

Effects of Electronic Prescribing on Adherence to Prescribed Medications in Community Settings: A Systematic Review

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Submitted to: Journal of Medical Internet Research
on: March 19, 2025

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Abstract

Background: A vast body of research highlights the development of medications with proven efficacy, yet the translation of these benefits into clinical practice is hindered by low adherence rates, particularly among those with chronic illnesses. Nonadherence not only compromises treatment effectiveness but also amplifies healthcare costs and complicates disease management. Medication adherence rates remain suboptimal, necessitating multifaceted strategies to address patient, physician, and system-related factors in community settings. Electronic prescribing (e-prescribing) emerges as a promising solution, offering numerous advantages such as enhanced efficiency, reduced errors, and improved adherence. However, the comparative impact of electronic versus paper prescriptions on medication adherence remains underexplored, prompting the need for systematic reviews to inform healthcare practices and interventions.

Objective: The objective of the study is to systematically review and summarize current evidence regarding the effect of e-prescriptions on adherence to prescribed medications compared to paper-based prescriptions.

Methods: This review employed a comprehensive search strategy across multiple databases, with inclusion criteria focused on outpatient studies published since 2010. Data extraction followed a rigorous two-level screening process, where titles, abstracts, and full texts were assessed for eligibility by independent reviewers. Grey literature was also searched using established methods. Data extraction involved collecting information on study methods, participants, interventions, outcomes, and other relevant details.

Results: Out of 1801 initially identified articles, 39 underwent full-text review, with 15 included in the qualitative synthesis. These studies, predominantly from the USA, varied in design and sample size. While 60% favored e-prescriptions, 20% favored traditional prescriptions, and 20% found no significant difference. Favorable outcomes for e-prescriptions included improved adherence rates. Studies favoring traditional prescriptions highlighted factors like claim reversals and primary non-compliance. Several studies found no significant difference in adherence between electronic and traditional prescriptions.

Conclusions: While some evidence suggests that e-prescriptions alone reduce primary nonadherence risk, many successful studies showing improved adherence used additional components like electronic health records (EHR) and decision support systems. These components, such as formulary decision support and patient adherence information, were reported to be associated with better adherence outcomes. Conversely, studies with no or unfavorable effects on e-prescriptions often lacked such additional components and focused on issues like prescription abandonment. The review underscores the importance of a comprehensive approach to e-prescription implementation, integrating self-management tools, and behavioral interventions to maximize adherence benefits in community settings.

(JMIR Preprints 19/03/2025:73599)

DOI: <https://doi.org/10.2196/preprints.73599>

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Original Manuscript

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Created by: Medication Adherence Review team, Health Information Research Unit, McMaster University

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A vast body of research highlights the development of medications with proven efficacy, yet the translation of these benefits into clinical practice is hindered by low adherence rates, particularly among those with chronic illnesses. Nonadherence not only compromises treatment effectiveness but also amplifies healthcare costs and complicates disease management. Medication adherence rates remain suboptimal, necessitating multifaceted strategies to address patient, physician, and system-related factors in community settings. Electronic prescribing (e-prescribing) emerges as a promising solution, offering numerous advantages such as enhanced efficiency, reduced errors, and improved adherence. However, the comparative impact of electronic versus paper prescriptions on medication adherence remains underexplored, prompting the need for systematic reviews to inform healthcare practices and interventions.

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The objective of the study is to systematically review and summarize current evidence regarding the effect of e-prescriptions on adherence to prescribed medications compared to paper-based prescriptions.

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Results

Out of 1801 initially identified articles, 39 underwent full-text review, with 15 included in the qualitative synthesis. These studies, predominantly from the USA, varied in design and sample size. While 60% favored e-prescriptions, 20% favored traditional prescriptions, and 20% found no significant difference. Favorable outcomes for e-prescriptions included improved adherence rates. Studies favoring traditional prescriptions highlighted factors like claim reversals and primary non-compliance. Several studies found no significant difference in adherence between electronic and traditional prescriptions.

Conclusions

While some evidence suggests that e-prescriptions alone reduce primary nonadherence risk, many successful studies showing improved adherence used additional components like electronic health records (EHR) and decision support systems. These components, such as formulary decision support and patient adherence information, were reported to be associated with better adherence outcomes. Conversely, studies with no or unfavorable effects on e-prescriptions often lacked such additional components and focused on issues like prescription abandonment. The review underscores the importance of a comprehensive approach to e-prescription implementation, integrating self-management tools, and behavioral interventions to maximize adherence benefits in community settings.

