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Title Page

Title: Copayments for prescription medicines on a public health insurance scheme in Ireland

Running Title: Copayments for prescriptions in Ireland

Authors

Corresponding author

Sarah-Jo Sinnott BPharm, MPharm PhD , MPSI
Department of Epidemiology and Public Health,
4th Floor Western Gateway Building,
University College Cork,
Ireland.
Email: sarahjosinnott@gmail.com

Co-authors

Charles Normand BA MA DPhil FTCD
The Centre of Health Policy and Management,
Trinity College Dublin,
Ireland

Stephen Byrne BSc (Hons) Pharmacy, PhD, Dip Stat, MPSI
Pharmaceutical Care Research Group,
School of Pharmacy,
University College Cork,
Ireland

Noel Woods BA MA PhD
Centre for Policy Studies,
University College Cork,
Ireland

Helen Whelton BDS, PhD, MDPH, FFD, PGDTLHE
School of Dentistry,
University of Leeds,
England

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Key Points:

1) The main public health insurance scheme in Ireland (GMS) provides primary care to approximately 40% of the population, generally on a means tested basis, but also on the basis of older age.
2) Until 2010 prescription medicines were free at the point of access on this scheme. In 2010 each prescription item was made subject to a €0.50 copayment. This was increased to €1.50 per item in 2013.
3) We found that both copayments had a larger impact on adherence to less-essential medicines than essential medicines, consistent with the prior literature.
4) Notably, in comparison to other essential medicines, relatively larger reductions in adherence to anti-depressant medicines were observed after each copayment intervention.
5) Further analyses of our results on anti-depressant medicines, in addition to analyses for clinical outcomes and variability according to socio-economic status within the GMS population, would increase our understanding of the wider impact of this copayment policy.

Abstract

Purpose

We assessed the impact of the introduction of a €0.50 prescription copayment, and its increase to €1.50, on adherence to essential and less-essential medicines in a publicly insured population in Ireland.

Methods

We used a pre-post longitudinal repeated measures design. We included new users of blood pressure lowering, lipid lowering and oral diabetic agents, thyroid hormone, anti-depressants, non-steroidal anti-inflammatory drugs (NSAIDs), Proton Pump Inhibitors/H_2 antagonists (PPIs/H_2) and anxiolytics/hypnotics. The outcome was change in adherence, measured using proportion of days covered. We used segmented regression with generalised estimating equations to allow for repeated measurements.

Results

Sample sizes ranged from 7,145 (thyroid hormone users) to 136,111(NSAID users). The €0.50 copayment was associated with reductions in adherence ranging from -2.1%[95% CI, -2.8 to -1.5] (thyroid hormone) to -8.3%[95% CI, -8.7 to -7.9] (anti-depressants) for essential medicines and reductions of -2%[95% CI, -2.3 to -1.7] (anxiolytics/hypnotics) to -9.5%[95% CI, -9.8 to -9.1] (PPIs/H_2) for less-essential medicines. The €1.50 copayment generally resulted in smaller reductions in adherence to essential medicines. Antidepressant medications were the exception with a decrease of -10.0% [95% CI, -10.4 to -9.6] after the copayment increase. Larger decreases in adherence were seen for less-essential medicines; the largest was for PPIs/H_2 at -13.5% [95% CI, -13.9 to -13.2] after the €1.50 copayment.

Conclusion

Both copayments had a greater impact on adherence to less-essential medicines than essential medicines. The major exception was for anti-depressant medicines. Further research is required to explore heterogeneity across different socio-economic strata and to elicit the impact on clinical outcomes.

Introduction

The dramatic collapse of the Irish economy in 2008 coincided with an all time high in pharmaceutical expenditure on the country's main public health insurance programme, called the General Medical Services (GMS) scheme. Spending for prescription medicines and devices on this scheme increased from €339 million in 2000 to approximately €1.2 billion in 2010.[1] Compared to Organisation for Economic Co-operation and Development (OECD) countries in 2009, the level of public spending for pharmaceuticals in Ireland was exceeded only by Greece, Canada and the U.S.[2] Given the economic landscape, and amid pressures from the EU-IMF-ECB troika to reduce public spending, a window of opportunity existed to implement cost containment strategies with the goal of achieving better value for money in pharmaceuticals.[3]

One such strategy was the introduction of a copayment policy. In October 2010, a €0.50 copayment per prescription item (capped at €10 per household per month) was introduced on the GMS scheme. This was later increased to €1.50 in January 2013 (capped at €19.50). The rationale behind copayments for prescription medicines is twofold. First is their role in moral hazard, an economic principle describing the inefficient use of prescription medicines by patients when supplied at zero cost by a third party payer e.g. the government.[4] Second is their role in saving costs or generating revenue.[4] Along with these intended effects, copayment policies also have some negative consequences for medication taking behaviours, impacting on patient outcomes.

