

Supplementary table 1. Details of demand side measures among the European countries.

Country	Measures among selected European countries to increase prescribing efficiency including generic PPIs and statins	Ref.
AT (Austria)	<p>Education</p> <ul style="list-style-type: none"> Quarterly publications sent by health insurance companies to physicians highlighting the cheapest branded generic currently available Guidelines issued annually and actively disseminated to all key stakeholder groups New IT systems available to physicians highlighting the cheapest generics currently available <p>Economics</p> <ul style="list-style-type: none"> Benchmarking physician prescribing costs with reprimands for excessive costs potentially leading to loss of income Direct financial incentives from increased prescribing of generics where seen as standard therapy <p>Enforcement – Statins only</p> <ul style="list-style-type: none"> Prescribing of atorvastatin and rosuvastatin restricted after the availability of generic simvastatin Physicians need the permission of the Chief Medical Officer of the patient's health insurance company for the patient to have atorvastatin and rosuvastatin reimbursed (failure to reach target lipid levels with generic simvastatin); otherwise 100% co-payment 	[4,58,70]
DE (Germany)	<p>National Level</p> <p>Education</p> <ul style="list-style-type: none"> Guidelines and prescribing guidance from both the Sickness Funds and Physician Associations. Therapeutic guidance and given by the federal joint committee (GBA) between the Sickness Funds and the Physician Association (KBV) Monitoring of prescribing coupled with academic detailing, financial penalties if targets are not met <p>Quality Circles</p> <p>Web-based training</p> <p>Engineering</p> <ul style="list-style-type: none"> Disease Management programmes Prescribing targets (linked with penalties – below) Contracts between pharmaceutical companies and individual Sickness Fund for specific products <p>Economics</p> <ul style="list-style-type: none"> Physician budgets based on benchmarking with colleagues and predetermined budgets based on contracts between the Sickness Funds and the Physicians' Associations (individual KVs) Financial penalties for excessive prescribing/ financial targets not met Patient co-payment for higher cost products than the reference product (molecule as well as the class for PPIs and statins in 2003) <p>Enforcement</p> <ul style="list-style-type: none"> Delisting of products from normal reimbursement list (atorvastatin in 2003) <p>Regional/ State Level (e.g. Hessen)</p> <p>Education</p> <ul style="list-style-type: none"> Local web based training and other initiatives orchestrated by the State Physician Association <p>Engineering</p> <ul style="list-style-type: none"> Prescribing targets. These include generics > 87.4 % of all prescriptions (simvastatin currently 90.6% of all statin prescriptions in Hessen), ezetimibe <3.2% of all lipid lowering drug prescriptions and me-too drugs at < 4.4 % of all prescriptions 	[24,26,53,71-77]