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Introduction

Medication Adherence refers to how closely a person's actions, such as medication intake, dietary adherence, and lifestyle adjustments, align with the agreed-upon recommendations from a healthcare provider (World Health Organization, 2003) and low adherence to prescribed medications is a concern for both acute and chronic conditions (Vermeire et al., 2001). A large body of research has contributed to the development of medications with proven efficacy and positive benefit-to-risk profiles. Clinical trials demonstrating the efficacy of these medications are typically followed closely to assure high adherence, however benefits are often greatly reduced or nullified in usual clinical practice where adherence rates are low (Nieuwlaat et al., 2014). Therefore, adherence is a vital link between an efficacious treatment and optimal patient outcomes (Brown & Bussell, 2011).

Despite the expansion of effective self-administered pharmacotherapies for many conditions, medication adherence rates remain variable and have not changed significantly over time; adherence rates averages around 50% and can range between 0% to over 100% (Choudhry et al., 2022; Cramer, 2004; Gialamas et al., 2009; Haynes et al., 1979; Naderi et al., 2012). In addition to potentially undermining the effectiveness of any treatment, nonadherence is associated with poorer prognoses, increased cost, enhanced complexity of disease management, and biased treatment effect estimates (Brown et al., 2016; Irvine et al., n.d.; Kane & Shaya, 2008; Osterberg et al., n.d.). Due to the scale and severity of medication non-adherence, evidence suggests that increasing adherence to interventions will have a greater impact on population health compared to intervention improvements, alongside substantial economic benefits (Haynes et al., 2000; Hubbard. E. Thomas, 2014; World Health Organization, 2003).

Current methods of improving medication adherence for chronic health concerns are often complex, labor-intensive, and ineffective. Cochrane review by Nieuwlaat et al. of 78 randomized trials found no simple intervention and only a few complex interventions to be effective at improving long-term medication adherence and health outcomes (Nieuwlaat et al., 2014). Strategies to improve adherence must address multiple factors, including patient-related factors, physician-related factors, and health system/team building-related factors (Brown & Bussell, 2011; World Health Organization, 2003). Creation, transmission, interpretation, and utilization of a medication prescription is a common theme among these proposed solutions.

Traditionally, prescriptions are written on paper and transmitted manually or via facsimile to the

dispensing pharmacy. In contrast, electronic prescribing (e-prescribing) encompasses computer-based systems to write drug prescriptions or support prescribing. E-prescribing is generally defined as the creation and transmission of a prescription or prescription-related information between a prescriber and dispenser (CMA & CPA, 2012). E-prescription is defined as the secure electronic process of creating and sending a prescription from an authorized prescriber to a patient's chosen pharmacy using clinical point-of-service (POS) solutions, seamlessly integrating clinical workflow and software (CMA & CPA, 2012; PrescribeIT, n.d.). E-prescribing systems can be incorporated into electronic health record (EHR) systems or be stand-alone systems in the ambulatory care setting (Porterfield et al., 2014). The application of stand-alone systems is limited to generating prescriptions, while -integrated systems closely interact with other components of an EHR, including computerized decision support, formulary, and safety alerts (DesRoches et al., 2010).

E-prescribing has been associated with several benefits, including improving health care services quality, increasing efficiency in prescribing and dispensing medications, promoting formulary adherence, reducing medication errors, enhancing health care cost savings, and increasing adherence to prescribed medications (Ababneh et al., 2020; Esmaeil Zadeh & Tremblay, 2016; Jani et al., n.d.; Lanham et al., 2016; McInnes et al., 2017; McMullin et al., 2004; Shawahna et al., 2011; Thatcher & Acharya, 2020; Vejdani et al., 2022). Benefits associated with e-prescribing vary depending on solution functionality, workflow integration, and other factors. A preliminary literature search revealed that most studies focused on the efficiency of the prescription process, stakeholder satisfaction, medication safety, and error minimization. There was a paucity of evidence that compared medication adherence rates between paper and e-prescriptions, especially in community settings. The only observed systematic review was narrowly focused on primary medication adherence and excluded important patient outcome measures, such as patient satisfaction (Aluga et al., 2021). Therefore, this systematic review was conducted to summarize current evidence on the effect of e-prescriptions medication adherence compared to paper-based prescriptions in community outpatient settings.