A study by Tambyln *et al.* is one of the most cited papers in the area of copayments for prescription medicines.[5] The authors found that the introduction of a 25% coinsurance fee for prescription medicines in older individuals and those who received welfare benefits in Quebec was associated with decreased adherence to essential medicines typically used in

chronic disease. Linkable hospital and pharmacy databases allowed the authors to associate these decreases in adherence with increased hospitalisations and mortality. This study is significantly relevant to the Irish setting given the socio-economic and demographic similarities between the GMS population and the population studied by Tamblyn *et al.* Qualification for the GMS is on the basis of means-testing, so the majority who qualify have low-incomes, and due to higher income thresholds, most people aged over 70 years also are also covered.[6] Other frequently cited papers that demonstrate a positive relationship between cost-sharing for prescription medicines and: hospitalizations and death[7]; nursing home admissions[8]; or use of mental health services[9] provide high quality evidence, but are less applicable to the Irish setting due to the more severe policies examined such as allowing patients to receive only three prescription items per month.

In light of the evidence for adverse consequences, an emerging international trend is to move away from conventional copayment policies. For example, in the United Kingdom prescription charges have been removed in Wales, Scotland and Northern Ireland. [10,11] Recent policy reform in the U.S. has created Value Based Insurance Design (VBID). VBID provides free or reduced price access to prescription medicines which provide value both at clinical and cost effective levels e.g., medicines used in diabetes or high blood pressure.[12] Discriminate pricing based on the value of medicines has also been proposed for the European setting.[4]

Considering the risk of copayments to public health, in addition to the risk of elevated healthcare costs due to potential increased use of hospital services, a study of the copayment system in Ireland was imperative. The introduction of the €0.50 copayment in 2010 and its increase to €1.50 in 2013 provided a natural experiment to analyse the policy implication on patient adherence to medicines.

Methods

Ethics

Ethical approval for this study was obtained from the Clinical Research Committee of the Cork Teaching Hospitals, Ireland.

Study design

We used a pre-post longitudinal design with monthly repeated measures. The effects of the €0.50 and €1.50 copayments were analysed separately.

Setting

The GMS scheme is the national tax-funded health insurance programme in Ireland for low income individuals/families and older people. [13] It provides hospital services and primary health care, including General Practitioner visits and prescription medicines, free at the point of access to approximately 40% of the population.[13] The initiation of the copayment system in 2010 ended free access to prescription medicines.

The Long Term Illness (LTI) scheme is a second, smaller public insurance scheme, which provides free medications to individuals who have been diagnosed with one of 16 chronic illnesses, for example, epilepsy or diabetes. Qualification is independent of income. There was no change to the LTI scheme during the course of this study. In their seminal paper that investigated the methods of studies examining drug policies Soumerai *et al.* recommended the use of before and after measurements along with the use of an appropriate comparison group to minimise fundamental threats to validity.[14] The LTI scheme served as a non-equivalent comparator group in our analyses for oral diabetes, blood pressure lowering and lipid lowering agents. The remaining medication groups in our study are not typically

covered by the LTI scheme, which precluded it as a comparator for those analyses. Instead, we relied on pre-post comparisons to estimate absolute reductions in adherence on the GMS, a design which still maintains methodological strengths.[14]

Data Source

We used national pharmacy claims data held in the Health Service Executive-Primary Care Reimbursement Services (HSE-PCRS) database. These data have been used in pharmacoepidemiological and health policy studies in the past[15,16] and have been shown to be accurate.[17] Data were at the individual level and included variables for age, gender, drug dispensed classified by World Health Organisation (WHO) Anatomical Therapeutic Class (ATC) code and the corresponding WHO Daily Defined Dose (DDD), the strength and quantity of medication dispensed and the date of dispensing.

Participants and medications

According to categories summarised in a Cochrane review[18], we designated "essential" or "less-essential" status to eight medication groups to assess whether the impact of the copayments differed depending on type of medication. Medications were identified by WHO-ATC code **(Supplementary Information 1).**

We employed a new user design to minimise the risk of prevalent user bias.[19] New users were defined as individuals who filled a new prescription for a medication without having had a prescription for that medication, or medication in that group, in the prior six months. Once identified as a new user of a medication, patients could enter the cohort at any time in the six months before copayment introduction/increase. Follow up began on first day of cohort entry and ran until 12 months post policy change for the €0.50 copayment. Follow up was for eight months post the €1.50 copayment due to incomplete data for 2013 at the time of analysis (**Figure 1**). Patients were excluded if not continuously eligible on the GMS

scheme or if in receipt of weekly phased prescriptions (**example flowchart in Supplementary Information 2)**. Phased prescriptions are monthly prescriptions that are typically dispensed on a week by week basis, for example in cases of complicated polypharmacy with the aim of improving adherence, or in cases of drug misuse**.**

Insert Figure 1*

Study Outcome

We evaluated adherence using the Proportion of Days Covered (PDC) method.[20] The PDC describes the proportion of days covered by a medication in a given interval and is typically made using two other variables; days' supply and dispensing date. In the absence of a days' supply variable in the HSE-PCRS database, a days' supply variable was estimated using the number of WHO DDDs.[21] This approach is often used in European pharmacy claims database studies.[22,23]