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EE (Estonia)	<p>Education</p> <p>Health Insurance Fund provides information to physicians to enhance their prescribing efficiency where concerns</p> <p>Engineering</p> <p>Price: volume agreements - obligatory for all reimbursed pharmaceuticals else 100% co-pay</p> <p>Pharmaceutical companies are required to state the rationale behind their requests with the Ministry not reimbursing if they feel suggested prices are too high</p> <p>If agreed volumes are exceeded, negotiations take place to determine the rationale and subsequent activities, which could include lowering reimbursed prices</p> <p>Economics</p> <p>Patients required to pay an additional co-payment for a more expensive product than the current referenced price product (molecule – ATC Level 5)</p> <p>In addition, statins – 75% to 90% reimbursed , rosuvastatin 50% reimbursed. PPIs – 50% reimbursed</p> <p>Enforcement</p> <p>Physicians are obliged to prescribe by INN name, and only use the brand (originator) name where medically necessary. Prescriptions are monitored</p> <p>Statins only reimbursed in patients with familial hypercholesterolaemia (total cholesterol >8mmol/l) or following a CV event (total cholesterol >4.5mmol/l)</p>	[77]
ES/ Catalonia (Spain)	<p>Education</p> <p>Benchmarking PHC (Primary Healthcare Centre) physician prescribing</p> <p>Academic detailing to enhance the prescribing of generics first line where seen as standard</p> <p>Production and dissemination of multidisciplinary guidelines on primary healthcare problems including hypercholesterolaemia, hypertension, diabetes, cardiac insufficiency and dyspepsia</p> <p>Production and dissemination of drug information bulletins</p> <p>Pharmacists and clinical pharmacologists providing information on therapeutics to PHC physicians to improve the quality and efficiency of their prescribing</p> <p>Educational courses on primary healthcare problems</p> <p>Engineering</p> <p>Indicators (Catalan Health Service or Primary Healthcare Centres and hospitals) include:</p> <ul style="list-style-type: none"> % generic utilisation % of new drugs prescribed that have limited value % of oral antidiabetic prescriptions as metformin % of prescriptions for renin-angiotensin drugs as ACE inhibitors, % simvastatin vs. all statins, % omeprazole vs. all PPIs and % alendronate vs. all bisphosphonates <p>Economics</p> <p>Drug budgets devolved to Primary Healthcare Centres with financial incentives as well as penalties for over budget situations</p> <p>Financial incentives in Catalonia were up to €0000/ physician in 2007 (up to 15% of their salary) with prescribing indicators accounting for 27% of the overall indicators used</p> <p>Enforcement</p> <p>Since 2007, it is mandatory for pharmacist to dispense the cheapest product if the prescribed product is more expensive than the current reference priced product</p> <p>If the drug prescribed is priced above the current reference price or when prescribed by INN name, the pharmacist must dispense the lowest priced molecule, which is usually a generic. This must be generic if the same price as the drug prescribed. In addition, no opportunity for patients to cover any additional costs for an originator themselves.</p>	[10]

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FR (France)	<p>Education Health insurance companies benchmarking GPs with their colleagues and providing continuous feedback on generic prescribing rates; however to date no incentives or sanctions influencing prescribing (this is changing – CAPI scheme below) Government promotional campaigns as well as targeted campaigns to enhance the acceptance of generics and INN prescribing among patients with INN prescribing allowed since 2001. Targeted campaigns aimed at increasing generic dispensing among patients not requesting generics when available Health insurance companies promoting generics on the back of reimbursement forms sent to patients</p> <p>Engineering Introduction of CAPI (Contrats d'amélioration des pratiques individuelles) in 2009 to improve prevention, consolidate the quality of care for patients with chronic diseases and optimise efficient prescribing. This includes prescribing targets/ goals for selected disease and therapeutic areas including antibacterials, PPIs, statins, antihypertensives, benzodiazepines, antidepressants, anticoagulants as well as drugs for breast cancer and diabetes. Currently only applies to a minority of GPs Targets established for generic substitution rates among community pharmacists Price: volume agreements for existing drugs with pay back mechanisms for over budget expenditure</p> <p>Economics Ambulatory care physicians agreed to prescribe by INN name in return for higher fees (initial target - 25% of all prescriptions). This is increasingly becoming obligatory in most situations GPs receive additional payment for improving care against agreed standards - CAPI targets (introduced in 2009). The system is voluntary with financial incentives for GPs to attain agreed target – up to €000/ GP (no penalties for failing); it is envisaged the CAPI scheme will be cost neutral Patients pay a higher co-payment for a more expensive product than the referenced priced molecule. Alongside this in 2006 there was an agreement with pharmacists whereby patients who refuse generic substitution will have to pay the full price of their prescription Patients pay up to 35% co-payment for PPIs and statins (0% if part of agreed long term illness); overall approximately 20% co-payment. This is typically covered by additional insurance taken out by patients Pharmacists also receive a fixed fee per prescription item dispensed combined with a regressive mark-up. In addition, guaranteed the same absolute margin whether they dispense generics or originator medicines. Since January 2008, community pharmacists receive a discount of 17% for generics and branded products with similar prices; the maximum discount for patent-protected products being 2.5%</p> <p>Enforcement Pharmacists can substitute if the generic drug is less expensive than the originator</p>	[2,77]

