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Investing in medication adherence improves health outcomes and health system efficiency: Adherence to medicines for diabetes, hypertension, and hyperlipidaemia

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INVESTING IN MEDICATION ADHERENCE IMPROVES HEALTH OUTCOMES AND HEALTH SYSTEM EFFICIENCY

Adherence to medicines for diabetes, hypertension, and hyperlipidaemia

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Executive Summary

Despite mounting evidence, amassed for more than four decades, poor adherence to medications still affects approximately half of the population that receives prescriptions, leading to severe health complications, premature deaths, and an increased use of healthcare services.

- Poor adherence is estimated to contribute to nearly 200 000 premature deaths in Europe per year. Patients with chronic diseases are particularly vulnerable to poor health outcomes if they do not adhere to their medications. Mortality rates for patients with diabetes and heart disease who don't adhere are nearly twice as high as for those who do adhere.
- It is estimated to cost EUR 125 billion in Europe and USD 105 billion in the United States per year in avoidable hospitalisations, emergency care, and outpatient visits.
- The three most prevalent chronic conditions diabetes, hypertension, and hyperlipidaemia stand out as the diseases with the highest avoidable costs, for which every extra USD spent on medications for patients who do adhere can generate between USD 3 to 13 in savings on avoidable emergency department visits and inpatient hospitalisations alone.

The prevalence of medication non-adherence varies considerably across conditions and patient groups. Most of the studies used different assessment methods making it difficult to compare adherence rates across health systems. Overall, among patients with diabetes, hypertension, and hyperlipidaemia:

- 4 to 31% of patients never fill their first prescription;
- of those who do fill their first prescription, only 50 to 70% are taking their medications regularly (i.e. at least 80% of the time); and
- less than half of these patients are still continuing to take their medications within two years of the initial prescription.

There are three broad reasons behind these low adherence rates to chronic disease medications:

- Firstly, poor awareness among all stakeholders. The problem of poor adherence to medication has generally been overlooked and rarely explicitly included in national health policy agendas. Consequently, few OECD countries routinely measure rates of adherence to medication. Even fewer use those measurements to systematically incentivise improvements in adherence and health outcomes. Health professionals physicians, nurses, and pharmacists underestimate the incidence of the problem in their patients. There is a dearth of evidence on cost effective interventions that improve adherence at a system level.
- Secondly, wrong targets for interventions and poor incentives. Discussions of non-adherence tend to attribute the problem exclusively to the individual patient, while the evidence suggests that health system characteristics in particular the quality of patient-provider interaction, cumbersome procedures for refilling prescriptions, or out-of-pocket costs of medications are lead drivers. Most interventions tackling poor adherence have focused on patients, particularly their forgetfulness and incorrect beliefs about medications, rather than taking a systems

level approach by understanding and changing the context in which healthcare is provided.

• Thirdly, lack of patient involvement. Patients with chronic conditions frequently feel that the decision about their therapy did not involve them and are inclined to rebuff it or lack motivation to follow the therapy consistently. From a patient perspective, a chronic condition poses not only health problems but also long-term personal and social challenges. Yet, the current disease focused, as opposed to person-centred approach to healthcare delivery leaves little or no room for consideration of the personal aspects of a patient's condition.

This paper identifies four enablers that are needed for improving adherence to medication at the system level: Acknowledge, Inform, Incentivise, and Steer and Support. No single intervention will guarantee that patients fill their prescriptions and take their medications as prescribed. The identified actions must be combined.

- Acknowledge: Medication non-adherence harms health and increases healthcare costs. The first step for the relevant stakeholders is to acknowledge that this problem exists and to adequately recognise its main drivers. Medication adherence needs to move up the policy agenda in order to raise awareness of the problem and mobilise adequate responses.
- **Inform: Few countries systematically monitor adherence.** Routine adherence measures as well as adherence-related quality and performance indicators should be encouraged in order to improve health system effectiveness and efficiency. The OECD can take stewardship in developing these indicators as part of the work on Healthcare Quality and Outcomes.
- Incentivise: Changes in financial incentives for providers and patients are essential. Shifting to payment systems that reward providers for the quality of patient outcomes would provide strong motivation to improve adherence. Medication adherence could also be considered as a measure for performance-based contracts with pharmaceutical companies. Where patients' co-payments for chronic medications exist, their reduction or removal should be considered to reduce financial barriers.
- Steer and Support: The adherence process begins with a patient and a prescribing clinician and a dispensing pharmacist who should all be supported by other health system stakeholders. Payers/system designers can develop IT systems that facilitate optimal prescribing and patient-clinician communication or renewing prescriptions by patients. Educators have a role in equipping health professionals with skills in managing adherence such as persondecision-making, centred communication, shared and socio-cultural competencies. Professional bodies can issue guidelines on how to personalise medication plans and decision aids facilitating shared patient-provider decisionmaking. Industry can contribute with solutions such as, for example, simplified medication regimens or packaging. There is also a scope for multi-partner initiatives to improve patients' health literacy.

Résumé

Malgré les preuves accumulées depuis plus de quatre décennies, aujourd'hui encore la moitié environ des personnes auxquelles on a prescrit des médicaments délivrés sur ordonnance suit mal son traitement, or ce manque d'observance est responsable de graves complications, de décès prématurés et de sollicitations plus nombreuses pour les services de santé :

- Le défaut d'observance thérapeutique serait la cause de 200 000 décès prématurés chaque année en Europe. Les personnes atteintes par l'une des principales maladies chroniques, en particulier, courent de sérieux risques à ne pas prendre correctement leurs médicaments. Chez les diabétiques et les personnes atteintes de cardiopathie, les patients qui négligent ainsi leur traitement connaissent une mortalité pratiquement deux fois supérieure à celle des patients qui s'y tiennent avec rigueur.
- On estime que le coût des hospitalisations, admissions aux urgences et consultations externes évitables s'élève chaque année à 125 milliards EUR en Europe et 105 milliards USD aux États-Unis.
- Les trois maladies chroniques les plus courantes à savoir le diabète, l'hypertension et l'hyperlipidémie – sont aussi celles avec les coûts évitables les plus élevés : chaque dollar supplémentaire dépensé en médicaments pour les patients attentifs à bien suivre les prescriptions qui leur ont été données génère entre 3 et 13 USD d'économies rien qu'en hospitalisations d'urgence et consultations externes épargnées.

La non-observance est un phénomène dont l'ampleur varie considérablement selon la maladie et la catégorie de patients considérées. Malheureusement, la plupart des études sur le sujet reposent sur des mesures indirectes obtenues par l'application de méthodes différentes, de sorte que la comparaison des taux d'observance entre les systèmes de santé s'avère malaisée. Dans l'ensemble, en ce qui concerne le diabète, l'hypertension ou l'hyperlipidémie :

- entre 4 et 31 % des malades ne se font pas délivrer les médicaments prescrits sur leur ordonnance initiale ;
- de ceux qui se font délivrer ces médicaments, seuls 50 à 70 % les prennent de manière régulière (c'est-à-dire au moins 80 % du temps) ; et
- moins de la moitié d'entre eux suit encore son traitement deux ans après l'ordonnance initiale.

Il y a trois grandes raisons au faible taux d'observance thérapeutique chez les malades chroniques :

• Premièrement, le manque de sensibilisation. Le problème du manque d'observance thérapeutique est en règle générale négligé et rarement visé en tant que tel par les programmes nationaux de santé publique. Par suite, peu de pays de l'OCDE mesurent régulièrement les taux d'observance, et bien moins encore récompensent systématiquement, sur la foi des relevés effectués, les progrès accomplis en matière d'observance et de santé. Qui plus est, des enquêtes auprès des professionnels de santé – médecins généralistes, personnel infirmier et pharmaciens – révèlent de leur part une tendance à sous-estimer le problème parmi leurs patients. Quant aux recherches censées montrer comment améliorer l'observance, elles sont lacunaires.

- Deuxièmement, des interventions qui se trompent de cible et des incitations insuffisantes. S'agissant de l'inobservance thérapeutique, on a tendance à imputer exclusivement au patient un problème qui semble pourtant tenir d'abord aux caractéristiques des systèmes de santé notamment à la qualité du rapport patient-soignant, à la lourdeur des procédures de renouvellement d'ordonnance ou au niveau de participation du patient au coût des médicaments. Les interventions menées contre le défaut d'observance sont dirigées pour la plupart vers le patient, cherchant en particulier à combattre ses oublis de traitements et rectifier certaines idées au sujet des médicaments, alors qu'il faudrait s'employer à comprendre et modifier le contexte de soin.
- Troisièmement, le manque d'implication des patients. Les patients atteints d'une maladie chronique ont souvent le sentiment que la mise en place de leur traitement a été décidée sans eux, un sentiment qui peut les amener au rejet de ce traitement ou les priver de la détermination nécessaire pour s'appliquer à le suivre. Si l'on se place du point de vue de ces patients, une maladie chronique ne les confronte pas seulement à des problèmes de santé mais aussi à des difficultés personnelles et sociales durables. Or la démarche de soin telle qu'elle se conçoit actuellement, c'est-à-dire axée sur la pathologie au lieu d'être construite autour du patient, ne laisse pas ou peu de place pour appréhender la maladie avec ses aspects intéressant l'individu.

Le présent document nous montre quatre leviers à actionner pour améliorer l'observance thérapeutique à l'échelle des systèmes de santé, auxquels correspondent quatre maîtresmots : Admettre, Informer, Encourager et Guider et Accompagner. Aucune intervention isolée ne sera à même de garantir que les patients se font délivrer les médicaments prescrits et qu'ils les prennent correctement. Les mesures mises en lumière doivent être appliquées ensemble.