Using the calculated days' supply and the first dispensing date, a medication supply diary was made for each patient indicating which days in the study period a patient had medication available to them. From this supply diary, monthly PDCs were measured, running consecutively from cohort entry to the end of follow up for each individual. Due to the new user design, adherence began at 100% for each patient and then, on average, followed the pattern established for new users, namely a gradual reduction to adherence of approximately 50%.[20] If a dispensing occurred before the previous dispensing ran out, the new dispensing was assumed to begin the day after the end of the prior dispensing and the diary was adjusted accordingly. The PDC was truncated at 1. If an individual was taking more than one medicine within a medication group, the number of days that a patient had at least one of their medicines available to them was calculated.[24] Switching medicines within a medication group was permitted.

In a sensitivity analysis to test the accuracy of using the number of DDDs to calculate the PDC, we assumed a 30-day supply for each dispensing because an individual is entitled to a maximum of one month supply on the GMS scheme.[25] We also tested the performance of quantity of medication dispensed in measuring the PDC.

Variables

The pre-post study design is strengthened by its inherent control for time-invariant confounders, such as socio-economic factors.[26] We adjusted our models for concurrent medication use inclusive of blood-pressure lowering, lipid lowering and oral-diabetes medicines along with insulin and aspirin. However, these variables did not alter the effect estimates for the intervention, therefore we present age and sex adjusted estimates only.

Statistical Methods

First, a segmented generalised linear regression model was fitted to estimate changes in PDC immediately after the policy change (change in intercept) and changes in PDC in the months following post policy (change in slope per month).[27] Policy effects were included in the model as interaction terms between the GMS group and the policy-specific intercept and slope terms. Then, we accounted for natural trends in adherence by subtracting the change in adherence in the LTI group from the concurrent change in the GMS group. We adjusted for correlations between repeated measures using generalised estimating equations.[28] A one month lag period was incorporated to allow the impact of the policy change to take effect, acknowledging that prescriptions are filled every 30 days. For medication groups without a comparator group we assessed the pre-post difference in adherence using a model without the interaction terms.

We conducted sub-group analyses to assess whether effect modification by age and/or gender may have occurred. Age was categorised as 18-29 years, 30-39 years, 40-49 years, 50-59 years, 60-69 years and 70+ years.

All data management and analyses were carried out in R studio version 2.15.3.

Results

The sample sizes for each medication group were quite large **(Tables 1 and 2)**. The LTI population was 5-7 years younger and had approximately 20% less females than the GMS population (**Table 1).** Diabetes medication usage was higher on the LTI scheme, which was expected. New users of less-essential medications were younger than new users of chronic disease medications in both €0.50 and €1.50 cohorts, except for anti-depressant medications **(Table 2).**

Insert Tables 1 and 2

After the €0.50 copayment was introduced, adherence in all medication groups fell. Adherence was decreased by -4.8% (95% CI, -5.7 to -4.0) for blood pressure lowering, by -3.0% (95% CI, -3.9 to -2.1) for lipid lowering and by -2.4% (95%, -3.5 to -1.3) for oral diabetes medications in GMS patients, relative to the LTI group **(Table 3).** Absolute reductions in adherence to thyroid hormone were of similar magnitude to other essential medications, but the drop in adherence to anti-depressant medications was much larger (-8.3% [95% CI, -8.7 to -7.9]). For two out of the three less-essential medicine groups, PPIs/H_2 and NSAIDs, the reductions in adherence were bigger than what was observed for most of the essential medicines (**Table 3).** In contrast, the reduction in adherence to anxiolytics/hypnotics dropped only by -2.0% (95% CI, -2.3 to -1.7). The change in slope in the post policy period

indicated a continued reduction in adherence for anti-depressant medications (-0.8% per month, 95% CI,-1.1 to -0.5) and PPIs/H_2 (-0.5% per month, 95% CI, -0.9 to -0.3). Using the results for slope changes in the controlled analyses as a guide to interpretation, these reductions may not be significant.

Insert Table 3

The reductions in adherence to blood pressure lowering, lipid lowering and oral diabetes medicines were of smaller magnitude after the increase in copayment from €0.50 to €1.50 compared to the introduction of the €0.50 copayment **(Figure 2)**. The same pattern was true for absolute reductions in adherence to thyroid hormone, but adherence to anti-depressant medicines decreased by a larger magnitude after the €1.50 copayment (-10.0%, 95% CI 10.4 to -9.6). Adherence to less-essential medications PPIs/H_2 and NSAIDs was also reduced by larger amounts after the increase in copayment to €1.50 **(Figure 2 and Table 3)**. In contrast, there was a very small reduction in adherence to anxiolytics/hypnotics (-0.8%, 95% CI -1.0 to -0.5). Changes in slope post policy indicate further reductions in adherence in the months following the increased copayment for thyroid hormone, anti-depressant medications, PPIs/H_2 and NSAIDs **(Table 3).** Using the estimates of slope changes in the analyses with a comparator group to guide interpretation; these slope changes may not be significant.

