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Characteristics and the determinants of high volume dispensing in long-term oral nutritional supplement users in primary care

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Abstract

Background: *Oral nutritional supplements (ONS) are recommended for patients at risk of malnutrition or malnourished. Appropriate ONS prescribing requires regular monitoring to assess its continued requirement. Previous research identified long-term ONS prescriptions (>6 months) without review, with 70% of these influenced by social factors.*

Aim: *To investigate the characteristics of ONS long-term users in Ireland and the determinants of larger volumes of ONS dispensing.*

Design and setting: *Secondary analysis of anonymous dispensed pharmacy claims data of patients dispensed standard ONS for 12 consecutive months in 2018 (n=912).*

Method: *Factors showing significant (p<0.05) univariate associations with above the median consumption of ONS units were entered into a multivariable model.*

Results: *Median age was 76 (range 18-101) years, with 66.9% of the sample being ≥65 years. Almost 70% of our sample was on polypharmacy (45.6%; ≥5 medications) or excessive polypharmacy (21.5%; ≥10 medications). Younger age and being on polypharmacy for drugs having an effect on the central nervous system (CNS) were significantly associated with being dispensed more ONS units in univariate and multivariate analysis. Those patients in the age range 18-44 were 2.5 fold more likely to be prescribed more ONS units (OR 2.5; 95%CI 1.5-4.25;p<0.001). Patients using CNS drugs or on CNS polypharmacy were more likely to be prescribed more ONS units (ORs 1.24 and 2.35; 95%CI 0.86-1.41 and 1.25-4.41 respectively; p=0.029).*

Conclusion: *Older age and polypharmacy characterize long-term ONS users in this study. Younger age and CNS medication polypharmacy are predictors of more ONS units prescribed over a year.*

How this fits in

Malnutrition or undernutrition, arising from a deficiency of energy and protein intake, occurs commonly among community-dwelling individuals in developed countries. In the UK, it is estimated that approximately 3 million people are at risk of malnutrition, of which nearly half are aged over 65 years, the majority living in the community. Both in the UK and Ireland, it is estimated that 10% of the population requiring care from a GP are at risk of malnutrition. Oral nutritional supplements (ONS) are recommended for patients at risk of malnutrition or malnourished. Appropriate ONS prescribing requires regular monitoring to assess its continued requirement. Previous research has identified long-term ONS prescriptions (>6 months) without review, with 70% of these influenced by social factors. In Ireland, GPs are the main prescribers of ONS in primary care. They are also commonly the first point of contact for individuals in the community who are malnourished or at risk of malnutrition. Identifying the characteristics of long-term ONS users and the determinants of being in receipt of larger volumes of ONS can help to identify potential modifiable factors that would lead to evidence-based ONS prescribing and a reduction in unnecessary prescribing.

Introduction

Oral nutritional supplements (ONS) are commercially manufactured products which provide macronutrients and micronutrients and are used to supplement the diet of individuals who do not achieve their nutritional requirements through food alone. These products can be milk, juice or soya-based and liquid, powder or semi-solid in consistency.[1] The UK National Institute for Health and Care Excellence (NICE) guidelines recommend the use of ONS for patients at risk of malnutrition or who are already malnourished.[2] Malnutrition or undernutrition, arising from a deficiency of energy and protein intake, occurs commonly among community-dwelling individuals in developed countries, with population groups such as the elderly and people living with chronic conditions being at risk.[3-6] Both in the UK and Ireland, it is estimated that 10% of the population requiring care from a General Practitioner (GP) is at risk of malnutrition.[7]

Malnutrition in the community is optimally treated by providing first-line dietary advice, a so-called "food-first" approach, in combination with ONS when necessary.[8, 9] Recent research investigating nutritional interventions in older adults at risk of malnutrition has indicated that ONS combined with dietary counselling is the most effective intervention, increasing both dietary intake and weight.[10] Criteria for the appropriate prescribing of ONS have been proposed; these encompass nutritional screening and assessment to ascertain the need for ONS; investigation of the underlying causes of malnutrition; establishing desirable outcomes to be obtained from the nutritional intervention (i.e. weight increase); and providing both dietary advice and continuous ONS monitoring to assess patient adherence and ongoing need.[11]