- Admettre : le défaut d'observance thérapeutique est une menace pour la santé et alourdit le coût des soins. Il s'agit en premier lieu que les diverses parties prenantes concernées reconnaissent l'existence du problème et en perçoivent bien les principaux ressorts. L'observance thérapeutique doit remontrer dans l'ordre des priorités publiques afin que l'opinion soit rendue plus sensible à ce sujet et que des solutions adaptées soit mises en œuvre.
- Informer : peu de pays procèdent à un suivi systématique de l'observance. Les mesures régulières et les indicateurs de qualité et de performance sont en ce domaine à encourager pour des systèmes de santé plus efficaces et plus efficients. L'OCDE peut prendre les rênes du développement d'indicateurs dans le cadre de ses travaux sur la qualité et les résultats des soins de santé.
- Encourager : il est indispensable de faire évoluer les incitations financières offertes aux prestataires et aux patients. L'introduction de systèmes de paiement prévoyant une récompense si la santé des seconds s'améliore ferait de l'amélioration de l'observance un impératif pour les premiers. On pourrait aussi envisager de faire de l'observance thérapeutique un critère d'évaluation dans le cadre des contrats de performance conclus avec les laboratoires pharmaceutiques. La réduction ou la suppression du ticket modérateur applicable aux médicaments seraient à étudier, lorsque ticket modérateur il y a.
- Guider et Accompagner : le processus d'observance commence avec un patient et un médecin prescripteur qui devraient pouvoir compter sur les interventions/outils d'autres parties prenantes du système de santé : payeurs et concepteurs de systèmes peuvent mettre au point des solutions informatiques

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qui aident le médecin à prescrire à son patient le traitement le plus indiqué dans son cas et leur permettent à tous deux de bien se comprendre ou qui facilitent autant que faire se peut les renouvellements d'ordonnance ; il revient aux formateurs de rendre les professionnels de santé aptes à encourager l'observance en leur enseignant notamment la communication centrée sur la personne et le partage de la prise de décisions, en plus de leur faire acquérir des compétences socioculturelles ; les organismes professionnels peuvent quant à eux fournir des guides sur la personnalisation des schémas thérapeutiques et des aides à la prise de décisions partagées entre le patient et le praticien ; l'industrie pharmaceutique, de son côté, apportera son concours à travers, par exemple, une simplification des posologies ou des emballages. Il est possible également d'engager des initiatives multipartites destinées à développer la culture médicale des patients.

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1. INTRODUCTION

1. The irrational use of medicines is a major challenge facing health systems worldwide. The WHO estimates that more than half of all medicines are prescribed, dispensed or sold inappropriately, and that half of all patients fail to take them correctly (WHO, 2004). In 1985, the WHO defined rational use of medicines to represent a situation where "Patients receive medications appropriate to their clinical needs, in doses that meet their own individual requirements, for an adequate period of time, and at the lowest cost to them and their community" (WHO, 1985).

2. The irresponsible use of available medicines involves cases in which no medicine is needed but is prescribed, cases in which the wrong medicines or ineffective or unsafe medicines are prescribed or dispensed, cases in which effective and available medicines are actually not used and those in which medicines are used incorrectly by patients. The focus of this working paper is limited to medication non-adherence as part of a broader responsible use of medicines framework.

3. The purpose of this paper was to review the international evidence on the magnitude of medication non-adherence, analyse its main drivers, and identify actions that healthcare stakeholders can take to address the avoidable costs currently incurred by health systems due to suboptimal medications use. The paper focuses on hypertension, diabetes, and hyperlipidaemia due to the large populations of patients with these conditions using available medication suboptimally by not taking it at all, starting too late, taking it irregularly, or discontinuing it prematurely. This means the beneficial effects of available medications are not fully realised. Suboptimal medication use leads to poor health outcomes and results in additional physician visits, hospitalisations, and ultimately premature deaths.

4. This work represents a synthesis of systematic reviews, meta-analyses, individual empirical journal articles, peer-reviewed reports, and grey literature, predominantly published in the last seven years. Relevant references identified from material included in this review and forward citation tracking have been used to supplement the initial results of the review. In addition, member countries were invited to complete a short questionnaire about policies and current practice. This questionnaire covered topics including monitoring of adherence, research on its prevalence, drivers, and impact on health outcomes as well as healthcare costs; and requested examples of relevant interventions focussed on hypertension, diabetes, and hyperlipidaemia.

5. The remainder of this paper is organised into four sections. Section 2 provides an overview of why it is necessary to invest in medication adherence. Section 3 provides an insight into what is known about the drivers behind medication non-adherence. Section 4 then presents a snapshot of national approaches or interventions that have been implemented in some OECD countries, drawing primarily from the short policy survey and supplemented by actions identified by the authors. Section 5 reflects on these developments and considers the extent to which measures could be more effectively introduced or strengthened.

2. WHAT IS MEDICATION ADHERENCE AND WHY ENCOURAGING IT IS IMPORTANT?

2.1. Poor medication adherence is associated with poor health outcomes and increased healthcare costs

6. Adherence to a medication regimen is "the extent to which patients take their medications as prescribed by their healthcare providers" (Osterberg & Blaschke, 2005). Poor adherence or non-adherence to medications includes patients who do not start their prescribed therapy at all, or discontinue it prematurely, or take their medications in doses or frequencies different from those recommended by the prescribing clinician. In this report the term adherence refers strictly to prescribed medication use.

7. Poor adherence to medications is a lost opportunity in terms of health outcomes and healthcare costs contributing to the inefficiency of health systems. Patients with chronic conditions such as hypertension, diabetes, and hyperlipidaemia are particularly vulnerable to poorer health outcomes if they do not adhere to their medications. For example:

- Mortality rates for patients with diabetes and heart disease who did not adhere are nearly twice as high as for those patients who did (Brown & Bussell, 2011; Cramer, 2004).
- The risk of heart attacks among patients who discontinued their statin therapy (a lipid-lowering medication) is three times higher than among those who continue taking this medication (Maningat et al., 2013).
- Patients who do not adhere to their prescribed beta-blockers, used to manage high blood pressure therapy are 4.5 times more likely to have complications from coronary heart disease than those who do adhere (Cramer et al., 2008).

8. Patients who take their prescribed medications regularly are more likely to enjoy better health outcomes, avoid complications and premature death and use less of emergency care and inpatient hospital services. Medication non-adherence leads to premature deaths as well as an increased use of healthcare services. Estimates suggest 200,000 that it contributes to nearly premature deaths and costs European governments EUR 125 billion annually in excess healthcare services (European Council Policymakers Debate, 2010). In the United States, it costs approximately USD 105 billion per year in terms of avoidable hospitalisations alone (Iuga & Mcguire, 2014; Aitken and Valkowa, 2013; New England Healthcare Institute, 2009). These estimates do not include avoidable costs of long-term care, diagnostic testing and pharmacy costs related to therapy intensification. Broader societal costs of increased disability, reduced productivity, and sick leave are also not considered.

9. Poor adherence leads to an increased use of secondary care services, such as outpatient care, emergency department visits, and hospitalisations, especially among patients with the most prevalent chronic conditions. Roebuck's large observational study of patients with diabetes, hypertension, hyperlipidaemia, or congestive heart failure (n=135,000) in the United States found that for all four conditions, hospitalisation rates were significantly higher for patients with low medication adherence. Higher levels of adherence were found to be associated with significantly lower annual inpatient hospital

days, ranging from 1.2 fewer days per patient for hyperlipidemia to nearly 6 days fewer for congestive heart failure (Roebuck et al., 2011). Other studies have shown that among diabetes patients, the one-year risk of hospitalisation was more than double for patients with low adherence than for patients with high adherence (Jimmy & Jose, 2011). Similarly, hypertension patients with poor adherence have a 1.5 times higher risk of hospitalisation compared to the risk of patients with good adherence (Kneeland & Fang, 2010). In terms of adherence to lipid lowering therapies (statins), the risk of emergency department visits was nearly 30% higher among non-adherent patients relative to adherent ones (Li & Huang, 2015; Gatwood & Bailey, 2014).

10. The increased risk of hospitalisations due to poor health outcomes translates to significant excess costs. Annual healthcare costs are much higher for patients with chronic diseases with poor adherence to medication (Aitken & Valkova, 2013; Osterberg & Blaschke, 2005; Martin et al., 2005). Among diabetes patients, for example, those with low levels of adherence have total annual healthcare costs per patient of USD 16,498, nearly twice the amount of patients with good adherence – USD 8,886 (Sokol et al., 2005). Roebuck's study also found that annual per-person savings due to good adherence amounted to USD 7,823 for congestive heart failure, USD 3,908 for hypertension, USD\$3,756 for diabetes, and USD 1,258 for hyperlipidaemia (Roebuck et al., 2011).

11. Encouraging medication adherence, especially in chronic conditions, has been shown to be cost effective whilst taking into account the increased expenditure on medications. The average cost-benefit ratios from adherence for the four conditions examined was 1:13.5 for hypertension, 1:8.4 for congestive heart failure, 1:8.6 for diabetes, and 1:3.8 for hyperlipidaemia, combining the increases in pharmaceutical spending with the decreases in medical spending. Hence, an extra USD spent on medications for adherent patients with congestive heart failure, high blood pressure, diabetes and hyperlipidaemia can generate between 3 to 13 USD in savings on emergency department visits and inpatient hospitalisations (Roebuck et al., 2011).