Methods

This systematic review followed the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) and Synthesis without Meta-analysis (SWiM) reporting guidelines (Campbell et al., 2020; Page et al., 2021). The focussed research question addressed by this review was: *What is the effectiveness of e-prescribing interventions (I) as compared to traditional prescribing (C) on patient adherence to prescribed medications (O) in a community setting (P)?*

Information sources and search strategy

Keywords and phrases identified from the PICO components, relevant synonyms, and Medical Subject Headings (MeSH) were combined using appropriate Boolean searches to create a custom literature strategy. We searched The Cochrane Library (via Wiley), MEDLINE, and Embase (via Ovid). We completed database searches for relevant articles on February 13, 2023. Reference lists of identified systematic reviews were also searched for inclusion in the screening process. The search strategy is available in Appendix A.

Inclusion and Exclusion Criteria

Complete inclusion and exclusion criteria are in Table 1. Studies were included if they satisfied all the criteria. We sought to include primary experimental and observational quantitative primary

studies on outpatients. Studies that solely reported on hospital inpatients were excluded. Since medication adherence is reported in a variety of measures in the literature, we sought to include studies that reported on any medication adherence measures such as pill counts, refill records, and or patient-important outcomes (BP, CD4 counts, patient satisfaction etc.)

Table 1: Inclusion and Exclusion Criteria

Component	Inclusion criteria	Exclusion criteria
Population	Outpatients, primary care	Inpatients
Intervention	Electronic prescription	
Comparator	Handwritten or paper-based prescribing	
Outcome	Any medication adherence measure and / patient important outcome	
Study design	Quantitative primary studies (experimental and observational), peer reviewed and non-peer reviewed reports	
Time of study	No limits*	
Language	English	Non-English publications
Location	No limits	

*Our target was to identify studies published since 2010 because we anticipated that most large-scale e-prescription implementations would post-date that year but did not enforce the limit on the search strategy so that relevant studies completed prior to this date were not missed.

We searched for grey literature via multiple methods. Primarily, we followed the Canadian Agency for Drugs and Technologies in Health (CADTH) guide to searching grey literature (CADTH Research Information Services, 2019). We also identified the websites of national health agencies and forums concerned with the prescription process in the USA, Canada, Australia, and European jurisdictions via Google searches and searched within the respective web domains for any relevant proceedings, reports, or white papers.

Study Selection

Citations retrieved were assessed in a two-level review process. At the first level, titles and abstracts of identified citations were screened based on the inclusion and exclusion criteria. This was followed by the full-text screening of citations that successfully passed the first-level screening. At each level, citations could be marked 'excluded,' 'included,' or 'undecided.' Two independent reviewers assessed eligibility during all screening stages, and an adjudicator resolved any disagreements. We used DistillerSR, a web-based systematic review software, to facilitate screening, data extraction, and adjudication of disagreements (Harrison et al., 2020).