It is recommended that patients prescribed ONS should be reviewed every 3 months or for those with longer term ONS requirements, every 6 months.[12] Previous research in Ireland identified a large number of patients prescribed ONS for more than 6 months without review, with 70% of prescriptions influenced by social factors, such as, living alone and difficulties with cooking and shopping.[13] The high cost for public health services associated with the prescribing of ONS has also been recognised in Ireland and the UK.[14, 15] Moreover, long term ONS prescribing can lead to patients' overreliance on these products to replace meals.[9]

The characteristics of long-term ONS users remain unexplored in the literature, and little is known about the determinants of higher volumes of ONS dispensed to individuals in the community. Therefore, this study aimed to investigate firstly, the characteristics of ONS long-term users residing in the community in Ireland, and the determinants of larger volumes of ONS dispensing among this population group.

Methods

Study design and study population

This was a retrospective secondary analysis of anonymous dispensed pharmacy claims data for individual patients ≥18years (n=912) who were in receipt of ONS for 12 consecutive months in 2018 on the General Medical Services (GMS) Scheme in Ireland. The GMS is means tested for those <70 years whereas those ≥70 years are eligible. Under the GMS scheme, persons are entitled to a medical card (MC) or a GP visit card (GPVC). MC holders receive free access to GP visits and prescribed medications, whereas GPVC holders are only entitled to free GP services. In 2018, 32.5% of the population of Ireland were eligible for the GMS Scheme; two million GMS cards were in circulation in 2018 with more than three quarters (76%) being MCs [15-17].

The study had ethical approval from the Irish College of General Practitioners (ICGP) Research Ethics Committee, and the University College Dublin (UCD) Human Research Ethics Committee (reference LS-18-50-Corish).

Database

A database of all prescriptions dispensed on the GMS Scheme is managed by the Health Service Executive (HSE) Primary Care and Eligibility Reimbursement Service (PCERS). Within this database, demographic data for claimants and prescribers are available.

Patients were residents within three large population areas north, south, east and west of Dublin (with surrounding areas). The areas examined contribute to 29.1% of the national population eligible for the GMS Scheme (Supplementary Table 3).

Definition of study variables

This study aimed to describe the characteristics of long-term ONS users, and analyse the associations between demographic and medical factors (type and units of ONS, and type of non-ONS medications dispensed) in a year.

- *Demographic and ONS-related factors*

The following information was analysed for the patient cohort; sex, age, living in residential care/independently, area of residence, GP practice area, number of individual ONS products dispensed and ONS units dispensed in 2018, whether in receipt of ONS in 2017. Standard ONS were classified based on their energy and protein content (Supplementary Table 2). Individuals dispensed over the median number of annual ONS units (>660) for the study population were categorised as 'high ONS users'.

The following information was analysed retrospectively for the patients' GP of choice; sex, age and practice area.

- *Non-ONS drugs*

The number and type of non-ONS drugs dispensed were analysed for our cohort. General polypharmacy was defined as being dispensed ≥5 drugs and excessive polypharmacy as being dispensed ≥10 drugs.[18, 19] Ninety-three percent were dispensed drugs working on the central nervous system, drugs working on the circulatory system, or both. As these categories represented the major medications in this cohort, drugs were further classified as CNS or circulatory as per the 2019 Monthly Index of Medical Specialities (MIMS) medicine formulary in Ireland.[20] The conditions treated by CNS and circulatory drugs in the study sample are presented in Supplementary Figure 2. For the purpose of the statistical analyses, CNS and circulatory drugs were coded as follows; no CNS/circulatory drugs, CNS/circulatory drugs (<5 drugs), and CNS/circulatory drug polypharmacy or excessive polypharmacy (≥5 drugs).

Statistical Analysis

Statistical analysis was carried out using SPSS version 24.0 (SPSS, Inc., Chicago, IL). Discrete variables are presented as percentages and continuous variables as medians and ranges. Sex differences were assessed using Mann-Whitney U and Kruskall-Wallis H non-parametric tests in the case of continuous variables, and using the χ^2 test in the case of discrete variables.