2.2. The magnitude of non-adherence is much larger than perceived

12. Measuring adherence might seem quite straightforward at first, but in practice it is far more complex. There are several ways to measure adherence and this, combined with varying definitions, makes it difficult to compare adherence rates across health systems. Overall, 4 to 31% of patients initiated on diabetes or hypercholesterolemia and hypertension medications never fill their first prescription (Blackburn et al., 2013; Shin et al., 2012; Raebel et al., 2012; Karter et al., 2009). For those who do fill the first prescription, only 50 to 70% are taking their medications regularly (i.e. at least 80% of the time) and less than half of these patients are still continuing to take their medications within two years of the initial prescription (Lee et al., 2016; Halava et al., 2016; Karter et al., 2009). The reported adherence rates are highly variable, which may in part be attributable to differences in the populations studied, the medication that patients were taking, and the adherence measures used among the included studies.

13. The general term adherence encompasses several constructs depending on when in a patient's medication journey adherence is being measured. Medication adherence refers to the degree or the extent to which a patient acts in accordance with the prescribed interval and dose of a dosing regimen. Medication persistence refers to the act of continuing the treatment for the prescribed duration. When patients do not fill their first prescription, it is called primary non-adherence to distinguish it from the far more commonly studied secondary non-adherence (when prescriptions are filled, but the medication is not taken as prescribed). Adherence is assessed in two ways, either through self-reported surveys or using administrative claims databases. Each method has its advantages and disadvantages and depends on the research question and availability of data. The most common measures used in studies based on claims databases is the medication-possession ratio (percentage of time a patient has access to medication) whereas for self-reported surveys, the Morisky Medication Adherence scale (self-reported scale for measuring medication-taking behaviour) is used (Lehmann et al., 2014; Clifford et al., 2014).

14. Primary non-adherence poses a problem because timely initiation of medications is critical for treating both acute and chronic conditions. Primary non-adherence has been difficult to assess till the advent of electronic prescribing (e-prescribing). This has greatly enhanced the ability to calculate it. Primary non-adherence rates for the three chronic diseases considered here range from 4 to 31% depending on the patient cohort, healthcare setting, healthcare system, and co-payments. Rates of primary non-adherence for diabetes therapies have been reported between 4 and 31% (similarly for hyperlipidaemia therapies, 5 to 22% and hypertensive therapies, 7 to 28%) (Blackburn et al. 2013; Shin et al. 2012; Thengilsdottir et al, 2015; Raebel et al. 2012; Tamblyn et al, 2014). Most studies rely on claims data and begin tracking adherence when the patient first fills a prescription and are thus in effect measuring the absence of "persistence" as never filling a second prescription. Studies show about 18-34% of patients failed to fill second prescriptions for either their diabetes, cholesterol, or hypertension medications (Karter et al., 2009; Svensson et al. 2015; Vrijens et al. 2017).

15. Secondary non-adherence is commonly understood as "non-adherence" and means that patients obtain their prescriptions but do not take their medication in doses and/or time intervals as recommended by their clinician. There is no real consensus on the optimal level of adherence. In some cases, researchers have concluded that 80% of the time is acceptable in many disease states. There are, however, others in which even greater levels of adherence are required to avoid negative outcomes. Rates for secondary adherence for the three chronic conditions ranged from 25% to 93%. 25 to 64% of patients initiated on statins for their high blood cholesterol were adherent based on adherence defined as more than 80% of medications dispensed (McGinnis et al., 2007; Lee et al., 2016; Maninget, 2013). A meta anlaysis found that overall the prevalence of adherence (the proportion of the study population that was classified as adherent to diabetes medication) varied widely from 38.5 to 93.1% (Krass, 2015). Studies using claims databases that defined adherence as an 80% ratio of days on which medication was dispensed reported adherence rates ranging from 52 to 74% (De Geest & Sabaté, 2003).

16. Persistence is reported either as a continuous variable in terms of the proportion of days for which therapy is available or as a dichotomous variable measured at the end of a predefined time period, for example, 6, 12, or 24 months. Persistence is low among people with chronic diseases and rates steadily decline from initiation to two years (Yeaw et al, 2009). Among diabetes patients, 73% of those who started the therapy continued their diabetes medication at 6 months and only 39% remained persistent (still taking their medications) at 24 months (ref). 25 to 50% of patients with hypercholesterolemia discontinued statin use within 6 to 12 months after initiation (Svensson et al. 2015; McGinnis et al. 2007). 16 to 50% of patients with hypertension discontinue their antihypertensive medications within the first year of treatment (Brown & Bussell, 2011). At 24 months, only 33% of patients prescribed a lipid-lowering drug and 41% of patients prescribed an antihypertensive persisted with therapy (Davis et al, 2011). These estimates exclude those who never filled the first prescription.

3. WHY DONT PATIENTS TAKE THEIR MEDICATIONS AS PRESCRIBED?

17. The previous section discussed both the importance and magnitude of adherence to medications among people with the three most prevalent chronic diseases. The evidence suggests that adherence rates continue to be suboptimal, despite the health beefits of therapy. This section investigates why medications adherence remains a challenge in all countries.

18. Medication adherence is influenced by a number of interconnected factors related to the patient, the provider, and the healthcare system. Discussions of non-adherence generally tend to attribute the problem predominantly to patients, in particular focusing on their forgetfulness – while the reviews of evidence from patient surveys and adherence interventions reveal the provider and the healthcare system characteristics are lead drivers (AlGhurar, Hughes, Simpson, & Guirguis, 2012; Kardas, Lewek, & Matyjaszczyk, 2013; Nieuwlaat, et al., 2014; Conn, Ruppar, Enriquez, & Cooper, 2016). The perception that nonadherence is a results of the patients' failure to follow instructions is an inadequate explanation for what is, more fairly, a complex behavioral process. Indeed, patient factors such as motivation, beliefs, perceptions about the need for medication, forgetfulness, and health literacy contribute to medication non adherence. However, poor adherence results from multiple barriers, many of which patients cannot control (Lauffenburger, & Choudhry, 2018).

19. Using the World Health Organisation's multidimensional model of adherence (World Health Organization, 2003) the barriers to adherence can be classified into five categories:

(i) healthcare system/health team barriers (e.g. poor quality of patient-provider interaction, cumbersome procedures, limited drug reimbursement);

(ii) condition-related factors (e.g. presence of comorbidities, lack of symptoms);

(iii) therapy-related barriers (e.g. side-effects, complexity of drug regimen);

(iv) patient-related factors (e.g. forgetfulness, wrong beliefs about diseases and medications, preferences, low health literacy); and

(v) socio-economic factors (e.g. poverty, low social support).

3.1. There are significant healthcare system and health team barriers to adherence

Barriers to more personalised and integrated care

20. Patient-provider interaction characterised by a personalised and integrated approach to the development of care plans, through person-centred communication and shared decision-making is a factor most often associated with good adherence to medicines for the three chronic conditions (Safran, Taira, & Rogers, 1998; Schoenthaler, Allegrante, Chaplin, & Ogedegbe, 2012; Kardas, Lewek, & Matyjaszczyk, 2013; Nieuwlaat, et al., 2014; Reiss-Brennan, et al., 2016; Conn, Ruppar, Enriquez, & Cooper, 2016). Effective person-centred communication is a dynamic and ongoing process that facilitates understanding the health needs (including health-related social needs) of a particular patient and devising care customised to these particular needs (Safran et al.,

1998; Lein et al., 2007; Reiss-Brennan et al., 2016). Shared decision-making means patients become equal partners in planning, developing, and monitoring care, which builds trust in the patient-provider relationship and ensures that the therapy's goals are relevant to patients within the larger context of their lives (Leppin, Montori, &Gionfriddo,2005; Ajayi, 2017).

21. Numerous barriers to a more personalised and integrated care exist due to the disease focussed nature of healthcare organisation, economic structure, managerial culture, and training. This results in fragmented care plans and prescribing clinicians rarely having resources (e.g. time, skills, health records) to extend the scope of attention beyond the organ affected by a given disease to a whole person context. As a result, patients with chronic conditions report disagreeing with their clinician's advice, feeling that the decision process about their therapy did not involve them, or they perceive that the therapy does not represent their best interests (Commonwealth Fund, 2012; Kardas et al., 2013; Cenci, 2016).

22. From the patient's perspective, a chronic condition poses not only a health problem but also a long-term personal and social challenge. Patients are often concerned about a therapy's side-effects on their daily functioning or might have specific preferences for a dosing regimen because of their work and other less flexible social routines. The disease-focused approach, however, leaves very little room for considering personal aspects of a patient's condition. Due to unaddressed concerns or preferences, patients are inclined to rebuff the treatment decision or lack sufficient motivation to follow the therapy consistently (Cenci, 2016; Ajayi, 2017). Patients' health literacy and shared decision making are central to their ability to adhere. A simple prescription without an explanation may at times disempower patients, who then feel that they did not reach a common understanding with their clinician (Cenci, 2016).

23. The barriers to more personalised and integrated care affect particularly chronic patients with co-morbidities. Little is known about adherence rates to multiple drug regimens, as the commonly used adherence measures are disease-focused as well. There is, however, evidence that patients with multiple co-morbidities often perceive their medication use as excessive and decide to discontinue one or more of their medications without consulting any health professional (Walid,Grenard & Marcum, 2011; Kardas et al.,2013). For some patients, a simple application of clinical guidelines developed for each condition separately, can result in more than ten medications a day, which may not always have clinical benefit and at times result in harmful side effects.