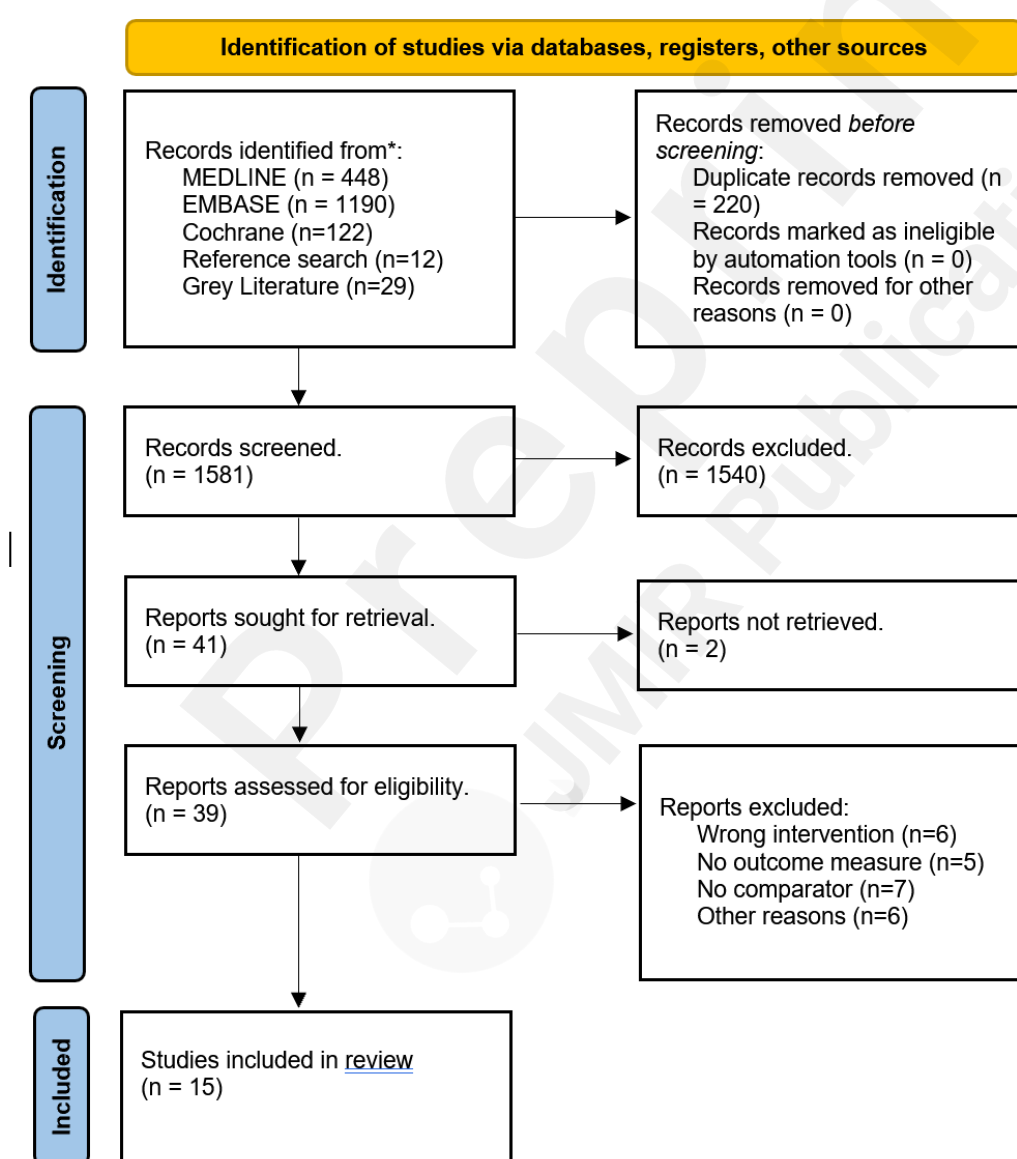
Data Extraction

Studies that passed the two-level screening were then moved to data extraction. We created and piloted a custom template to extract relevant information from the included studies. Extracted data included study methods, participants, study design, sample size, setting, interventions, outcomes, study duration, and additional notes pertaining to any of the aforementioned items. Two reviewers independently extracted all data, and a third adjudicator resolved disagreements.

Results

Study Selection

Figure 1: Study flow diagram illustrating the screening and selection process.



A total of 1760 articles were identified through a systematic search of databases (MEDLINE = 448; EMBASE = 1190 and Cochrane database = 122). An additional 41 articles were identified via grey literature search and reference searching, bringing a total of 1801 items identified. After removing duplicates, 1581 articles were subjected to level 1 screening of which 1540 were excluded. We

sought to retrieve full-text documents of the remaining 41 articles, 2 of which were unobtainable. The remaining 39 articles were screened based on the inclusion and exclusion criteria, 15 of which were included in the final review.

Characteristics of Included Studies

Study characteristics are summarized in Table 2. All the included studies were peer-reviewed journal articles. Eleven studies (73%) employed observational study designs (cross-sectional, retrospective cohort, and case-control) (Adamson et al., 2017; Anderson et al., 2015; Bergeron et al., 2013; Ekedahl & Månsson, 2004; Fischer et al., 2011; Forestal et al., 2016; Hou et al., 2012; Michelis et al., 2011; Pevnick et al., 2014; Shrank et al., 2010; J. Y. Smith et al., 2016). The remaining 4 (27%) studies were randomized controlled trials (Del Ma et al., 2003; Fernando et al., 2012; Hill et al., 2010; Williams et al., 2010). Eleven (73%) of the studies were conducted in the USA, one in Sweden, and one in Australia. The remaining three studies did not declare their country setting explicitly and were labeled as location not specified. The included studies reported population sample sizes ranging from 143 patients to 10 million index prescriptions.