Univariate analysis and multivariable analyses were performed with high ONS users as the dependent variable. Data were analysed using cross-tabulations and the Chi-square statistical test in the univariate analysis and binary logistic regression in the multivariable analysis, presenting adjusted odds ratios (OR) and 95% confidence intervals (CI).[21] Independent variables were included in the logistic regression analysis if they were significant in the univariate analysis.[22] Statistical significance was taken as a P-value of <0.05.

Results

Sample characteristics

The median age of the study population was 76 years with ~67% of the sample being ≥65 years of age (Table 1). Women in the sample were older than men (82 versus 65 years old respectively) (P<0.001) (Supplementary Table 1). 18.2% of individuals were in residential care. Most patients were on one ONS product (90.0%) and the majority were in receipt of ONS in 2017 (96.2%). Men were dispensed more units of ONS in 2018 than women (684 units versus 576 respectively, P=0.017) (Supplementary Table 1). Over two-thirds of the sample either had polypharmacy or excessive polypharmacy. Women were dispensed more

concomitant drugs compared to men (median 7 versus 5 drugs respectively, p<0.001) (Supplementary Table 1). 75.4% were dispensed CNS drugs and 61.7% were dispensed circulatory drugs. The most commonly dispensed CNS drugs were those used to treat mood disorders and anxiety, and the most commonly dispensed circulatory drugs were those used to prevent MI and to treat hypertension (Supplementary Figures 2 and 3 respectively).

Most GPs were males and in the 45-64 years age category. The median number of long-term ONS users per GP was 2.0 (1-17). Just under one-third of GPs had more than two long-term ONS users under their care.

[Please insert Table 1]

Sample characteristics segregated by residential status

Table 2 shows that individuals living in residential care were older than those living independently (median 87 versus 71 years respectively, p<0.001). Individuals in residential care were also more likely to be dispensed more than one ONS product and be on polypharmacy or excessive polypharmacy (18.6% versus 8.2%, and 79.1% versus 64.5% respectively, both p<0.001).

[Please insert Table 2]

Characteristics of dispensed ONS

The most commonly dispensed ONS were high-energy standard-protein sip feeds with/without fibre followed by very high energy sip feeds with/without fibre. Together these represented 59.5% of all ONS products dispensed (Figure 1).

There were differences in ONS dispensing patterns within age categories; a larger proportion of patients aged 18-44 years and 45-64 years was in receipt of high-energy standard protein sip feeds compared to those aged ≥65 years (49.1%, 50% and 25.2% respectively, p<0.001) (Figure 2).

Figure 1. Percentage of ONS product type dispensed to ONS long-term users (n=912) as per Supplementary Table 2.

[Please insert Figure 1]

Figure 2. Percentage of ONS product type dispensed to ONS long-term users (n=912) segregated by patient age category. (p<0.001)

[Please insert Figure 2]

Univariate and multivariable analysis using median ONS units as the dependent variable

Univariate analysis showed that the variables associated with high ONS use were patient gender, patient age category, type of ONS, patient general polypharmacy, and patient CNS and circulatory drug prescription (Table 3). There was a higher proportion of patients with no polypharmacy (<5 drugs) in the high ONS user group compared to those with polypharmacy (≥5 drugs) or excessive polypharmacy (≥10 drugs) (57.3%, 46.6% and 46.4% respectively, p=0.009).

Multivariable analysis shows that patient age category, ONS type and CNS drugs dispensed were significant predictors of high ONS use (Table 4). Compared to those individuals ≥65 years, individuals in the 18-44 years and 45-64 years age categories had higher odds of being high ONS users (ORs 2.5 and 2.4; 95%CI 1.5-4.25 and 1.67-3.71 respectively) (p<0.001). Patients dispensed CNS drugs (<5) or on CNS polypharmacy or excessive polypharmacy had higher odds of being a high ONS user (ORs 1.24 and 2.35; 95%CI 0.86-1.41 and 1.25-4.41 respectively) (p=0.029).

[Please insert Table 3 and 4]

Discussion

Summary

In this study, long-term ONS users in the community setting were characterized by female sex, older age, and polypharmacy. Gender differences existed among these ONS users, with females being older than males. Interestingly, when we looked at the determinants of higher dispensing of ONS units, patients' younger age and CNS drug prescription were predictors of more ONS units dispensed over a year.