Cumbersome procedures for refilling prescriptions

24. Due to the long-term nature of chronic conditions, the ease or difficulties with which patients can renew/refill prescriptions also significantly affects adherence. Patients with chronic diseases frequently report having no time to refill prescriptions. Cumbersome procedures involving for example, monthly visits to healthcare facilities to pick up a renewed prescription, queuing at pharmacies, or the need to carry around paper records contribute to non-adherence (Alghurair et al., 2012).

25. A US study found that the system-level factors influencing the ease of renewing prescriptions had a consistent relationship with medication adherence in Medicare aged patients, and that optimising these factors almost doubled the level of "good" adherence in this population (Schmittdiel, et al., 2015). Initiatives like long-term medication supply, online refills of prescriptions, mail order pharmacy use, and calendarised blister

packaging all have been shown to significantly improve adherence (Schmittdiel, et al., 2015; Zedler et al., 2011).

Patient out-of-pocket payments and limited prescription coverage

26. In many OECD countries, patients with chronic diseases do not pay the full costs of prescription medicines directly. Where such costs are only partially covered by insurers, patients report taking less medication than prescribed, due to the related out-of-pocket costs. This is more pronounced among patients with low incomes and/or multiple health conditions who use significantly less medications than prescribed due to costs (Piette et al., 2004; OECD, 2015; Morgan & Lee, 2017). In this context, there is a need for patient-provider communication focusing on a patient's personal financial situation and not just the disease only.

27. Evidence suggests that patient-physician discussions about medication adherence problems owing to costs rarely occur. A physician noting a lack of improvement in a patient's condition, but unaware that the patient did not adhere to their medications might decide to prescribe another medication or move to second line therapy. This often means discarding the previous prescription before all of the purchased medication is used, which further exacerbates the financial pressure. In some circumstances, a stronger dose or second line therapy might have higher out of pockets costs. Important opportunities for discussing options such as switching to generics, lower-cost branded medications, or providing information on possible financial assistance are missed. Patients who simultaneously suffer from a number of health conditions might be selective about the treatments they forego due to out-of-pocket costs. When the financial pressures are not discussed together with the prescribing physician, the choices made by patients alone may result in poor health outcomes (Alexander, Casalino, & Meltzer, 2003; Piette, Heisler, & Wagner, 2004; OECD, 2015).

3.2. Condition-related factors exacerbate medication non-adherence

28. Condition-related barriers to adherence among chronic patients include the asymptomatic nature of some of the conditions or the disappearance of symptoms during the therapy, the presence of co-morbidities, and condition-related limitations such as the inability to open a medication bottle or read the print on the medication (AlGhurar, Hughes, Simpson, & Guirguis, 2012; Kardas et al., 2013).

29. Chronic conditions at the onset are not necessarily accompanied by obvious symptoms, which may result in a reduced sense of urgency on the patient's part or even denial of the diagnosis - "I do not feel sick – I don't need the medicine" (New England Health Care Institute, 2009; Alghurair et al., 2012). Similarly, the sense of urgency on the patient's part might be reduced by the disappearance of symptoms after the initiation of the therapy. The above-discussed barriers to more person-centred communication between patients and physicians often mean that the asymptomatic nature of a condition is not addressed at the time of the initial prescription, which exacerbates this type of condition-related barriers to adherence.

30. Presence of co-morbidities is also classified as condition-related barrier to adherence (Walid,Grenard & Marcum, 2011). However, as discussed earlier, the underlying cause most probably is the health system's failure to adopt a multidisciplinary and participatory approach to the development of care plans for patients with multiple co-morbidities, which would ensure adequate support in medication taking. Patients might also experience problems with adherence due to the condition-related limitations in physical and sensory abilities. Evidence suggests that in some cases patients simply cannot open a medication bottle and/or read the print on medication, including instructions for drug dosage (Alghurair et al., 2012; Figueiredo, et al., 2016).

3.3. Therapy-related factors often interfere with patient preferences

31. Therapy-related barriers to adherence among patients with chronic conditions include medication side effects, treatment complexity, route of administration, and requirements for storage and handling (Jin, Sklar, Min Sen Oh, & Chuen Li, 2008).

32. The most commonly reported therapy-related barrier to adherence is the actual or expected occurrence of adverse effects, especially when patients perceive them as decreasing their functional abilities required in daily work and social routines (ABC Project, 2012; AlGhurar et al., 2012). Other frequently reported therapy-related factors behind non-adherence are the complexity of drug regimens – complex and/or frequent dosing, high number of prescribed medications – and route of administration, in particular, the inconvenience associated with the administration of injection formulations. These aspects of therapies pose barriers especially when they interfere with the patients' work schedules or other daily routines (Alghurair et al., 2012).

33. The aforementioned barriers are not insurmountable by the health care team. In most cases, an alternative medication regimen that reduces the burden of adherence could be prescribed. The adverse effects could be minimised by, for example, finding what is the lowest effective dose of a given medication for the patient. Drug regimens could be simplified by choosing medications given fewer times per day and better aligning dosing intervals to a patient's daily routines. However, in order to so, both the patients and physicians need to discuss the issues at hand and both participate in weighting advantages and disadvantages of various alternatives. Resolving the problem may also involve consulting other clinicians (Rose, Fischer, & Paasche-Orlow, 2017). However, the quality of the patient-provider interaction is sub-optimal at times and the possibilities for patient engagement or collaboration among various clinicians is limited. Therefore, patients' preferences remain unaddressed even where it would be feasible.

34. Other therapy-related reasons behind poor adherence include aspects related to medication storage and handling. At work, for example, patients may experience obstacles to adherence if the medication needs to be stored in an inconspicuous location (Kibicho & Owczarzak, 2011). Patients with unmet social needs might not have access to basic household equipment such as a refrigerator (Kardas et al., 2013).

3.4. Patients' beliefs about diseases and medications are not always taken into account

35. The general perception on patient-related factors purports that medication nonadherence is usually accidental, while the evidence suggests that it is more intentional than not. Patients' may not conform to their prescribed course of treatment due to a conscious decision based on their beliefs about diseases and medications. In contrast, simple forgetfulness and confusion are relatively less common drivers behind non-adherence to medication. Oftentimes, nonadherent patients report forgetfulness instead of the true cause, as the suboptimal quality of patient-provider interaction does not invite them to reveal and discuss the true causes underlying nonadherence (Commonwealth Fund, 2012; Alghurair, Hughes, Simpson, & Guirguis, 2012; Olson, 2012; Kardas et al., 2013).

36. Knowing the patient as a person allows the health professional to understand elements that are crucial to the patient's adherence: beliefs, attitudes, subjective norms, cultural context. For example, a patient with hypertension and a family history of heart disease might believe that nothing can be done to prevent a heart attack and decide not to start on the course of medication. Similarly, vulnerable persons who often feel they lack control in their lives, might believe that they would fail to follow consistently a long-term chronic condition therapy and decide not to start it at all. The lack of patient-physician partnerships when choosing amongst various therapeutic options exacerbates the patient-related barriers to good adherence (Brown et al.,2016; Ratanawongsa et al., 2013).

37. One of the greatest challenges for healthcare professionals is convincing the patient that there is a causal link between therapy and health. Unless an individual patient starts believing that his/her disease or condition poses a threat, he/she may not see the need to adhere to a prescribed therapeutic regimen. Patients' perceptions at times reflect a healthcare team's inability to elicit patient trust, which would allow for their therapy related concerns to be resolved effectively. Hence, they might be difficult to counter by relying purely on additional educational materials. In general, beliefs about diseases and medication can be influenced, for example, by carefully choosing the wording of the message delivering the diagnosis, but are rarely addressed by health systems (NEHI, 2009; Alghurair et al., 2012; Crum and Zuckerman, 2017).

3.5. Unmet social needs are also associated with non-adherence

38. As mentioned earlier, patients with chronic diseases report taking less medication than prescribed due to limited prescription coverage and the related out-of-pocket costs. In particular, patients with low incomes use significantly less medication than prescribed (Piette, Heisler, & Wagner, 2004; OECD, 2015; Morgan & Lee, 2017). These problems are exacerbated by other unmet social needs such as shortage of basic food or household equipment – a refrigerator, for example (Kardas et al., 2013).

39. Adherence is also a challenge for patients with chronic diseases who have poor social support – patients living alone and/or lacking a social network (Kardas et al., 2013). A meta-analysis showed a significant relationship between adherence and practical and emotional support, family cohesiveness and conflict, marital status, and living arrangement of adults. Practical support – family or friends engaging patients in the practical aspects of medication purchasing and administration - had the highest correlation with adherence. Adherence is 1.74 times higher in patients from cohesive families and 1.53 times lower in patients from families in conflict (DiMatteo, 2004).

40. Unmet social needs are increasingly recognised as critical component of effective healthcare. Health systems are still ill equipped to address them. Healthcare providers have weak incentives or none at all to routinely identify unmet social needs. Healthcare providers are often without means to act due to limited flexibility and/or funds to cover any not strictly medical costs of care as well as a lack of integration with social service providers, even when aware of them (Blumenthal & Abrams, 2016; McMullen & Katz, 2017).

4. WHAT ARE HEALTH SYSTEMS DOING TO SUPPORT MEDICATION ADHERENCE AMONG PATIENTS WITH CHRONIC DISEASES?

41. The previous sections looked at defining the problem of medication nonadherence among patients with selected chronic conditions and understanding the underlying drivers. This section provides an overview of the current initiatives to improve medication adherence across the OECD countries.