Table 2: Characteristics of Included Studies

Primary Author	Publication type	Year	Study design	Country	Population/sample size	Duration of study
Smith J.Y.	Journal article	2016	Retrospective cohort	USA	25229 providers	January 2009 to December 2011
Forestal	Journal article	2016	Cross-sectional study	USA	148,325 prescriptions	September, 2014
Hou	Journal article	2012	Retrospective cohort	NS	7120 patients	April 1, 2009 to March 31, 2011
Michelis	Journal article	2011	Retrospective cohort study	USA	2218 patients	Calendar year 2017
Williams	Journal article	2010	Randomized controlled trial	USA	2698 patients	August 1, 2007 to July 31, 2008 (12 months)
Hill	Journal article	2010	Randomized controlled trial	USA	245 patients	March 2007 to September 2008 (19 months)
Bennett	Journal article	2003	Randomized controlled trial	Australia	179 patients	6 months
Adamson	Journal article	2017	Retrospective cohort	USA	2496 patients	January 1, 2011 to December 31, 2013
Anderson	Journal article	2015	Retrospective cohort	NS	143 patients	3 months
Bergeron	Journal article	2013	Cross-sectional study	NS	344 patients	September 2009 to March 2011
Ekedahl	Journal article	2004	Cross-sectional study	Sweden	411818 prescriptions	March 2000 to May 2000
Fernando	Journal article	2012	Randomized controlled trial	USA	10349139 prescriptions	June 22, 2010 to December 25, 2010
Pevnick	Journal article	2014	Case control	USA	12,389 prescriptions	June 3, 2003 to July 21, 2006
Shrank	Journal article	2010	Cross sectional study	USA	10349139 prescriptions	July 2008 to September 2008

Fischer	Journal article	2011	Cross sectional study	USA	280081 patients	July 2007 to July 2009
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Summary of results from included studies

A summary of the findings from the included 15 studies are presented in Table 3. All the studies used e-prescribing as the intervention and paper and/or other prescription transmission methods (e.g. telephone, telefax, pharmacy orders) as the comparison. E-prescribing was used either as a stand-alone system or integrated with EMR. Different measures of medication adherence were used, such as self-reporting, pharmacy records, claim data, and patient interviews. Nine studies (60%) reported results favouring e-prescriptions while 3 (20%) were against. The remaining 3 studies (20%) found no significant difference in medication adherence between e-prescriptions and traditional prescriptions.

The results of the included studies vary significantly in the PICO measure, preventing the completion of a meta-analysis. The heterogeneous nature of the research methods also prevented a formal assessment of the quality of the evidence. The included articles are summarized below.

Studies that favour e-prescriptions

Smith et al. (2016) analyzed pharmacy fill data from SureScript and provider enrollment records from January 2009 to December 2011. They compared differences before and after adoption of e-prescribing among prescribers, looking specifically at 90-day retail fills, initial fills (primary adherence), and subsequent refills between the treatment group (adopters of e-prescribing) and the control group (non-adopters). comprised 6295 providers, while the control arm comprised 18934 providers. E-prescribers demonstrated significantly higher rates of 90-day retail fills (+2.8 fills per provider, $P < .001$), primary adherence (+12.0 fills per provider, $P < .001$), and subsequent adherence (second fill: +4.5 fills per provider, $P < .001$; and third fill: +2.4 fills per provider, $P < .001$) compared with non-e-prescribers. They concluded that provider adoption and the use of e-prescribing applications with formulary decision support were associated with significant prescriber and patient behavior change in a large, nationally representative population.

Hou et al. (2012) conducted a retrospective analysis using de-identified pharmacy claims data from a pharmacy benefit manager between April 1, 2009, and March 31, 2011, to assess medication adherence rates of patients utilizing an online prescription management account compared with non-users. The eight therapeutic groups examined were antidepressants (58), antidiabetics (27), antihyperlipidemics (39), antihypertensives (36), beta blockers (33), diuretics (37), thyroid agents (28), and ulcer drugs (49). Adherence was measured using the proportion of days covered (PDC). Results were reported for all therapeutic groups combined and stratified by individual therapeutic groups. Overall, patients utilizing the online account had a significantly higher weighted average PDC (73.19% vs. 61.64%, $P < .0001$). Users exhibited a higher average PDC across all therapeutic groups, apart from the beta-blocker group, which did not reach statistical significance. The percentage of patients achieving an average PDC of $>80\%$ was also greater in the users' group across each therapeutic group.