Insert Figure 2

Sub-group analyses revealed that males had larger reductions than females in adherence to thyroid hormone immediately after each policy (after the 50c policy, -4.3% (95% CI, -5.6 to -2.9) *vs* -1.5% (95% CI, -2.2 to -0.8) respectively and after the €1.50 policy -2.6% (95% CI, -3.9 to -1.3) *vs* -0.17% (95% CI, -0.9 to 0.6) respectively). Additionally, males and those aged >70yrs had larger decreases in adherence to NSAIDs immediately after each policy. Effect modification by age or gender also occurred in the anxiolytics/hypnotics group, the PPI/H_2

group, the lipid lowering medicine group and anti-depressant medication group **(Supplementary Information 3).**

Our sensitivity analyses demonstrated that using number of DDDs to calculate the PDC was the most conservative method, in comparison to using an assumed 30 day supply or quantity dispensed. This was especially true for less-essential medicines, which are often used on an as required basis (**Supplementary Information 4).**

Discussion

In this pre-post longitudinal study, we found that both €0.50 and €1.50 copayments were associated with larger reductions in adherence to less-essential medicines than essential medicines directly after the policy changes, consistent with previous systematic review findings.[18,29] Further decreases in the months following the changes in copayments were very gentle and/or insignificant, which also concurs with the literature.[30,31] These results indicate that the impact of the policies was in the period immediately following the policies. In the long term, adherence continued at this new reduced level, as opposed to decreasing even further in the following months.

The major exceptions to the observed trends were for anxiolytics/hypnotics and anti-depressant medications. The minimal reductions in adherence to anxiolytics/hypnotics echo findings as far back as the 1970s when Reeder *et al.* reported little change in the utilisation of sedative/hypnotic mediations after the implementation of a $0.50 copayment in a Medicaid population in the United States.[30] In more recent times, Ong *et al.* in 2003 did not find any reductions in utilisation of anxiolytics and sedatives when a copayment was increased in Sweden, even though it was a much more expensive copayment than examined in our study.[32] The consistency of these findings over numerous decades points to persistent insensitivity towards copayments for these drugs, likely due to their addictive nature.

Our finding that adherence to anti-depressant medications was reduced more than other essential medicines is different to what has been previously reported. A study by Goldman *et al.* found that reductions in use of anti-depressant medications were similar to, or less than, reductions in use of other essential medicines when a copayment was doubled.[33] In Sweden, an increase in copayment saw a reduction in utilisation of anti-depressant medications for females only. [32] In the Irish setting, there was no effect modification by gender, but the

decrease we observed was driven by people aged 18- 29 years. There was no change in adherence to anti-depressant medications in Iceland after a €1 increase in 2010.[34] The discordance between our results and those reported in the Icelandic study are particularly remarkable given that the policy interventions occurred in similar economic circumstances in 2010. Differences in the demographics of the populations, the types of anti-depressants included and the fact that our study did not have a control group for anti-depressants may explain why our findings differ to previous reports. Further, our results may have been vulnerable to confounding by the underlying economic recession during the study period. In this period, diagnoses of depression increased, as did suicides.[35,36]

Is the small copayment, such as those studied in this paper, a useful policy tool? A key consideration is that the effect on essential medicines was generally smaller than for less-essential ones. But within these two categories there are exceptions, and care is needed to avoid the consequences of reduced use of, for example, antidepressants. We also need a better understanding of the clinical consequences of reductions in use of essential medicines, even if these reductions are small – for instance, how important was the ~4% reduction in use of blood pressure lowering drugs with regard to outcomes such as heart attack or stroke. Conversely, the reductions observed for the less-essential medicines may be thought desirable given that some of these drugs have been found to be inappropriately prescribed in Ireland. [16,39] However, if a reduction in the use of inappropriately used medicines was a key goal, then other measures may be required when the results for anxiolyics/hypnotics are considered.

Our findings are in line The Rand Health Insurance Experiment (HIE), which is to date the strongest study in the area of cost-sharing. The HIE found that after randomising families to different levels of cost-sharing, there was little difference between the groups for medications used in chronic disease but the use of less-essential medicines decreased for people who paid

more for them.[37] Our results also echo observational studies dating as far back as the 1970s that examined similar small copayments to the ones we studied.[38,39] Given the amount of time that has passed with natural changes in currency, the actual price paid in our study represents a smaller proportion of income. This suggests the practice of paying a small amount may be sufficient to thwart moral hazard rather than the price, a feature which is supportive of a small copayment.