Strengths and limitations

A strength of this study is that, to our knowledge, it is the first to investigate the characteristics of long-term ONS users and the determinants of higher prescribing of ONS units in the community setting. Despite the population being limited to three areas in Dublin, the database represents almost one-third of all patients living in Ireland who are eligible nationally for the GMS Scheme and gives insight into urban and suburban dwelling individuals who are free-living or in residential care.

A limitation of the study is the lack of other contextual variables needed to explore in more detail the characteristics of our sample such as presence of chronic conditions, access to dietetic services, level of social support, and hospitalization. Moreover, due to the eligibility criteria, the GMS scheme over-represents socio-economically deprived individuals and the population in this study may be affected by multimorbidity and depression to a greater extent than a less deprived sample of a similar age. Furthermore our database only represents those individuals in the GMS who are MC holders as GPVC holders are not entitled to free/reduced cost dispensed medications. The polypharmacy variable was constructed from a list of drugs prescribed for each patient for which pharmacy claims were presented for payment. We do not have information on the duration of prescription or whether these were repeat prescriptions. Moreover, the data contained in the PCERS database are for dispensed and not prescribed ONS, therefore, it is impossible to know whether patients are taking their ONS as prescribed or to ascertain the adequacy of the ONS prescription.

Comparison with existing literature

To our knowledge, there are no previous studies which have characterized adult long-term ONS users in the community. It is interesting that different studies investigating the factors associated with and the determinants of malnutrition in older adults have identified older age, female sex and polypharmacy with increased risk of malnutrition.[23, 24] The association between age and malnutrition is unclear and could be mediated instead by the progressive deterioration of health and functional ability associated with ageing, also known as frailty.[24]

Although female sex has been associated with a higher risk of developing malnutrition, this finding is not consistently observed in systematic reviews.[24, 25] It may be that the

increased risk of developing malnutrition in females is linked to more disabilities and greater functional decline compared with males.[24, 26] Our cohort of long-term ONS users was predominantly female and females were dispensed significantly more concomitant drugs than males, possibly indicating that they are also frailer.

Contradictory results have also been reported on the association between polypharmacy and malnutrition.[24] Polypharmacy could increase the risk of malnutrition due to its side-effects, including, among others, poor appetite.[24] More than 66% of our sample of long-term ONS users were either on polypharmacy or excessive polypharmacy; however, a larger percentage of those who were not on polypharmacy or excessive polypharmacy were in receipt of more ONS units than the median. This could suggest that those on polypharmacy or excessive polypharmacy were a frailer cohort with lower levels of energy intake, supported by the fact that a larger proportion of elderly people (≥65 years) had polypharmacy or excessive polypharmacy compared to the younger age groups (Supplementary Figure 1).

Different patterns of ONS prescribing were observed in our sample of long-term ONS users when categorized by age, with a larger percentage of those between 18-64 years prescribed high-energy standard-protein sip feeds, and a larger percentage of those ≥65 years being prescribed the other ONS categories. This may be explained by the deficits in the ability of older people to meet their energy and protein requirements.[27] Interestingly, although it could be expected that more ONS units would be prescribed for those in residential care, being a frailer cohort, there was no difference between the units dispensed for this cohort and those living independently in the community. A more supportive environment with foods for individuals in residential care could partially explain the equal units dispensed in both settings.[28]

Implications for research and/or practice

Our population of long-term ONS users in Ireland are characterized by older age. Decreased functional ability during ageing can negatively impact on the ability to shop and cook meals which, in turn, detrimentally influences nutritional status. In fact, previous research in Ireland reported that social factors such as difficulties with cooking and shopping provide the rationale for prescribing ONS in 70% of cases.[13]

Furthermore, in our cohort, CNS medication polypharmacy was a predictor of more ONS units prescribed over a year in long-term users. Little is known about mental health and ONS prescription; however, mental health problems, particularly anxiety and depression, commonly occur in older people, who are vulnerable to develop malnutrition.[23, 29] Thus, mental health problems could be directly associated with the development of malnutrition.[23, 29, 30] A Swedish study in 2011 reported that mental health symptoms were strongly associated with the risk of malnutrition in community-living elderly.[29] A bidirectional association between mental health and malnutrition has been suggested. Depression can cause a decrease in

appetite; however, malnutrition is linked to micronutrient deficiencies which can negatively impact on mental health.[31, 32] It is interesting to observe how in our study, younger age was also a predictor of higher dispensing of ONS units; this finding deserves further exploration, if possible alongside information relating to chronic health conditions and hospitalization, as this could indicate social prescribing of ONS to young adults with mental health issues and chaotic lifestyles.[33] (Supplementary Figure 2).