Michelis (2016) conducted a retrospective cohort study by querying the electronic medical records of a single multispecialty outpatient academic medical practice to identify patient encounters during which consecutive lipid panels were drawn in 2007 ($n = 2218$). Logistic regression was used to examine whether the odds of reaching LDL goals were influenced by e-prescribing and adjusted for

characteristics, such as physician age and speciality, known to affect prescribing patterns and goal attainment. Of the 796 patients not initially at LDL goal, 393 (49%) were at goal at follow-up. 51% of these patients were in the e-prescription group vs. 44% in the manual prescription group. Patients with an e-prescription were 59% more likely to attain their guideline-based LDL goal (odds ratio [OR] = 1.59; 95% confidence interval [CI]: 1.12–2.25). The authors suggested that superior LDL goal attainment may be attributed to the lower cost of medications. Patients with an e-prescription were significantly more likely to receive a generic, more affordable, statin than patients with a manual prescription (38.0% vs. 22.9%; $P = 0.0004$).

Williams et al. (2010) assessed the effect of using an e-prescribing application in a cluster randomized controlled study that supplied patient adherence information to primary care providers on inhaled corticosteroid (ICS) nonadherence. Providers (88 intervention; 105 control) and patients (1335 intervention; 1363 control) were randomized together by practice. Patients were aged 5 to 56 years, had a diagnosis of asthma, and had existing prescriptions for ICS medication. Adherence was estimated using prescription and fill data. In contrast to clinicians in the control arm, providers in the intervention arm had access to updated information on patient ICS adherence through an electronic prescription software. They could also access additional details about patient ICS use by selecting an option that inferred clinician intent. Detailed adherence information viewed by their primary care provider in the first 9 months had significantly higher adherence at the study end compared with patients in the intervention arm whose provider did not view adherence information (35.7% vs. 12.3%; $P = .002$) and compared with patients in the control group (35.7% vs. 23.3%; $P = .026$). Clinician intent was inferred by the type of adherence information viewed, either general or detailed. While general adherence data was readily available whenever the e-prescribing application was opened, merely viewing it did not necessarily indicate an intention to engage with or act upon the information. Conversely, accessing detailed adherence information required an extra step of selecting a separate link after encountering the general adherence message, implying that the clinician was specifically interested in obtaining further insight into the patient's medication usage pattern.

Hill et al. (2010) in a randomized controlled trial, assigned 245 patients between 19–50 years of age who underwent annual gynecologic examinations to either verbal counseling about the use of calcium carbonate with vitamin D supplement ($n=122$) or verbal counseling and an e-prescription ($n=123$). Telephone interviews at 3 and 6 months determined compliance. At 3 months, 66.0% of women who received an e-prescription reported compliance ($P = .001$) compared to the control group which reported that 28.4% of women were compliant. E-prescriptions were 2.2 times more likely to report taking the calcium than control subjects, who did not receive the e-prescription (95% confidence interval, 1.5–3.1).

Adamson et al. (2017) conducted a retrospective review of medical records between January 1, 2011, to December 31, 2013 among a cohort of new patients prescribed dermatologic medications at a single, urban, outpatient dermatology clinic to study whether e-prescribing affects rates of primary nonadherence. The primary outcomes were the overall rate of primary nonadherence, defined as filling and picking up all prescribed medications within a 1-year period, and the difference in primary nonadherence between patients who received e-prescriptions and those who received paper prescriptions. A total of 4318 prescriptions were written for 2496 patients (mean [SD] age, 47.7 [13.2] years; 849 men and 1647 women). The overall rate of primary nonadherence was 31.6% ($n = 788$). Based on multivariable analysis, the risk of primary nonadherence was 16 percentage points lower among patients given an e-prescription (15.2%) than patients given a paper prescription (31.5%).