42. Several reviews have assessed and mapped the availability of initiatives to improve medication adherence (Conn et al., 2016; Costa et al., 2015; Nieuwlat et al., 2014; Kardas et al., 2013; ABC Project, 2012). A number of consistent themes were identified by these systematic reviews. Most of the reviews identified nil to modest improvements in medication adherence after interventions. The interventions were found to be localised one off initiatives aimed at modifying individual patient behaviour only. The interventions mainly take a form of general information campaigns on the benefits of adherence, followed by smaller initiatives at the provider level – either pharmacists or primary care physicians. The majority of interventions do not seem to be informed by prior analysis of the nature of reasons behind non-adherence There is insufficient evidence to assess the cost effectiveness of most interventions.

43. These reviews were mostly based on the peer-reviewed literature, thus a survey was administered to OECD countries' representatives to obtain a better understanding of current national initiatives. The results provided a mixed picture across the OECD countries in the development of policies and interventions for medication adherence. Table 1 gives an overview of current medication adherence initiatives that were identified exclusively from survey responses. Subsections 4.1 to 4.5 discuss these initiatives in more detail.

44. The survey indicated that non-adherence is not considered a priority on the national policy agenda in many countries at present. The authors did not find sufficient evidence to suggest that a visible increase in efforts have been undertaken at the national level after the seminal report on medication non-adherence and call to action by the WHO in 2003. Interventions to enhance or support medication adherence are not well co-ordinated nor part of a larger strategic policy programme. Most of the interventions aimed at modifying individual patient behaviour only. Relatively few initiatives addressed the broader determinants of non-adherence related to healthcare system and healthcare team. Many interventions were not evaluated in terms of their effectiveness, cost-effectiveness, or improved patient health outcomes.

Country	Routine monitoring of	Studies assessing non-	Interventions to
	adherence at a national	adherence rates, drivers	promote adherence
	level	and impact on health	
		outcomes and costs	
Australia	No	Yes	PDI, DTI
Belgium	No	Yes	No
Canada	No	Yes	PDI
Czech Rep.	No	No	No
Estonia	No	Not reported	Not reported
France	No	Yes	PDI
Hungary	No	Yes	PDI
Iceland	No	No	No
Israel	Not at a national level,	Yes	PDI, DTI
	but at physician level		
Japan	No	Yes	PDI
Korea	No	Yes	No
Latvia	No	No	No
Norway	No	Yes	DTI, PDI
Poland	No	Work-in-progress	IC (PDI is planned)
Portugal	No	Yes	IC
Slovenia	Not at a national level,	Yes	PDI
	but at physician level		
Sweden	Yes	Not reported	Not reported
Switzerland	No	No	PDI
Turkey	Not at a national level,	Yes	PDI
	but at physician level		
United	No	Yes	PDI, IC, DTI
Kingdom			
United	Not at national level, but	Yes	PDI, IC, DTI
States	at Centre for Medicare		
	and Medicaid level		

Table 1. Medication adherence initiatives identified from the survey responses - OECD countries.

Key: PDI - Provider delivered intervention with financial incentives for the providers. **IC** -Public information/education campaigns targeting patients. **DTI** - Data & technology infrastructure.

Source: Survey administered to health authorities of OECD countries in April 2017.

These findings are largely in line with those reported in the 2012 European 45. Commission study Assessing Barriers to Adherence – ABC Project – Box 1. The study found that most initiatives in the European Union addressing adherence took place at the patient level, for instance, the provision of education and information about newly prescribed medications and the benefits of adherence. This was followed by initatives focused on improving patient-physician interactions, for instance, through the implementation of a partnership approach. The lowest amount of activity was reported for policy solutions at the government or healthcare payer level, which included investments in research to identify effective interventions demonstrating value for money and increasing public awareness of medication non-adherence. The study also emphasised the "hidden" nature of non-adherence in both policy and practice. Despite policy documents making reference to adherence, these references are often distributed among a number of other topics, such as patient safety, rather than falling under the discrete label of medication adherence. This reduces the visibility of adherence as a focus in the policy arena (ABC project, 2012).

Box 1. ABC Project - Assessing Barriers to Adherence - main findings.

The 2012 European Union study Assessing Barriers to Adherence – ABC study – stresses the need for creating a health policy agenda that promotes patient non-adherence to medications as a priority concern based on a qualitative analysis of the available evidence as well as expert opinions. The countries (e.g., The Netherlands, Finland, Germany, and Malta) that have managed to elevate medication adherence to a critical healthcare issue on the national policy agenda share characteristics such as co-ordinated multi-stakeholder forums and system-level support and drive.

The ABC study found very little interest in medication adherence among key stakeholder groups in the European Union. As part of the project, surveys were sent to healthcare professionals (nurses, pharmacists, physicians), medical, pharmacy and nursing schools, as well as pharmaceutical companies:

- A survey sent to healthcare professionals nurses, pharmacists, physicians in Austria, Belgium, England, France, Germany, Hungary, The Netherlands, Poland, Portugal, and Switzerland found that heath care professionals reported being limited in the extent to which they intervene to assist patients having long-term conditions with medication adherence. Approximately half of the healthcare professionals in the survey ask patients with long-term conditions whether they have missed any doses of their medication on a regular basis. Pharmacists persistently report that they intervene less than physicians or nurses to support patients in taking their medications. The results did not vary significantly by country.
- Only ten out of 201 medical, nursing, and pharmacy schools in the European Union responded to the survey to assess whether schools include medication adherence as part of the core curriculum. Half of the schools reported not having specific content on how to assess medication adherence in their curriculum and 25% reported no specific content on how to improve or promote adherence. The median number of teaching hours spent on medication adherence was reported to be three contact hours in the entire programme.
- Only nine out of the 98 pharmaceutical companies responded to the survey on their current adherence promoting activities. Only four of the nine companies indicated that medication adherence was addressed in their strategic plan and that they were involved with medication adherence programmes.

Source: (ABC Project, 2012)

4.1. Routine monitoring & reporting may provide the impetus to improve adherence

46. The United States and Sweden are the only OECD countries that report on adherence and persistence measures on a routine basis at the system level. In other countries: Israel, Slovenia, and Turkey, primary care physicians monitor adherence routinely at the patient level (first column in Table 1). Very few countries report or use adherence measures as either quality improvement or performance measures, however, most countries if not all have conducted several research studies measuring adherence and/or persistence for a range of diseases.

47. The experience of Sweden and the United States with system-level reporting is summarised below:

• Sweden: Sweden measures and reports one adherence measure annually; the percentage of patients starting on antihypertensive therapy who were still following the regimen after 12–18 months. This indicator is reported in a series of annual reports

entitled *Regional Comparisons* with indicator-based comparisons of healthcare quality and efficiency among the counties of Sweden.

United States: Since 2012, the Centres for Medicare and Medicaid Services (CMS) use its Medicare STAR program to measure adherence to three categories of drugs for management of cardiovascular disease risk factors: angiotensin converting enzyme inhibitors and angiotensin receptor blockers (ACEI/ARBs) to hypertension; statins to control LDL-cholesterol; control and oral antihyperglycemics to control glycosylated hemoglobin (HbA1c). Qualified Health-Plans issuers in the Health Insurance Marketplace need to report the adherence measures using the standard Proportion-of-Days-Covered (PDC) method separately for the three drug categories. The implementation of these measures emphasises the responsibility of health-plans issuer to monitor and improve medication adherence among their patients. Patient and provider indicators of medication adherence are tied to performance measures and are publicly reported at provider and system levels. Based on their annual ratings, plans face rewards, such as quality bonus payments or marketing advantages, and consequences, such as the potential loss of patients.

48. Most countries (n=13 of the surveyed countries) reported research studies being conducted on medication adherence either by universities or research institutions (Table 1, second column). These studies assess the magnitude of adherence and persistence as well as the impacts of medication non-adherence in terms of health outcomes and healthcare costs of patients. (The results of these studies have been incorporated in Sections 2 and 3).

49. Measuring and reporting adherence at the physician level has also been suggested as a mechanism to improve adherence. One of the ways to do this is providing physicians with feedback on their individual patient's level of adherence. Israel and Slovenia are leading the way with innovative initiatives aimed at the providers.

- Israel: Health funds in Israel have consolidated primary care services into interprofessional teams to enhance support for patients with chronic diseases. The funds provide doctors with extra resources to support patients through a patientprovider partnership, regular monitoring of a patient's health indicators, including adherence to medication, and support tailored to the specific needs of patients. Physicians receive feedback on adherence rates among their patients, which highlights patients with low adherence (measured as a share of filled prescriptions by patients or through electronic pill boxes that register the time when the lid has been open). The adherence measures are also reported at a clinic level. These efforts are complemented by the Quality-Indicators-in-Community Healthcare programme consisting of 35 quality indicators, including selected health outcomes. This approach has focused on changing the structure of supply to influence provider behaviour, with some funds seeking to influence providers also through financial incentives. Evidence available from the second largest health fund -Maccabi - suggest that poor glycaemic control decreased by 29% and control of cholesterol increased by more than 90% (OECD, 2012).
- Slovenia: patients with chronic diseases are routinely monitored at the individual level by general practitioners within Family-Medicine Model Practices. The latter are practices led by a General Practitioner supported by a registered nurse as well as a graduate nurse with specialised training in screening for chronic-disease risk factors, preventive counselling, and care coordination for patients with stable

chronic diseases. The graduate nurse provides patients with intensive health education, motivational interviewing, and explains the importance of regular taking of medications or refers to structured education programmes. Moreover, the nurse assesses the attainment of individually set objectives (regarding target values of specific parameters) and probes for the presence of possible side effects of medications. The goal behind this model of practice is to optimise care for patients with chronic diseases – including optimal use of medication – and empower patients to participate in their care and engage in self-management.