However, caution must be exercised in advocating for a small copayment given the limitations of our study. We did not have a comparator population for each of the medication groups in our study. Despite this, our use of the LTI group, while a non-equivalent comparator, was most useful for studying adherence in three chronic disease medications, reflecting any extraneous influences on adherence e.g. changes in national chronic disease health policies.[40] Pharmacy claims data do not indicate consumption of medications, just dispensing. Our categorisation of medication groups as essential or less-essential does not take into account instances where less-essential medicines may be a required therapy e.g., PPIs in peptic ulcer disease. Related to this, we measured adherence to less-essential medicines using the same method for essential medicines. Less-essential medicines, especially NSAIDs, may be used on "as required" basis to which our method may be somewhat insensitive. However, it is difficult to measure adherence to medicines that are used sporadically, thus we used the method that is most frequently cited in the literature for claims data. . We have not assessed clinical outcomes, rather we used adherence as a surrogate outcome.[41]

Our study was strengthened by using a population level database, thus we had full dispensing information for the entire GMS population. Although the GMS population is by definition comprised of low-income people, some socio-economic variation may still persist within the population. While we carried out subgroup analyses according to age and gender, we did not

have access to socio-economic data, which calls for further research. Our data were at the individual level, thus avoiding ecological fallacy.[14] We employed the most appropriate study design and statistical techniques to study drug policy interventions.[14,27]

Conclusion

Our results show that small copayments for prescription medicines in Ireland are associated with larger decreases in the use of less-essential medicines than essential ones. The exception was medicines used in depression, a result which requires further investigation and caution.

The extent to which small copayments can reduce moral hazard and increase revenue without significant harm to patients may depend on copayment policies being combined with other policy interventions. First, supply side measures should continue to be implemented, controlling the cost of medicines to the government, and thus reducing the burden of patient cost-sharing. Secondly, awareness and understanding of the role of essential medicines should be emphasised by healthcare professionals, promoting rational choices amongst patients.

Importantly, the effects of a €2.50 copayment (introduced December 2013) in this Irish publicly insured population have yet to be assessed. This, along with careful monitoring of vulnerable groups and accessing data on clinical outcomes is crucial to the future development of this copayment policy. Until such research is completed, further increases to the price would not be a prudent way forward given that copayments have been associated with negative patient outcomes in the past.

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Table 1 Baseline characteristics of new users of essential medicines for the €0.50 copayment and the €1.50 copayment

	€0.50		€1.50	
	GMS	**LTI**	**GMS**	**LTI**
Blood pressure lowering medicines	n=39,314	n= 3,831	n= 37,007	n=3,112
Mean Age –yrs (SD)	62.1 (±16.4)	56.3 (±19.7)	60.4 (±16.7)	57.7 (±21.3)
Female – n (%)	21,935 (55.8)	1,210 (31.6)	20,200 (54.6)	985 (31.7)
Medication use at baseline – n (%)				
Aspirin	4,089 (10.4)	371 (9.7)	3,590 (9.7)	281 (9.0)
Lipid lowering medicines	5,268 (13.4)	433 (11.3)	5,440 (14.7)	401 (12.9)
Oral diabetes medicines	1,054 (2.7)	552 (14.4)	1,073 (2.9)	557 (17.9)
Insulin	236 (0.6)	277 (7.2)	296 (0.8)	229 (7.4)
Lipid lowering medicines	n= 33,394	n=4,217	n=29,619	n=3,351
Mean Age –yrs (SD)	63.6 (±13.6)	56 (±18.9)	63.2 (±13.4)	57 (±10.7)
Female – no. (%)	17,942 (53.7)	1,327 (31.5)	15,300 (51.7)	1,095 (32.7)
Medication use at baseline – n (%)				
Aspirin	5,076 (15.2)	523 (12.4)	4,206 (14.2)	385 (11.5)
Blood pressure lowering medicines	9,117 (27.3)	671 (15.9)	8,323 (28.1)	570 (17)
Oral diabetes medicine	1,536 (4.6)	856 (20.3)	1,540 (5.2)	781 (23.6)
Insulin	367 (1.1)	338 (8.0)	373 (1.3)	301 (9.0)
Oral diabetes medicines	n= 7,145	n= 4,076	n= 7,007	n=3,011
Mean Age –yrs (SD)	62.8(±15)	55.4 (±11.4)	61.4(±15.8)	56.1 (±22)
Female – n (%)	3,395 (47.5)	1,306 (32.0)	3,253 (46.4)	1,028 (34.1)
Medication use at baseline – n (%)				
Aspirin	1,710 (23.9)	392(6.2)	1,638 (23.4)	251 (8.3)
Lipid lowering medicines	2,213 (31)	437(10.7)	2,181 (31.1)	394 (13.1)
Blood pressure lowering medicines	2,799 (39.2)	459 (11.3)	2,775(39.6)	372 (12.4)
Insulin	229 (3.2)	206 (5.2)	300 (4.3)	200 (6.6)
Thyroid hormone	n= 7,654	-	n=8,104	-
Mean Age –yrs (SD)	58.9 (±17.6)	-	57.3 (±18.1)	-
Female – n (%)	5,946 (77.7)	-	6,095 (75.2)	-
Medication use at baseline – n (%)				
Aspirin	267 (3.5)	-	1,049 (12.9)	-
Lipid lowering medicines	1,357 (17.7)	-	1,592(19.6)	-
Blood pressure lowering medicines	1,638 (21.4)	-	1,869(23.1)	-
Oral diabetes medicines	267(3.5)	-	343(4.2)	-
Insulin	95(1.2)	-	106(1.3)	-
Anti-depressant medicines	n=39,432	-	n=45,220	-
Mean Age –yrs (SD)	52.8 (±19.8)	-	50.2 (±19.7)	-
Female – n (%)	25,945 (65.8)	-	28,842 (63.8)	-
Medication use at baseline – n (%)				
Aspirin	6291 (16.0)	-	6,144 (13.6)	-
Lipid lowering medicines	7,715 (19.6)	-	8,598 (13.6)	-
Blood pressure lowering medicines	9,816 (24.9)	-	10,707 (23.7)	-
Oral diabetes medicines	1,574 (4.0)	-	1,878 (4.2)	-
Insulin	433 (1.1)	-	523 (1.2)	-