Anderson et al. (2015) conducted a retrospective review of medical records from an outpatient

dermatology clinic to estimate acne treatment primary nonadherence rates and to determine the relationship between primary nonadherence and the number of acne treatments prescribed. The primary study outcomes were the overall rate of primary nonadherence and the rate for each treatment-number subgroup. Secondary outcomes included the association of sex, age, medication type, and e-prescription status with primary nonadherence. Four patients (9%) who were given 1 treatment, 19 (40%) who were given 2 treatments, and 15 (31%) who were given 3, or more, treatments did not fill all their prescriptions. Univariate analysis showed less primary nonadherence with e-prescriptions than paper prescriptions ($P < .001$).

Pevnick et al. (2015) conducted a retrospective analysis of 14,682 initial pharmaceutical claims for angiotensin receptor blockers and inhaled steroid medications among 14,410 patients of 2189 primary care physicians (PCP) to assess the effect of e-prescribing with formulary decision support on preferred formulary tier usage, copayment, and concomitant adherence. Adherence was quantified using the proportion of days covered (PDC). They projected that a patient of a PCP who frequently used e-prescribing would report an increase in PDC of 3.6% when compared to patients whose PCPs did not use e-prescribing frequently.

Fischer et al. (2011) retrospectively analyzed e-prescribing data and filled claims for all patients who received e-prescriptions from an e-prescribing system in the calendar year 2008. Among other characteristics, they classified prescriptions based on method of prescription delivery, including whether it was printed for the patient, transmitted electronically to the pharmacy, or transmitted directly to a mail-order service. The main analysis evaluated primary nonadherence for newly e-prescribed medications, defined by no filled claims in the prior 6 months. They compared primary nonadherence rates across prescriber, patient, and prescription characteristics. They reported that prescriptions that were transmitted electronically to the pharmacy had 46% lower odds of being unfilled than those that were printed.

Studies that favoured traditional prescriptions

Forestal et al. (2016) conducted a cross-sectional study using a sample of reversed claims from the Pharmaceutical Assistance Contract for the Elderly (PACE) program for September 2014 to assess whether prescription origin is among the factors associated with initial medication adherence, using claim reversals as a proxy measure. The total number of reversed claims for new prescriptions (15,966) was categorized by prescription origin (written, telephone, electronic, fax, and pharmacy). Using a chi-square analysis, the reversed claims were compared among prescription origins to determine if there was a difference in the proportion of e-prescriptions reversed compared with those from another origin. When compared with all other prescription origins, e-prescriptions (E) were more likely to be reversed at day 0 ($E=50\%$, any other [AO]=49%, $P<0.05$) and after day 0 ($E=58\%$, [AO]=42%, $P<0.05$). They found that e-prescriptions are associated with a higher rate of claim reversals, potentially indicating lower initial adherence. This could be due to patient forgetfulness, and/or prescriptions not being presented to the pharmacy by the patient. The growing adoption of e-prescriptions merits particular attention since it may be a factor in initial medication adherence in the elderly.

Ekedahl (2004) conducted a cross-sectional study in 3 healthcare districts (population 240,000) in the southernmost part of Sweden on unclaimed e-prescriptions transmitted to 21 pharmacies during a period of 3 months (2000). This study also included semi-structured interviews with patients not claiming their e-prescriptions transmitted to 4 pharmacies during a period of 3 weeks (2001) to assess the extent of and the reasons for unclaimed prescriptions, primary non-compliance, after

automated transmittals to pharmacies. The main outcome measure was the proportion of unclaimed e-prescriptions. In total, 2171 (2.37%) e-prescriptions remained unclaimed at the pharmacies. From March through May 2000, 89,533 e-prescriptions were dispensed, constituting 21.7% of all dispensed prescriptions. In total, 2,171 unclaimed e-prescriptions to 1,893 patients were identified. The non-redeemed e-prescriptions constituted 85.4% of all unclaimed prescriptions and 2.37% of all e-prescriptions. There was a large variation in the proportion of e-prescriptions out of all dispensed prescriptions between the participating pharmacies (range 5.9; 40.0%), and the primary non-compliance rate per pharmacy varied 3-fold, from 1.4 to 4.2% ($2.42 \pm 0.72\%$; mean $\pm$ SD). However, there were no correlations between primary non-compliance rates, whether to pharmacy size or the ratio of e-prescriptions/all dispensed prescriptions.