4.2. Provider-delivered interventions have been shown to have a modest impact on improving adherence

50. Almost all of the surveyed countries reported interventions delivered by healthcare providers (PDI in Table 1), notably pharmacists or primary care physicians. Healthcare providers (e.g., physicians, pharmacists, and nurses) are ideal actors to implement adherence promoting interventions because of their existing relationships with patients, ongoing monitoring of patients' health outcomes and familiarity with individual patients' unique treatment needs. Most of these interventions required additional support to providers, mostly financial incentives.

51. Several countries described pilot programmes delivered by pharmacists to improve medication adherence. These interventions generally use an educational component combined with behavioural strategies. Most of these pilots have been or are currently being evaluated. Results vary in terms of the effectiveness of these interventions and cost-effectiveness is rarely established.

- United Kingdom: In 2011, National Health Service (NHS) England has launched the "New Medications Service" (NMS) the largest national intervention aiming to support patients in optimising their use of medications. The NMS is performed by community pharmacists when a patient is prescribed a new medicine for one of four therapy areas hypertension, type-2 diabetes, anticoagulation/antiplatelet therapy, or asthma/chronic obstructive pulmonary disease. Around 7 to 14 days after the patient presents at the pharmacy with the prescription, the pharmacist offers a consultation to find out if the patient is having any problems taking their medicine and provides support to remove any barriers to adherence. Within the NHS community-pharmacy contractual framework, the NMS is classified as an Advanced Service, whereby accredited pharmacies can opt to provide the service. NMS generated a mean of 0.06 (95%CI: 0.00, 0.16) more QALYs per patient, at a mean reduced cost of -£190 (95%CI: -929, 87). Therefore, the NMS service dominates current practice, with an ICER (Incremental cost-effectiveness ratio 95% credibility range) of -£3 005 (-£17 213, £4 543).
- **Canada:** A pilot community-pharmacist programme "Health Inform" based on providing periodic patient education was conducted in 2005. The programme mailed out brochures from the participating pharmacy to its patients that included: information on the disease, the medication's action and side effects, the administration of the medication, as well as the benefits of the commitment to take the medication as prescribed. The programme required the pharmacists to seek permission for such mailing. Pharmacists were reimbursed for enrolling the patients in the program. The pilot study was evaluated and reported that at the end of one year, enrolled patients demonstrated higher persistence to statins, bisphosphonates, and antihypertensives than those who were not invited to the

programme (i.e., "comparison patients") by 11.7%, 11.9%, and 14.3%, respectively (McLean, 2007).

- Switzerland: In spring 2016, the Federal Office of Public Health, the Association of Pharmacies, and the Association of Insurers launched a pilot project that aims at improving adherence among patients with diabetes. The pilot involves 20 pharmacies with 10 patients per pharmacy. Medication adherence is monitored using an electronic pill box during the 12 months. Pharmacists, using the pharmacy databases, identify non-adherent patients and devise a personalised intervention in collaboration with a prescribing physician. The interventions involve additional consultations, re-validation of treatment plans, and/or motivational discussions. The project assesses the interprofessional collaboration by collecting information on satisfaction with the collaboration, means of communication, and the quality of the exchange. The project will be evaluated in 2018. A similar approach has been under consideration in **Poland.**
- **Japan:** A pilot community-pharmacist project the "COMPASS project" was trialled to improve the blood glucose level through improving adherence to medications in patients with type-2 diabetes. The intervention was provided by pharmacists who use coaching skills and motivational interviewing as well as provide advice to patients. This project is currently being evaluated. Another approach is to provide patients with electronic medication notebooks in which they are to record their medication history. There are fee incentives in place whereby there is an additional payment for pharmacist when they provide patients with guidance on medications.
- Australia: In 2016, a New Medicine Support Service (2015-16) programme was piloted across nine pharmacies in New South Wales. This service aimed at improving medicine adherence by providing pharmacist support to patients newly prescribed a medicine for long-term conditions, including dyslipidaemia, hypertension, and type 2 diabetes. The New Medicine Support Service (2015-16) was evaluated with focus on referrals back to General Practitioners. Referrals occurred for 13% of patients at the intervention stage and 5% of patients at the follow-up stage. For the remainder of participants, reassurance and advice to carry on using their medications was sufficient.

52. Most countries have in place guidelines, frameworks, and financial incentives for primary care physicians to improve quality of care for patients with chronic diseases. However, there were no specific physician delivered adherence interventions that countries reported. Most of the physician delivered interventions are part of broader chronic disease management plans.

• France: In France, a number of different programmes have been established to improve diabetic care outcomes. The physician receives an additional annual payment for patients diagnosed with the listed condition. This payment covers the care co-ordination required to implement specific care protocols. A pay-for-performance (P4P) scheme, initially introduced in 2009 as the Contrat d'Amélioration des Pratiques Individuelles (CAPI, Contract to improve individual practices), and now known as the Rémunération sur Objectifs de Santé Publique (ROSP, Remuneration of public health objectives) incentivises improvements in quality of care and more efficient prescribing. Currently, the ROSP includes 29 indicators from four different areas: organisation of practice, chronic conditions, prevention, and efficiency. Eight of the indicators measuring care for chronic

conditions relate to diabetic patients. The calculation of the performance payment for each physician is rather complex taking into account the doctor's individual performance, the average performance of all doctor's per indicator and the target objectives which are set annually by the Haute Autorité de Santé (HAS, the public entity responsible for setting healthcare quality standards). The indicators are a mix of measures for procedural quality (e.g. number of HbA1c tests) and intermediate outcomes (e.g. share of diabetics below HbA1c thresholds). They also include cholesterol thresholds and indicators to measure the intake of statins and aspirin among diabetics at high risk of developing cardiovascular diseases (CNAMTS, 2014; Cashin et al., 2014). The bonus payments GPs can generate through the ROSP accounted for 4.1% of total GP payment in 2014 (Rapport de la Commission des comptes de la sécurité sociale, 2015). In 2015, the average bonus was around EUR 6 800 (CNAMTS, 2016). An additional service for patients with diabetes called "SOPHIA" was put in place in 2009. SOPHIA provides diabetes counselling and education by nurses over the phone employed by the statutory health insurance. GPs are also financially rewarded for submitting a completed medical questionnaire to health insurance funds for each patient registering for this service.

• Norway: Patients in Norway are listed with one physician (General Practitioner) only, who follows them over time and coordinates care with specialists and other healthcare professionals. The physician discusses with the patients the effects, side effects, and patient preference (dose and timing) regarding their medication. This often includes measurements and blood tests for evaluating the effect of the prescriptions. It is also usual to ask the patient if they remember taking their medicine as prescribed. The current guidelines for chronic conditions (diabetes, cardiovascular disease) include advice regarding follow-up. The GP is responsible for each patient's medication list and is responsible for follow-up of individuals according to the guidelines. With the introduction of electronic prescribing, the GP can see any prescription, date of prescription, and date the medication is dispensed from the pharmacy. This allows the physician to remind patients in case they do not take out their medication at proper intervals.

53. The literature supports that provider delivered interventions tend to be effective, although even the most effective interventions have shown modest improvements in adherence among patients with the three most prevalent chronic conditions. The provider interventions with the largest effect were characterised by face-to-face tailored ongoing support that examined the patients' personal context, such as daily routines and habits, and then linked medication administration to those routines (Conn, Ruppar, Enriquez, & Cooper, 2016; Costa, et al., 2015; ABC Project, 2012; Niewlaat, et al., 2014).

4.3. Many interventions are focussed on providing information to patients

54. Various interventions to address poor adherence have focused on changing patients behaviour directly, particularly their forgetfulness and beliefs about medications, through information dissemination campaigns (IC in Table 1). This can range from providing leaflets and brochures at the provider level, either at a physician office or a pharmacy, public education campaigns, as well as online tools.

55. Public educational campaigns to promote medication adherence and raise awareness among patients and their family caregivers about the importance of taking

medication as prescribed are often seen as a vital first step toward better health outcomes. Examples of such campaigns include:

- **Portugal:** The *Responsável do Medicamento campaign* is part of a broader responsible use of medications campaign. It is a joint campaign by the pharmacists' association and INFARMED (the national authority in charge of medications and health products). It is a multi-stakeholder campaign with a website, events, posters, a pledge, and social media.
- United Kingdom: The *Adherence, Let's take care of it* campaign aims to increase awareness of the issue of medication non-adherence. The campaign includes a website, National Medication Adherence Week, social media, and a pledge. The campaign started in 2015 and is funded by Omnicell, a private company offering automated medication dispensing systems.
- United States: Script your future is a campaign including co-ordinated national communications, paid advertising, and targeted outreach in six cities. The goal is to raise awareness among patients and their family caregivers about the importance of taking medication as prescribed as a vital first step toward better health outcomes. The campaign focuses on patients affected by three chronic conditions diabetes, respiratory disease, or cardiovascular disease. The campaign is led by the National Consumers League a private, non-profit advocacy group.

56. The particular examples of such campaigns in the OECD countries have not been evaluated with regard to their effectiveness or cost-effectiveness. The systematic reviews of adherence interventions show that interventions such as simple reminders or campaigns aiming to inform and educate patients or their families tend to be ineffective or low in effectiveness, as compared to the interventions involving face-to-face interactions with healthcare professionals (Conn, Ruppar, Enriquez, & Cooper, 2016; Costa, et al., 2014; IMS, 2012)

57. Pharmaceutical companies also provide information to patients about their medications and the importance of taking them. For example, Novartis launched a customisable patient adherence and education programme; BP Success Zone Patient Management Program (BPSZ)¹ to help patients monitor their blood pressure, manage medication regimes, and track improvement while providing educational information, diet plans, and exercise programmes to help enhance their overall health. Another example is eResources4Health, created by Daiichi Sankyo, an unbranded health education Webbased tool that contains more than 100 unbranded, customisable health resources. It is intended to educate people with chronic diseases with appropriate self-management tools and help them work more closely with their healthcare providers². There is limited published information on the effectives or cost-effectiveness of these initiatives.