Values missing for thyroid hormone and anti-depressant medicines in the LTI column because these drugs are typically not covered on the LTI scheme

Table 2 Baseline characteristics of new users of less-essential medicines for the €0.50 copayment and the €1.50 copayment

	€0.50	**€1.50**
	GMS	**GMS**
PPIs/H_2 receptor antagonists	n=74,986	n=88,917
Mean Age –yrs (SD)	56.2 (±19.1)	52.8 (±19.6)
Female – n (%)	43,979 (58.6)	51,836 (58.3)
Medication use at baseline – n (%)		
Aspirin	14,289 (17.8)	13,027 (14.7)
Lipid lowering medicines	17,602 (21.9)	18,562 (20.9)
Blood pressure lowering medicines	22,874(28.5)	23,181 (26.1)
Oral diabetes medicines	3,510 (4.4)	3,952 (2.6)
Insulin	829 (1.0)	912 (1.0)
NSAIDs	n=136,111	n=132,589
Mean Age -yrs (SD)	53 (±19.5)	50.5 (±19)
Female –n (%)	82,565 (60.7)	79,747 (60.1)
Medication use at baseline –no. (%)		
Aspirin	26,152 (19.2)	21,117 (15.9)
Lipid lowering medicines	33,208 (24.4)	30,110 (22.7)
Blood pressure lowering medicines	41,320 (30.4)	35,902 (27.1)
Oral diabetes medicines	6,690 (4.9)	6,494 (4.9)
Insulin	1,554 (1.1)	1,484 (1.1)
Anxiolytics/Hypnotics	n=64,462	n=73,665
Mean Age -yrs (SD)	55 (±19.1)	53yrs (±19.1)
Female –n (%)	40,824 (63.3)	45,975 (62.4)
Medication use at baseline –n (%)		
Aspirin	11,700 (18.2)	12,037 (16.3)
Lipid lowering medicines	14,845 (23.0)	17,294 (23.5)
Blood pressure lowering medicines	18,729 (29.1)	21,049 (28.6)
Oral diabetes medicines	2,775 (4.3)	3,465 (4.7)
Insulin	685 (1.1)	853 (1.2)

NSAIDs : Non-steroidal anti-inflammatory drugs
PPIs/H2: Proton Pump Inhibitors/H2 antagonists