Finally, the majority of our cohort was already in receipt of ONS in 2017 indicating that, once the ONS prescription is commenced in patients with the characteristics described in this study, its discontinuation is unlikely to happen. Oral intake of a high-calorie high-protein diet should be promoted whenever possible in patients at risk of or with malnutrition, with ONS being used as an adjunct to the diet for a limited period when necessary.[12] It has been previously reported that primary healthcare professionals occasionally prescribe ONS for patients at risk or with malnutrition in the community when food modification has not been possible due to social factors.[34, 35] Also, better compliance with ONS has been reported by individuals living alone and with difficulties cooking and shopping. Further research should explore whether social support for long-term ONS users would reduce their need to be prescribed ONS. It would also be interesting to compare the characteristics of individuals on long-term ONS but not included on the GMS scheme with our sample. GPs may benefit from collaboration with other healthcare professionals with expertise in nutrition, such as community dietitians, in the treatment of patients with malnutrition.[9] Box 1 provides links to guidelines on ONS prescribing and reviewing.

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Box 1. Links for guidance on ONS prescribing/reviewing

- **Prescribing Pathway for the Initiation and Renewal of Standard Oral Nutritional Supplements (ONS) for Adults Living in the Community**
  https://www.hse.ie/eng/about/who/cspd/ncps/medicines-management/oral-nutritional-supplements/prescribing%20pathway%20and%20list%20.pdf
- **Managing malnutrition in the community.   Pathway for using oral nutritional supplements (ONS) in the management of malnutrition.**
  https://www.malnutritionpathway.co.uk/library/ons_pathway.pdf

Table 1. PCERS patients and GPs characteristics

Characteristic		
Individuals on ONS, n=912	**%**	**Median (range)**
Gender		
Males	43.5	
Females	56.5	
Age		76.0 (18-101)
Age category		
≥18-44 years	11.3	
≥45-64 years	21.8	
≥65	66.9	
Patient Dublin area		
South/South East	16.0	
West/South West	41.4	
North/North West	42.5	
Residential status		
Living in residential care	18.2	
Living independently	81.7	
Number of ONS products in 2018		1 (1-4)
Number of ONS units in 2018		660 (12- 3250)
Patients on more than 1 ONS	10.0	
Patients on ONS previous year	96.2	
Number of medications	6.0	(0-18)
Polypharmacy		
No polypharmacy (< 5 drugs)	32.9	
Polypharmacy (≥ 5 drugs)	45.6	
Excessive Polypharmacy (≥ 10)	21.5	
Patient CNS drug dispensed[&]		
No CNS drug	24.8	
CNS drug (< 5 drugs)	65.9	
CNS Polypharmacy or Excessive Polypharmacy (≥ 5 drugs)	9.3	
Patient circulatory drug dispensed[$]		
No circulatory drug	38.4	
Circulatory drug (< 5 drugs)	42.7	
Circulatory Polypharmacy or Excessive Polypharmacy (≥ 5 drugs)	19.0	
General practitioners, n=405		
Gender		
Males	59.0	
Females	41.0	
Age		53 (33-72)
Age category		
≥18-44 years	23.2	
≥45-64 years	61.5	
≥65	15.3	
GP Dublin area		
South/South East	23.2	
West/South West	35.1	
North/North West	39.3	
Other*	2.5	
Number of patients on ONS		2 (1-17)
GPs with > 2 patients on ONS	27.9	

[&] Central Nervous System (CNS) medication include drugs to treat anxiety; Insomnia; psychoses; Mood disorders; Obsessive Compulsive Disorder; Nausea; vomiting; vertigo; epilepsy and seizures; Parkinson's; Alzheimer's; Multiple Sclerosis; Attention Deficit Hyperactivity Disorder, and narcolepsy. [$] Circulatory medication include drugs to treat hypertension; oedema; heart failure; arrhythmias; angina; prevent MI, stroke, and vascular events; hypercholesterolaemia; vascular diseases such as Raynaud's and pulmonary arterial hypertension; haemorrhage; anaemia and neutropenia. *A minority of patients attended GPs with practices in different areas to their residential area

