Jan;85(1):280S-284S.
24. Huang HY, Caballero B, Chang S, Alberg A, Semba R, Schneyer C, *et al*. (2006) Multivitamin/mineral supplements and prevention of chronic disease. *Evid Rep Technol Assess*. (Full Rep) May;139:1-117. [US Agency for Healthcare Research and Quality (AHRQ)]
25. Pocobelli G, Peters U, Kristal AR, White E. (2009) Use of supplements of multivitamins, vitamin C, and vitamin E in relation to mortality. *Am J Epidemiol*. Aug 15;170(4):472-483.
26. White E, Patterson RE, Kristal AR, Thornquist M, King I, Shattuck AL, *et al*. (2004) Vitamins And Lifestyle Cohort Study: Study Design and Characteristics of Supplement Users. *Am J Epidemiol*. 159:83-93.
27. Feher M, Schmidt JM. (2003) Property Distributions: Differences between Drugs, Natural Products, and Molecules from Combinatorial Chemistry. *J Chem Inf Comput Sci*. 43(1):218-227.
28. Thiel RJ. (2000) Natural vitamins may be superior to synthetic ones. *Med Hypotheses*. 55(6):461-469.
29. Smallbone DF. (2000) What do we mean by food form vitamins and minerals? *The Nutrition Practitioner*. February, 2(1):44-46.
30. Hakimi R. (2008) Diagnosis and treatment methods of alternative medicine in private health insurance – a quantitative analysis. [Article in German] *Versicherungsmedizin*. 60(1):27-31.
31. Verkerk RH, Hickey SA. (2009) Critique of prevailing approaches to nutrient risk analysis pertaining to food supplements with specific reference to the European Union. *Toxicology*. doi:10.1016/j.tox.2009.12.017.