Table 3 **Impact of €0.50 copayment introduction on adherence**

	Short term % change in adherence (95% CI)			**Long term % change in adherence (per month) (95% CI)**		
	GMS	LTI	DIFF	GMS	LTI	DIFF
Essential medicines						
Blood pressure lowering medicines	-5.0 (-6.8 to -3.4)	-0.2 (-1.1 to 0.6)	-4.8 (-5.7 to -4.0)	-0.5 (-0.9 to -0.1)	-0.9 (-1.2 to -0.7)	0.5 (0.3 to 0.6)
Lipid lowering medicines	-4.7 (-6.5 to -2.9)	-1.7 (-2.6 to -0.8)	-3.0 (-3.9 to -2.1)	-1.2 (-1.5 to -0.7)	-1.1 (-1.3 to -0.8)	-0.1 (-0.2 to 0.1)
Oral diabetes medicines	-4.0 (-6.0 to -1.9)	-1.6 (-2.5 to -0.6)	-2.4 (-3.5 to -1.3)	-0.5 (-0.9 to 0.2)	-0.9 (-1.3 to -0.5)	0.4 (0.3 to 0.8)
Thyroid hormone	-2.1(-2.8 to -1.5)	-	-	-0.4 (-0.8 to -0.1)	-	-
Anti-depressant medicines	-8.3(-8.7 to -7.9)	-	-	-0.8 (-1.1 to -0.5)	-	-
Less-essential medicines						
PPIs/H_2 antagonists	-9.5 (-9.8 to -9.1)	-	-	-0.5 (-0.9 to -0.3)	-	-
NSAIDs	-5.7 (-5.9 to - 5.5)	-	-	0.4 (0.1 to 0.7)	-	-
Anxiolytics/Hypnotics	-2.0 (-2.3 to -1.7)	-	-	-0.2 (-0.5 to 0.01)	-	-
Impact of €1.50 copayment introduction on adherence						
Essential medicines						
Blood pressure lowering medicines	-5.3 (-7.1 to -3.5)	-0.9 (-1.8 to 0.01)	-4.4 (-5.3 to -3.5)	-1.2 (-1.6 to -0.6)	-1.4 (-1.7 to -1.0)	0.2 (0.04 to 0.4)
Lipid lowering medicines	-4.7 (-6.8 to -2.6)	-3.5 (-4.5 to -2.5)	-1.2 (-2.3 to -0.1)	-1.6 (-2.1 to -1.0)	-1.7 (-2.0 to -1.3)	0.1 (-0.1 to 0.3)
Oral diabetes medicines	-4.9(-7.2 to -2.7)	-5.2 (-6.3 to -4.2)	0.3 (-0.9 to 1.5)	-1.8 (-2.3 to -1.6)	-1.9 (-2.1 to -1.7)	0.1 (-0.2 to 0.1)
Thyroid hormone	-0.7 (-1.4 to -0.1)	-	-	-1.0 (-1.3 to -0.5)	-	-
Anti-depressant medicines	-10.0 (-10.4 to -9.6)	-	-	-1.5 (-1.8 to -1.2)	-	-
Less-essential medicines						
PPIs/H_2 antagonists	-13.5 (-13.9 to -13.2)	-	-	-1.2 (-1.5 to -0.9)	-	-
NSAIDs	-8.9 (-9.2 to -8.7)	-	-	-1.4 (-1.6 to -1.1)	-	-
Anxiolytics/Hypnotics	-0.8 (-1.0 to -0.5)	-	-	-0.2 (-0.6 to 0.1)	-	-

NSAIDs : Non-steroidal anti-inflammatory drugs
PPIs/H2: Proton Pump Inhibitors/H2 antagonists
Values missing for thyroid hormone, anti-depressant medications and all less-essential medicines because these drugs are typically not covered on the LTI scheme.