Table 2. PCERS patients characteristics segregated by residential status

Characteristic	Median or %†		P-value
	Living in private nursing home	Living independently	
Age, n=912 (years)	87 (58-101)	71 (18-100)	**p<0.001**
Gender			
Males	11.3	88.7	
Females	23.7	76.3	**p<0.001**
Patient Dublin area, n=912			
South/South East	17.4	15.7	
West/South West	47.3	40.1	
North/North West	35.3	44.2	p=0.11
Number of ONS units in 2018, n=912	600 (30-3192)	672 (12-3250)	p=0.54
Patients on more than 1 ONS, n= 912	18.6	8.2	**p<0.001**
Patients on ONS previous year	92.8	96.9	**p=0.023**
Number of medications	7 (0-18)	6 (0-18)	**p=0.021**
Polypharmacy			
No polypharmacy (< 5 drugs)	21.0	35.6	
Polypharmacy (≥ 5 drugs)	55.7	43.4	
Excessive Polypharmacy (≥10)	23.4	21.1	**p=0.001**
Patient CNS drug dispensed[&]			
No CNS drug	17.4	26.4	
CNS drug (< 5 drugs)	74.3	64.0	
CNS Polypharmacy or Excessive Polypharmacy (≥ 5 drugs)	8.4	9.5	**p=0.032**
Patient Circulatory drug dispensed[$]			
No circulatory drug	33.5	39.5	
Circulatory drug (< 5 drugs)	51.5	40.7	
Circulatory drug Polypharmacy or Excessive Polypharmacy (≥ 5 drugs)	15.0	19.9	**p=0.035**

[&] Central Nervous System (CNS) medication include drugs to treat anxiety; Insomnia; psychoses; Mood disorders; Obsessive Compulsive Disorder; Nausea; vomiting; vertigo; epilepsy and seizures; Parkinson's; Alzheimer's; Multiple Sclerosis; Attention Deficit Hyperactivity Disorder, and narcolepsy. [$] Circulatory medication include drugs to treat hypertension; oedema; heart failure; arrhythmias; angina; prevent MI, stroke, and vascular events; hypercholesterolaemia; vascular diseases such as Raynaud's and pulmonary arterial hypertension; haemorrhage; anaemia and neutropenia.

Table 3. Univariate analysis with characteristics of patients and GPs in the ONS user and high ONS user groups

Characteristics	< 660 ONS units		>=660 ONS units		P-value
	n	%	n	%	
Patient Gender					
Male	181	45.6	216	54.4	
Female	274	53.2	236	46.8	**0.023**
Patient Dublin area, n=912					
South/South East	84	57.5	62	42.5	
West/South West	184	48.7	194	51.3	
North/North West	187	48.2	201	51.8	0.130
Residential status					
Living in a private nursing home	90	53.9	77	46.1	
Living independently	365	49.0	380	51.0	0.27
Patient age category					
≥18-44 years	34	33	67	69	
≥45-64 years	63	31.7	136	68.3	
≥65	358	58.7	252	41.3	**<0.001**
Type of ONS*					
ONS type 1	239	45.7	284	54.3	
ONS type 2	208	64.0	117	36.0	**<0.001**
Patient General Polypharmacy					
No Polypharmacy (< 5 drugs)	128	42.7	172	57.3	
Polypharmacy (≥ 5 drugs)	222	53.4	194	46.6	
Excessive Polypharmacy (≥10 drugs)	105	53.6	91	46.4	**0.009**
Patient CNS drug dispensed[&]					
No CNS drug	125	55.3	101	44.7	
CNS drug (< 5 drugs)	302	50.2	299	49.8	
CNS Polypharmacy or Excessive Polypharmacy (≥5 drugs)	28	32.9	57	67.1	**0.002**
Patient circulatory drug dispensed[$]					
No circulatory drug	146	41.7	204	58.3	
Circulatory drug (< 5 drugs)	207	53.2	182	46.8	
Circulatory Polypharmacy or Excessive Polypharmacy (≥5 drugs)	102	59.0	71	41.0	**<0.001**
GP gender					
Male	294	49.5	300	50.5	
Female	161	50.6	157	49.4	0.781
GP age category					
≥18-44 years	113	46.3	131	53.7	
≥45-64 years	263	51.8	245	48.2	
≥65	79	49.4	81	50.6	0.370
GP Dublin area					
South/South East	102	54.0	87	46.0	
West/South West	161	49.1	167	50.9	
North/North West	182	47.6	200	52.4	
Other	10	76.9	3	23.1	0.116