¹<u>http://www.bpsuccesszone.com</u>

² http://www.pharmavoice.com/article/payers/

4.4. Financial incentives play a role in improving adherence

58. Payment reforms and financial incentives for providers have the potential to improve medication adherence. Shifting to payment systems that reward providers for better patient outcomes and encouraging co-ordination of care is critical for providing the incentives and investments that are required for improving adherence. Most of the effective provider delivered interventions reported by the countries rely on financial incentives for health professionals or organisations to provide the additional service of improving adherence.

59. Medication adherence is increasingly being considered as a measure for performance based reimbursement contracts. A US study found that higher private healthplan level averages of medication adherence were associated with significantly lower rates of disease-related complications for both diabetes and congestive heart failure. The authors concluded that medication adherence measures are potentially useful tools for improving the performance of health plans and providing incentives for plans to improve adherence could be an effective level to improve the overall quality of care (Seabury et al, 2015).

60. Some have argued for medication adherence to become a part of reimbursement through value-based pricing and performance-based contracting between payers and pharmaceutical companies (Barlas et al., 2016). Such contracts align payer and manufacturer incentives to improve adherence to medications. An example is the performance-based agreement between the pharmaceutical company Merck and the insurance Cigna in 2009 regarding the cost of diabetes medications Januvia and Janumet. Under the agreement, Merck offers Cigna discounts on the two medications if the percentage of patients who are adherent to diabetes medications increases. The discounts also increase if patients blood glucose is under control. Within this agreement, Cigna's efforts to improve adherence are rewarded with the discounts on drugs, while the pharmaceutical producer benefits from higher volumes of sales. The agreement is also helping Cigna to offer lower co-payments for adhering patients. Cigna has assigned the two drugs a preferred status on its drug coverage lists and committed to apply a range of initiatives to help patients improve adherence, including phone calls to investigate why they are failing to take their treatments. The infrastructure necessary for implementation of the agreement, such as collection of pharmacy data and lab results for internal use, was already in place as Cigna had an active diabetes management programme. In 2010, Cigna announced that its medicine adherence programmes have helped patients with diabetes reduce emergency room and other hospital visits by 50% for those reaching blood glucose goals, and reduced diabetes-related costs by 24%. Among the 165,000 members taking the two oral diabetes drugs, blood sugar levels improved by over 5% on average. Participants also registered a 4.5% increase in blood glucose testing. Medical adherence improved across the board, rising to 87% for those taking Januvia and Janumet (Neumann et al., 2011).

61. Regarding financial incentives of patients, a host of observational studies demonstrate that reducing patient co-payments for highly effective chronic therapies can substantially improve adherence, especially in countries with high co-payments (Morgan & Lee,2017; OECD, 2015; Kesselheim et al, 2015). Others suggest that simply reducing co-payments may not be sufficient and have proposed that providing financial rewards for better adherence may be an even more effective mechanism to promote behaviour change (Bosworth et al, 2011). Whereas physician pay-for-performance has received substantial attention in the medical literature, patient pay-for-performance is a concept that needs

further research to understand its long-term effectiveness and cost-effectiveness (Jochelson, 2007).

4.5. Data and technology infrastructure could be leveraged to boost adherence

62. Data and technology infrastructure (DTI in Table 1) could be developed or, where existing, leveraged to encourage adherence. A common trait among successful adherence interventions is that they leverage information technology and patient-level data. The initiatives focus on understanding the patients' attributes using data and tailoring interventions to those attributes. As such, the technology infrastructure supports further interventions such as patient follow-up and personalised support provided by healthcare professionals who are trained and empowered to work closely with patients to improve adherence (Cutler, 2010).

63. Several OECD countries, for example, Norway, Denmark, Finland, Sweden, England, Estonia, and the United States have e-prescribing infrastructures in place, based on survey results and literature. When medication information is shared electronically, prescribers have access to information that allows them to assess a patient's medication regimen at the point of care and to identify non-adherence. Electronic systems may also be able to notify a prescriber or pharmacist about refills, which can help trigger an intervention to avoid a potential gap in medication use.

64. Kaiser Permanente in the United States has been at the forefront of adherence interventions relying on data and technology infrastructure. These include using e-prescribing to identify patients who do not fill their prescriptions as well as mail orders, online refills, and home delivery options for the ease of refilling prescriptions by patients. Patients also have access to their electronic personal health records. Kaiser Permanente has consistently scored 5-star rating (excellent) for the Medicare STAR quality rating system's measures of medication adherence for diabetes, hypertension, and high cholesterol in nearly all of its regions. This level of achievement reflects a comprehensive strategy that includes multiple interventions and the whole-system approach to tackling medication non-adherence.

65. The pharmaceutical industry is investing in the use big data for improving the understanding of patient non-adherence. For example, Sanofi has been working with the Duke Clinical Research Institute (DCRI) and the Center for Assessment Technology and Continuous Health (CATCH) in the United States on tools to help predict how people with type-2 diabetes will adhere to their medication. Another example is the partnership between Novo Nordisk, IBM Watson, and Glooko, which will combine Novo Nordisk's insulin therapy and education expertise, Glooko's software, apps, and data expertise, and IBM Watson's intelligent computing power to create personalised digital tools, and even a virtual "diabetes coach". One of the goals of this partnership is to improve adherence to insulin therapy among patients with diabetes.³

³ https://www.novonordisk.com/bin/getPDF.2069517.pdf

66. There are also technological advances that attempt to facilitate remote patientprovider interactions, depending upon the desired level of involvement. Consumer eHealth tools and mobile phone applications represent an attempt to nudge patients to play a more active role in managing their medication. These tools, for example, provide electronic reminders, allow patients to track their adherence, and provide real-time information back to the provider for intervention and/or targeted follow-up. The motivation behind such interactive capabilities comes from the known association between patient engagement and improved treatment adherence.

67. Innovation has also taken place in the form of smart digital pills, and mobile technology. Proteus Digital Health, for instance, has developed digital pills with embedded ingestible sensors, which track medication adherence and send data to a provider or care giver. Another example is the smart pill bottle - developed by Adhere Tech – that lights up, buzzes, and sends text and voice messages to remind patients of their pre-scheduled dosages. There are also solutions that could prove appropriate for patients who are unintentionally non-adherent due to forgetfulness and lack of planning. Care4Today[™] Mobile Adherence – a secure messaging platform, mobile application, and website – is designed to improve adherence to treatment regimens through reminders to take medications, refill prescriptions, and visit healthcare providers. The mobile platform is developed by Janssen Healthcare Innovation and is product agnostic. Theses examples are just a few to illustrate industry led innovations. However, these have not been fully evaluated with regard to their effectiveness and cost-effectiveness yet. Such data could be useful for assessing in what ways payers/system designers and industry could partner to encourage adherence.

5. WHAT ARE THE ENABLERS FOR EMBEDDING MEDICATION ADHERENCE IN HEALTH SYSTEMS?

68. As this working paper and many studies have shown, persistent poor adherence to medications is associated with poor health outcomes and increased health expenditure, especially among patients with chronic diseases. While much progress has been made in improving outcomes across the board, greater efforts to maximise the value of medications must be made if we are to close this gap. This report has identified four enablers that could embed improved medication adherence at the system level. These actions can be summarised as: Acknowledging, Informing, Incentivising, and Steering and Supporting. No single intervention will guarantee that patients fill their prescriptions and take their medications as prescribed. The identified actions must be combined with a strong patient-centred focus and involve all actors.

69. The evidence demonstrates that adopting a person-centred approach for medication use that incorporates patient beliefs, preferences, goals, and barriers to medication-taking (e.g., costs, technological ability, concerns about medication use) leads to better health outcomes. Addressing the adherence issue, however, requires the involvement of all health system actors working as a team, with patients as the main player. Policy makers, health/social-care organisations and professionals, payers, health-workforce educators, professional/regulatory bodies, the research community, as well as the industry need to be involved.

5.1. Acknowledging: Medication adherence needs to be on the policy agenda

70. Medication non-adherence leads to poor health outcomes and increases healthcare costs among patients with the three most prevalent chronic conditions. Medication non-adherence is a problem that applies to all chronic diseases, diminishing the ability to treat not only diabetes or heart disease, but also osteoporosis, asthma, and many other diseases and results in suffering, death, and suboptimal utilisation of health care resources. Although the challenge of poor medication adherence has been discussed and debated for at least four decades, the problem has generally been overlooked as a health care priority. Compounding the situation, adherence problems have been exacerbated by limited evidence on how to improve it cost-effectively as well as the fragmented approach by which hospitals, primary health care organisations, and other parts of the health system interact with patients and providers to encourage adherence. Medication adherence should be elevated as an important health care issue and be on the policy agenda in order to develop a systematic approach to improving it.

71. Despite this profound impact, patient adherence is not on the radar of policy makers and many health professionals, which has meant inconsistent government policies and a lack of resources for research, education, and professional development.