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GB - Eng (England)	<p>Education</p> <p>Physicians typically trained in medical school to prescribe by INN name with follow up in the community coupled with IT systems. Follow up includes decision support software as well as the prescribing of generics seen as good-quality prescribing. This has resulted in current average INN prescribing of 83% across all products rising to over 99.5% in certain cases once generics are available, e.g. generic simvastatin</p> <p>National guidance and guidelines, practice based formularies, benchmarking and academic detailing</p> <p>Engineering</p> <p>'Better Care Better Value' indicators to enhance the prescribing of low cost statins and PPIs versus single sourced statins and PPIs and statins</p> <p>Active generic switch programmes as well as active therapeutic switch programmes, and decision support software</p> <p>Economics</p> <p>Devolved budgets to PCT (Primary Care Trusts) alongside PCT Commissioning and Practice Based Commissioning (PBC)</p> <p>Practice based financial incentives</p> <p>Payment by results</p>	[20,21,24,101,115]
GB – Scot (Scotland)	<p>Similar to England for Education and Engineering</p> <p>However in Scotland:</p> <p>Budgets lie with the Health Boards with drug budgets established for health centres (mechanism not uniform across Health Boards. The same applies to high cost drugs) but not devolved to them (unlike England)</p> <p>Consequently, GPs are responsible for their drug budgets but not accountable</p> <p>Financial incentives in place to encourage appropriate prescribing</p>	–
HR (Croatia)	<p>Education</p> <p>National formulary providing prescribing guidance</p> <p>Limited number of treatment guidelines – though not enforced</p> <p>Engineering</p> <p>Price: volume agreements – applies to new drugs (currently not for statins and PPIs)</p> <p>Economics</p> <p>Co-payments for the statins and PPIs, e.g. for the statins:</p> <p>Since 2003 – 25% co-payment for secondary prevention in patients with ischaemic heart disease or cerebrovascular disease and with patients with diabetes with a TC > 5mmol/l; 75% for patients for primary prevention if 10year chance of CHD >20% or above 60 years of age. No reimbursement if initiation undertaken in patients above 70 years of age</p> <p>2006 – similar to 2003 for secondary prevention, primary prevention includes TC >7mmol/l after 3 months diet</p> <p>2007 – no co-payment for patients meeting criteria for primary and secondary prevention;</p> <p>co-payment if patients' wish a more expensive drug than the current referenced priced product</p> <p>For the PPIs</p> <p>50% co-payment but only in patients where H2 blockers no longer working for oesophageal reflux, Zollinger Elisonov syndrome or eradication of <i>helicobacter pylori</i></p> <p>Differential co-payments for different molecules versus the current reference standard</p> <p>Enforcement</p> <p>Access to patient history to check criteria for reimbursement, e.g. statins and PPIs</p>	–
IE (Republic of Ireland)	<p>Education</p> <p>Published guidelines – however not enforced</p> <p>Overall, currently no incentives or sanctions encouraging GPs to prescribe generic drugs rather than originators or single sourced products in a class. This is likely to change with the planned introduction of reference pricing for the molecule in 2011</p>	[12]