*This variable only includes those patients who were on one ONS type,ONS type 1 includes the 2 most common type of ONS as per Figure 2 (High energy and very high energy standard protein sip feed with or without fibre), ONS type 2 includes the other ONS types represented in Figure 2 (High energy shots, High protein sip feed, High energy semi-solid, Textured modified high energy/high protein sip feeds) [&]Central Nervous System (CNS) medication include drugs to treat anxiety; Insomnia; psychoses; Mood disorders; Obsessive Compulsive Disorder; Nausea; vomiting; vertigo; epilepsy and seizures; Parkinson's; Alzheimer's; Multiple Sclerosis; Attention Deficit Hyperactivity Disorder, and narcolepsy. [$]Circulatory medication include drugs to treat hypertension; oedema; heart failure; arrhythmias; angina; prevent MI, stroke, and vascular events; hypercholesterolaemia; vascular diseases such as Raynaud's and pulmonary arterial hypertension; haemorrhage; anaemia and neutropenia.

Table 4. Multivariable analysis with characteristics of patients significant in univariate analysis in the ONS users and high ONS users groups

Characteristics	Unadjusted*				Adjusted£			
			95% CI				95% CI	
	OR	P	Lower	Upper	P	OR	Lower	Upper
Patient Gender								
Male	1.0$					1.0$		
Female	0.74	**0.023**	0.57	0.96	0.993	0.987	0.74	1.35
Patient age category								
≥18-44 years	2.88		1.85	4.50		2.50	1.50	4.25
≥45-64 years	3.10		2.20	4.31		2.49	1.67	3.71
≥65	1.0$	**<0.001**			**<0.001**	1.0$		
Type of ONS@								
ONS type 1	1.0$					1.0$		
ONS type 2	0.47	**<0.001**	0.36	0.63	**<0.001**	0.57	0.42	0.77
Patient Polypharmacy								
No polypharmacy (< 5 drugs)	1.0$					1.0$		
Polypharmacy (≥ 5 drugs)	0.65		0.48	0.88		0.82	0.56	1.20
Excessive Polypharmacy (≥ 10)	0.645	**0.010**	0.45	0.93	0.55	0.78	0.465	1.31
Patient CNS drug dispensed&								
No CNS drug	1.0$					1.0$		
CNS drug (< 5 drugs)	1.225		0.90	1.67		1.24	0.86	1.78
CNS Polypharmacy or Excessive Polypharmacy (≥ 5 drugs)	2.52	**0.002**	1.49	4.25	**0.029**	2.35	1.25	4.41
Patient circulatory drug dispensed$								
No circulatory drug	1.0$					1.0$		
Circulatory drug (< 5 drugs)	0.63		0.47	0.84		0.97	0.66	1.41
Circulatory Polypharmacy or Excessive Polypharmacy (≥ 5 drugs)	0.50	**<0.001**	0.34	0.72	0.96	0.93	0.57	1.54