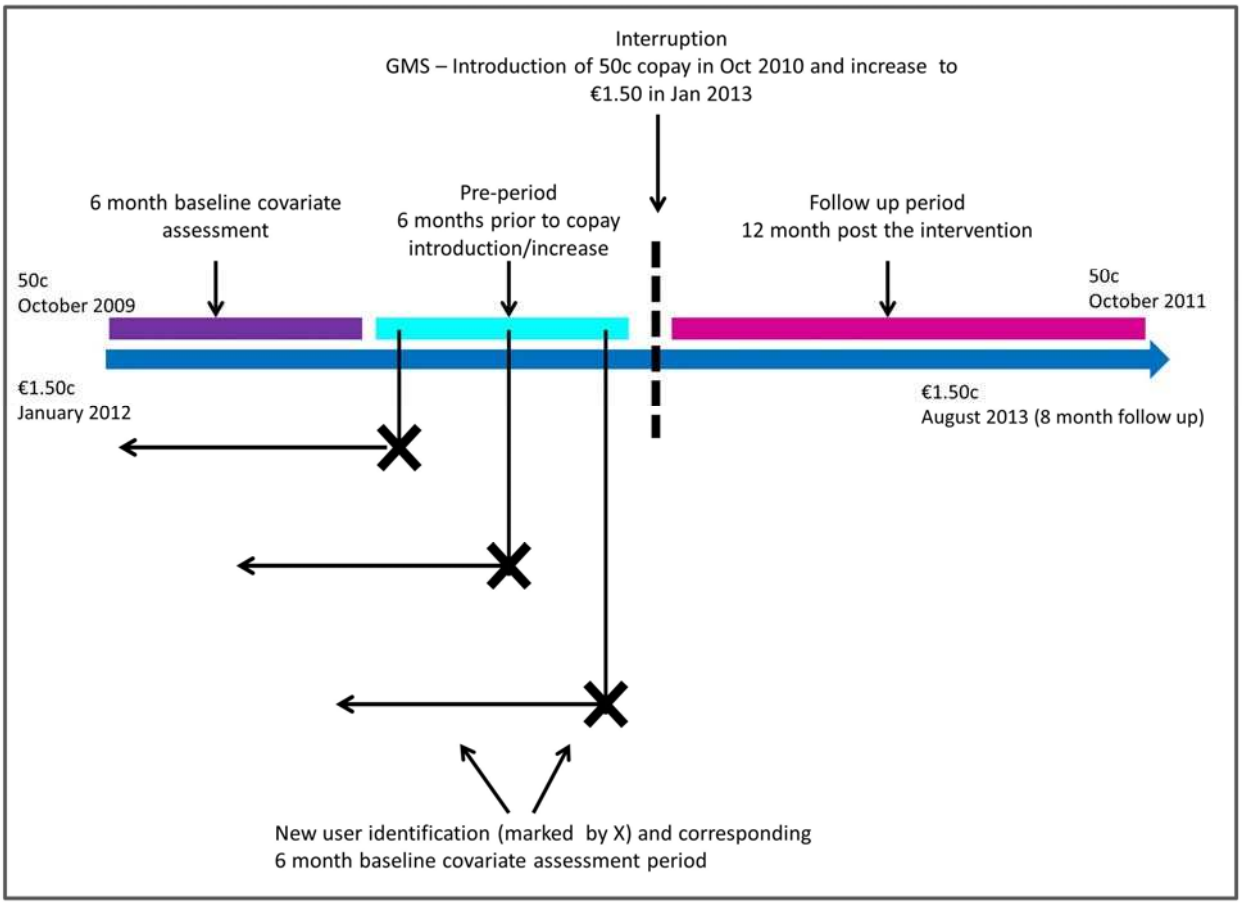

Figure 1: Demonstration of new user identification, cohort entry and follow up for 50c and €1.50 policy interventions

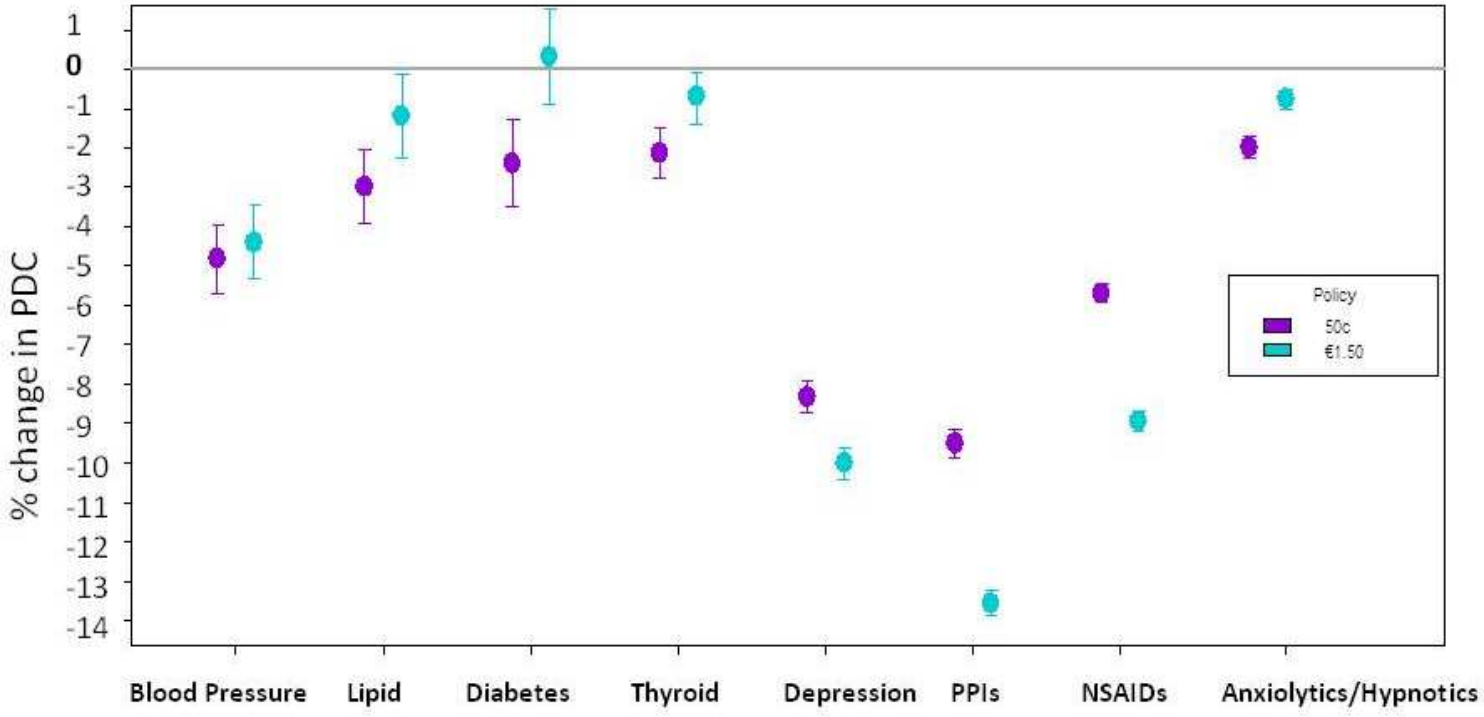

Figure 2: Results for the short term effects of 50c and €1.50 copayment policies plotted for each medication group.

Results plotted for blood pressure lowering,lipid lowering and oral diabetes medications are relative differences. Results plotted for remaining medication groups are absolute differences in adherence observed in the GMS group.

NSAIDs – Non-steroidal anti-inflammatory drugs.

PPIs/H2 – Proton Pump Inhibitors/H2 antagonists