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IT (Italy)	<p>Education</p> <p>National and regional guidelines and formularies, academic detailing and monitoring physician prescribing. However, there has been significant variability regarding activities amongst the Regions</p> <p>Local projects among the Regions/ localities to enhance prescribing in prevalent disease areas including CV diseases through educational input</p> <p>Engineering</p> <p>Ambulatory care prescribing costs capped by law with pay back mechanisms for excessive costs</p> <p>Economics</p> <p>Financial incentives for GPs to follow agreed guidance/ guidelines (Region/ locality dependant)</p> <p>Patients pay an additional co-payment for a more expensive product than the referenced price molecule</p> <p>Enforcement</p> <p>Prescribing restrictions instigated nationally by the reimbursement agency (AIFA Notes) where concerns with the value of products in all potential populations, e.g. statins only reimbursed for secondary and not primary prevention, with sanctions for abuse</p>	I[6,24,77-79]
LT (Lithuania)	<p>Education</p> <p>Some guidelines in place to encourage the rational use of medicines. However, not obligatory</p> <p>Audits undertaken where the State Patient Fund expects excessive prescribing costs. Sanctions can include refunds where excessive prescribing costs</p> <p>Economics</p> <p>Patients pay an additional co-payment for a more expensive product (molecule – ATC Level 5) than the current reference price. In addition, since 2010 obligation by pharmacists to display prices in pharmacies and stock the cheapest generic</p> <p>At least 50% co-payment for the PPIs for majority of indications, lower co-payment for the statins – 20%. However, statins only reimbursed for secondary prevention and only for 6 months</p> <p>Engineering</p> <p>Since 1 July 2004, physicians should prescribe by INN name unless concerns with issues such as the bioavailability and side-effects with the generic</p> <p>Many physicians though still prescribed by originator name as there have been limited sanctions to date and pharmaceutical companies continue to market their brands (originators) to physicians, as well as help alleviate additional co-payments via discounts to community pharmacies</p> <p>However in 2010, compulsory INN prescribing apart from biologicals unless prior permission obtained from the hospital or Polyclinic Therapeutic Committee</p> <p>Price: volume agreements – applies to new drugs (not currently PPIs and statins)</p> <p>Enforcement</p> <p>Prescriptions are monitored to make sure physicians comply with reimbursement restrictions, e.g. statins</p>	[77]

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NO (Norway)	<p>Education</p> <p>There are some guidelines in Norway – but these are not enforced. In addition, no incentives or sanctions influencing prescribing</p> <p>Enforcement (statins initially in 2005 and esomeprazole in February 2007)</p> <p>The Norwegian Medicine's Agency (NOMA) instigated prescribing restrictions by law ('preferred product status') from 2004 rather than reference pricing in a class or related classes to conserve resources</p> <p>The first 'preferred group' introduced in March 2004 was the thiazides as the first line treatment for essential hypertension in naïve patients</p> <p>In June 2005, prescribing restrictions were introduced for certain statins with the new regulation stating that all new patients treated for hypercholesterolemia should be prescribed simvastatin and all current statin users switched to simvastatin where possible within one year. Prescribing of other statins was permitted but only on good medical grounds, with physicians clearly stating the rationale with the potential for spot checks where abuse was suspected</p> <p>Esomeprazole was restricted from February 2007 due to its high acquisition costs versus other PPIs and no major demonstrable differences in therapeutic effect. Under this scheme, lansoprazole, omeprazole and pantoprazole should be prescribed first line as the 'preferred products' unless there is a good medical rationale. However in Norway, specialists have to verify the diagnosis and recommend therapy before PPIs are reimbursed</p> <p>Overall impact</p> <p>One year after implementation, simvastatin was prescribed in 92% of all new users with 39% of atorvastatin users switched to simvastatin</p>	[80,116]
PO (Poland)	<p>Education</p> <p>There are currently limited demand side measures in Poland including physician education; however, this is variable amongst the Regions</p> <p>Economics</p> <p>There is reference pricing for the class (therapeutic – ATC level 3, and Pharmacologic – ATC level 4) along with the molecule (ATC Level 5) with patients paying an additional co-payment for a more expensive product than the current reference price for the molecule or class</p> <p>There are also variable co-payments by disease area/ product in addition to the current co-payment/ package as well as any extra co-payment for a more expensive products. This is currently 30% for both the statins (apart from rosuvastatin which is not reimbursed) and the PPIs (omeprazole, lansoprazole and pantoprazole) with esomeprazole not reimbursed</p> <p>Enforcement</p> <p>Pharmacists are obliged to inform patients about generic products if they have the same active ingredient, same dosage, package and route of administration as the prescribed product but cheaper unless substitution is forbidden by the physician</p>	[81]