72. Due to the limited visibility of adherence on health-policy agendas, the research on effectiveness of initiatives is incomplete and the cost-effectiveness of interventions is

rarely evaluated. Individual interventions are piloted and then discontinued as budgets and priorities shift before their impact is known. Successes are not always expanded across the system. Even the most successful interventions tend to be low in effectiveness. This may often be due to a lack of recognition of the root causes of discontinuing and not adhering to treatment and failing to address the issue holistically.

73. The existing evidence suggests that no single strategy will guarantee that patients fill their prescriptions and take their medications as prescribed. Therefore investment in multifaceted interventions addressing health system in general and interaction with health professionals in particular are most promising. The research in this field still needs advances such as more objective adherence measures, improved design of long-term interventions, and larger patient groups to provide stronger evidence base (Kardas et al., 2013; Clyne et al., 2016; Nieuwlaat et al., 2014)

5.2. Informing: The need for routine monitoring and reporting of adherence

74. Very few countries measure and report adherence and persistence measures routinely at the system level. Developing and reporting adherence measures as quality improvement indicators or as performance measures could help in improving health system efficiency. These measures need to be comparable in order to benchmark and assess best practice between countries and interventions. The OECD can take stewardship of developing these indicators as part of the Healthcare Quality and Outcomes work.

75. Reporting of medication adherence measures could serve two main purposes: to provide transparency and inform decision-making about overall priorities and systemlevel strategies; and to inform quality improvement activities of service providers. In order to achieve these purposes a combination of both national level reporting and reporting at lower levels, for example, at the local or provider level, would be useful.

76. Measuring the quality of care provided to patients is an increasingly common element of evaluating and improving healthcare delivery. Measuring and reporting defining performance indicators allows making policy priorities explicit, responsibilities/expectations, facilitating accountability, and focusing resources. Measuring alone is insufficient, rather the public reporting of performance data has been recommended as one key strategy for stimulating improvement of quality of care by putting the focus on transparency and accountability of healthcare providers. The introduction of public reporting programmes at different levels of the health sector is a challenging but rewarding strategy. Existing research covering different clinical outcomes supports the idea that public reporting could, in fact, stimulate providers to improve healthcare quality.

77. There is a scope for cross-national comparisons of adherence rates and empirical analyses of the causes of differences between countries so that lessons can be learned from those countries with the best adherence rates, including how they have used different policy and interventions.

78. Data on adherence and the technology infrastructure provide support for further interventions to boost adherence such as personalised support for patients who experience problems with adherence. When medication-use information is shared electronically, prescribers can assess a patient's medication regimen at the point of care and identify non-adherence. Electronic systems may also be able to notify a prescriber or a pharmacist about refills, which can help trigger an intervention to avoid a potential gap in medication use.

5.3. Incentivising: Changes in financial incentives for providers and patients are key

79. Shifting to payment systems that reward providers for better patient outcomes is critical to providing the incentives and investments that are required for improving adherence. Health professionals, prescribing clinicians especially, face serious limitations in promoting adherence, including reimbursement schemes that reward brief encounters with patients and do not reimburse services like counselling and motivational discussions with patients. As a result, there is a limited scope for the discussion of individual aspects of a patient's condition and personalisation of the medication regimen.

80. Rewarding the time spent by health professionals on resolving patient concerns about medications does not necessarily create a financial burden on organisations and providers but, by facilitating treatment adherence, it can significantly improve health outcomes and reduce total treatment time and costs. The clinically significant gain in involving patients occurs in terms of obtaining information that is crucial to understanding and managing patient needs. The data generated from person-centred communication can lead to a better understanding of specific approaches that work best for an individual patient (Reiss-Brennan et al., 2016). Evidence suggests that the physicians' "whole person" knowledge of patients increases the number of patients adhering to the recommended course of treatment by 50 to 230% (Safran et al., 1998; Stweart et al., 2000; Nieuwlat et al., 2014). In general, an investment in person-centred communication and shared decision-making has positive effects for patients' long-term health status, improves the patient-provider working relationship, and, ultimately, patient as well as practitioner satisfaction (Lein & Wills, 2007).

81. The existing provider payment-related constraints undermine also the effectiveness of other adherence-improving initiatives such as physician access to electronic pharmacy records. Studies have shown that despite the ability to electronically review adherence through pharmacy refill records of medications at the time of the patient visit, the primary-care providers' assessments of adherence did not agree with the more objective pharmacy fill assessments about half of the time. A reason for this has been that the review of such refill records requires time, for which primary care doctors are not reimbursed (Meddings et al., 2012).

82. Reducing patient co-payments for highly effective chronic therapies can substantially improve adherence, especially in countries with high co-payments. Providing financial rewards for better adherence may be an even more effective mechanism to promote behaviour change. It is, however, a concept that needs further research to understand its long-term effectiveness and cost-effectiveness.

83. There are arguments for medication adherence becoming part of a reimbursement system founded on value-based pricing and performance-based contracting with pharmaceutical companies. Examples of such contracts are in place and it would be useful to review the impacts of such agreements.

5.4. Steering and Supporting: The need to remove system-level barriers to adherence and improve patient-provider interactions

84. The adherence process begins with an individual patient and a prescribing clinician and a dispensing pharmacist, who should be supported by a suite of interventions/tools developed by other health system stakeholders: payers/system designers, health educators, professional regulatory bodies, and the industry.

85. Payers/system designers should focus on removing system-level features that create practical barriers to adherence. This means investing in information technology systems that, among other functions, ease the providers' access to and review the complete information on patients' medication regimens in one place. Interventions should also address barriers faced by patients such as cumbersome procedures for routine renewing/refilling of prescriptions for long-term therapies. Initiatives like long-term medication supply, online refills of prescriptions, and calendarised blister packaging all have been shown to improve adherence. Simpler interventions that focus on improving adherence by providing behavioural nudges, when broadly implemented on a population level, may provide substantial cumulative public health benefit by significantly leveraging therapeutic efficacy.

86. The limited support patients receive with their medicine taking is in part due to health professionals rarely receive formal training in how to assess and tackle the problem. There is a strong case for educators to reflect on the nature and the extent of the education and training provided to healthcare professionals for supporting patients in their use of medicine.

87. Improving how patients take their medicines requires that health professionals are equipped with skills specific to delivering care in the person-centred instead of the disease-centred model, i.e. that the providers should seek and gain an understating of the patients' individual needs, perspectives, and values, convey to patients the information they need to participate in their care, and build trust and understanding (ABC Project, 2012; White et al., 2012). The goal in the skills development is to ensure the patients' narratives about their experience of illness are cost-effectively translated into improved care plans, i.e. that the time investment and the quality of patient assessment become optimally balanced.

88. Health professionals also need support through evidence-based tools such as clinical guidelines. In particular, clinical guidelines developed for the purpose of a personalisation of treatment are needed. Clinical management in the context of multimorbidity and polypharmacy requires the person-centred approach and can be a challenge for clinicians. Similarly, a challenge is posed by the growing number of patients with chronic conditions in nearly all age groups along with the expanding number of medications, often involving different mechanisms of action and safety profiles. Some patient characteristics support more and other support less aggressive therapy. Specifically for patients with long life expectancy and without disease complications a more aggressive medication could be more suitable than for older patients with comorbidities or low ability to safely follow the more intensive therapy. Developing toolkits that guide clinicians through the process of establishing therapy goals and matching patients to therapies can be useful in supporting adherence.

89. Engaging patients in an open, transparent manner might lead to discussing with them complex health-care choices, for instance, adverse-effect profiles of different medications or risks related to different dosing regimens. In order to facilitate such discussions without undue burden, health professionals need support in form of decision aids – written materials, videos, or interactive electronic presentations designed to inform patients about care options and guiding patient-provider discussions. The decision aids should be certified or issued by professional regulatory bodies to assure that they are evidence-based, balanced, and able to meet patients' informational needs.

90. There is also a scope for the industry to contribute with innovative solutions such as simplified medication regimens, smart pills and packaging, or technological advances (e.g. apps) that could facilitate the follow-up on adherence. These solutions might ease following the therapy, facilitate remote patient-provider communication, provide electronic reminders to patients, or allow patients to track their adherence.

6. CONCLUSIONS

91. The potential benefits of enhancing medication adherence as a health care priority are considerable. Poor adherence to medications among patients with chronic diseases is a lost opportunity in terms of maximising health outcomes and health system efficiency. This is pertinent given the small percentage of patients with chronic disease who do take their medications as prescribed.

92. Non-adherence to medication is a multidimensional health care problem. The causes may be related to the patient, treatment, disease, health care provider and the health system. There is variation in the extent of initiatives to promote medication adherence among OECD countries. Most initiatives are focused on pharmacist delivered interventions.

93. This report has set out a number of key enablers for sustaining a medication adherence strategy, which should be the focus for any leadership team wishing to embed and sustain rational use of medicines strategy. These actions can be summarised as: Acknowledging; Informing; Incentivising; Steering and Supporting. Addressing nonadherence through a patient-centred approach to health care necessitates the involvement of all health system stakeholders: patients, policy makers, health care organisations and professionals, payers, educators, professional regulatory bodies, industry and the research community. In order to mobilise them, medication adherence needs to be placed on the national policy agenda, starting with adherence being routinely observed and continuing towards the development of adherence quality and performance indicators. Such indicators could help in improving health system efficiency through establishing and influencing the relationship between the spending on pharmaceuticals and the gains in health outcomes. Improving how patients take their medicines requires that health professionals are equipped with skills specific to delivering care in a person-centred instead of the disease-centred model, i.e. that the providers should seek and gain understating of patients' individual needs, perspectives, and values, convey to patients the information they need to participate in their care, and build trust and understanding.

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