OR= Indicates Odds Ratio; **1.0$**= Indicates refernce group; *Binary logistic regression carried out with each variable individually as predictor of dependent variables; £Binary logistic regression carried out with full model adjusted for all variables as predictors of dependent variables; @This variable only includes those patients who were on one ONS type. ONS type 1 includes the 2 most common type of ONS as per Figure 2 (High energy and very high energy standard protein sip feed with or without fibre), ONS type 2 includes the other ONS types represented in Figure 2 (High energy shots, High protein sip feed, High energy semi-solid, Textured modified high energy/high protein sip feeds) &CNS drugs include drugs to treat anxiety, Insomnia, psychoses, Mood disorders, Obsessive Compulsive Disorder, Nausea, vomiting, vertigo, epilepsy and seizures, Parkinson's, Alzheimer's, Multiple Sclerosis, Attention Deficit Hyperactivity Disorder, and narcolepsy $Circulatory medication include drugs to treat hypertension; oedema; heart failure; arrhythmias; angina; prevent MI, stroke, and vascular events; hypercholesterolaemia; vascular diseases such as Raynaud's and pulmonary arterial hypertension; haemorrhage; anaemia and neutropenia.
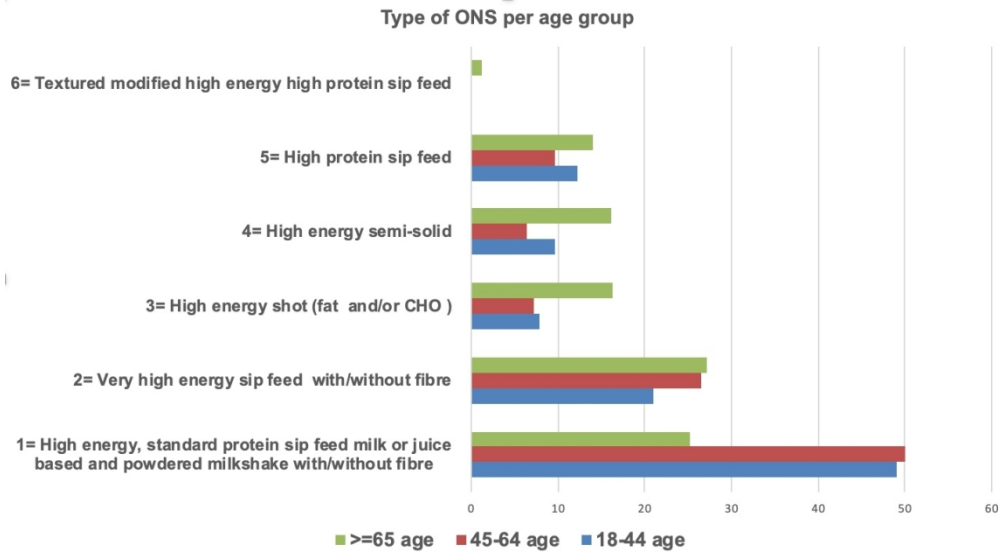
Figure 2. Percentage of ONS product type dispensed to ONS long-term users (n=912) segregated by patient age category. (p<0.001)
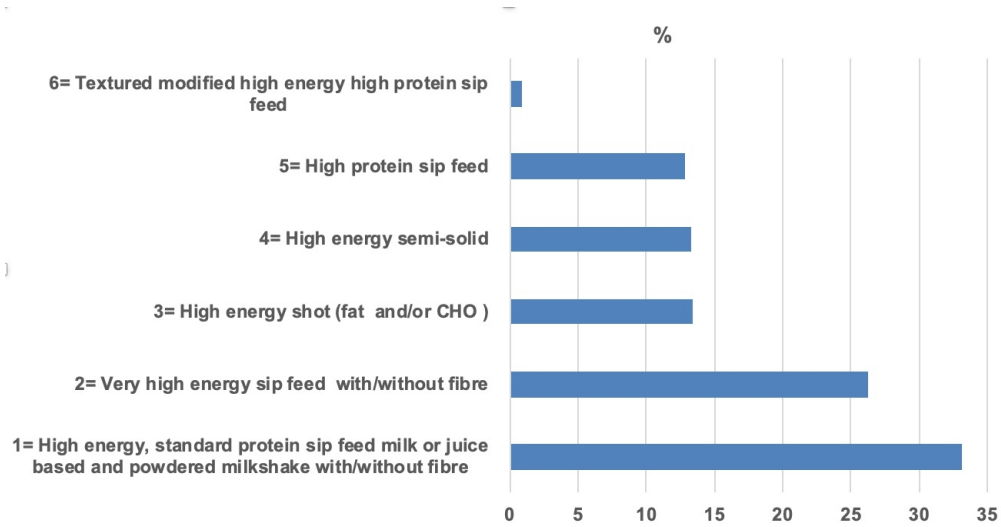
250x140mm (144 x 144 DPI)

Figure 1. Percentage of ONS product type dispensed to ONS long-term users (n=912) as per Supplementary Table 1.

229x119mm (144 x 144 DPI)