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PT (Portugal)	<p>Education Treatment guidelines (although not mandatory) alongside pharmacy educational programmes Information campaigns to patients and healthcare professionals promoting the quality of generics and their impact with controlling pharmaceutical expenditure. Patient campaigns via TV, radio, leaflets in hospitals, healthcare centres and pharmacies as well as bill boards and the internet Physicians updated every quarter by INFARMED (Portuguese Medicines Agency) of available generics (Pharmaceuticals Generics Guide and Reference Price Guide); also available electronically Currently though no incentives or sanctions for physicians to prescribe generic drugs with hardly any monitoring of physician prescribing behaviour</p> <p>Economics Reference Price System (RPS) introduced in 2002 defining a fixed amount paid by the National Health Service (NHS) for the molecule (homogeneous group) with patients required to fund the difference for a more expensive product In June 2009 new legislation was approved reimbursing generics 100% for pensioners whose income is below the national minimum wage; subsequently withdrawn. In June 2010, new legislation was approved reimbursing 100% only the 5 cheapest generics in a homogeneous group for pensioners whose income is below the national average</p> <p>Engineering Price: volume agreements between the Portuguese Pharmaceutical Industry (APIFARMA) and the Ministry of Health Enforcement Since 2002, obligation by physicians to prescribe by INN name for medicines with approved generics; however physicians can prohibit substitution where concerns Since 2002, pharmacists are allowed to substitute generics (where physicians prescribe INN name and do not prohibit substitution), and should inform patients about the prices of generics. There is though currently no financial incentives by law to encourage pharmacists to preferentially dispense generics</p>	[77,101]
RS (Republic of Serbia)	<p>Economics Patients required to pay an additional co-pay for a more expensive product than the reference price for the molecule (same INN name – ATC Level 5) The availability of generics has been enhanced by less aggressive patent laws similar to the situation in Poland (above)</p> <p>Enforcement Prior authorisation scheme for selected premium priced drugs based on step therapy approaches</p>	–
SE (Sweden)	<p>Education Guidance and guidelines including the Wise Drug List in Stockholm County Council Benchmarking of prescribing coupled with continuous feedback Computerised decision support tools to enhance the quality and efficiency of prescribing Mandatory to have at least one DTC in each County enhancing the rational use of drugs</p> <p>Engineering Structured programmes for the introduction of new drugs (Region dependant) Prescribing targets to enhance the prescribing of generics first line where standard such as generic omeprazole versus all PPIs and generic simvastatin versus all statins</p> <p>Economics Financial incentives to GPs for achieving agreed prescribing targets Devolved drug budgets with the opportunities for savings for achieving targets Patient co-payment for more expensive brands than the reference price for the molecule</p> <p>Enforcement National prescribing restrictions on new and existing drugs where concerns with their value in all or some populations. This includes ARBs, rosuvastatin and atorvastatin Compulsory generic substitution with the cheapest available product for the molecule - enhanced by the introduction of technical support systems enabling pharmacists to continually stock the cheapest product Physicians can indicate 'no substitution' although this is rare in practice. In addition, the Medicines Product Agency indicates to physicians and pharmacists which products are not substitutable</p>	[3,9,26,61,62,108]

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SI (Slovenia)	<p>Education The Health Insurance Institute organises regular therapeutic meetings for physicians to enhance the quality of their prescribing Audits and benchmarking of prescribing habits among ambulatory care physicians</p> <p>Economics Financial penalties for physicians linked with inappropriate prescribing ascertained via prescribing audits Additional co-payments for patients for more expensive compounds than the reference molecule</p> <p>Enforcement Prescribing restrictions for certain drugs</p>	–
TR (Turkey)	<p>Education Limited activities to date. This will grow with the instigation of a family physician system (some pilots are currently in operation)</p> <p>Enforcement There are some restrictions for prescribing ; however not currently for either the PPIs or statins</p>	–

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