Shrank et al. (2010) conducted a cross-sectional cohort study to evaluate the rates and correlates of prescription abandonment. Retail pharmacy data provided by a large national pharmacy chain in the US was used for this study. Pharmacy data contained all prescriptions (regardless of insurer), the mode of transmission (for example, electronic), and whether the script was bottled and then returned to stock (RTS). They assigned each prescription to 1 of 3 mutually exclusive outcomes: 1) filled prescription, indicating that the patient purchased the prescription; 2) RTS, indicating that the patient abandoned the prescription; or 3) RTS with fill, indicating that the patient abandoned the prescription and was returned to stock, but the patient purchased a prescription for a medication in the same medication class at the same or another pharmacy. Their cohort consisted of 10,349,139 index prescriptions filled by 5,249,380 patients during the identification period. They noted that prescriptions delivered electronically to the pharmacy had a 64% increase in the probability of being abandoned compared with those not electronically delivered ($P < 0.001$).

Studies that reported no difference

Bennett et al. (2003) conducted a randomized controlled trial to assess the effect of a computerized decision support system in conjunction with an e-prescribing application on medication adherence. They randomized 179 patients to receive generated consumer product information, computer-generated medication timetable, both, or usual care. Adherence was measured using data from the Health Insurance Commission (HIC). Values of more than 30 days suggested low adherence, and those less than 30 days suggested over adherence. Results suggest that there was no effect of the intervention on medication adherence.

Bergeron et al. (2013) investigated differences before and after the rollout of e-prescribing in patients' primary adherence to newly prescribed medications, patients' understanding of how to use their medications, and multiple pharmacy use using post-visit interviews and follow-up phone calls with 344 patients. Overall, rates of abandoned prescriptions were 6.9% before e-prescribing, 10.6% 1 to 6 months after e-prescribing, and 2.5% 12 to 18 months after e-prescribing ($P = .07$). There was a decrease in patient's ability to demonstrate proper use of their new medicine after e-prescribing (69.0% before e-prescribing, 67.1% 1-6 months after e-prescribing, 51.9% 12-18 months after e-prescribing; $P = .02$). There was an increase in the percentage of patients using multiple pharmacies after e-prescribing was implemented.

Fernando et al. (2011) randomized patients with prescriptions for nonnarcotic medications to a control group who were discharged with standard written prescriptions or an intervention group who had their prescriptions electronically delivered to the pharmacy of their choice. All study participants were contacted 7 to 31 days after ED discharge for a structured telephone interview. There was no difference in primary prescription non-compliance between the two study groups ($p = 0.58$).

However, electronically delivered prescriptions significantly reduced the median pharmacy wait time from 15 to 0 minutes ($P < 0.001$) and improved patient satisfaction at the pharmacy ($P = 0.034$). Neither subsequent physician nor ED visits were increased by primary prescription non-compliance.

Discussion

This systematic review aimed to determine the impacts of e-prescribing compared to traditional prescribing methods on medication adherence among outpatients. The multifactorial nature of the problem of medication adherence makes it difficult to propose a single-pointed solution. However, an evaluation of the evidence assembled in this report allows generalizations to be drawn and key factors for successful e-prescription implementation and improved medication adherence to be identified. Although some evidence suggests that e-prescription by itself was associated with a lower risk of primary nonadherence (Adamson et al., 2017; Anderson et al., 2015; Fischer et al., 2011), a greater proportion (66%) of the studies that reported increased adherence with e-prescription systems that employed additional supportive components of the prevalent EHR and e-prescription platforms (Hill et al., 2010; Hou et al., 2012; Michelis et al., 2011; Pevnick et al., 2014; J. Smith et al., n.d.; Williams et al., 2010). Smith et al. used a Decision Support System (DSS) that provided formulary and eligibility information. They argued that when providers are made aware of formulary benefit information conveyed through e-prescribing, they may be more likely to pay attention to this information when presented, shift their overall prescribing habits.

Michelis et al. and Pevnick et al. additionally found formulary decision support made available at the point of care beneficial. There are a few possible explanations for this relationship. Physicians who e-prescribe have built-in access to patient-specific information related to medication costs and, as a result, may be more likely to prescribe affordable medications that improve adherence. This assumption is directly in line with previous findings that higher copayment burden results in a higher risk of prescription abandonment. Williams et al. observed that patients in the intervention group whose clinicians opted to view detailed information had improved adherence over the study period, whereas adherence tended to fall among patients whose clinicians did not view this information.

Hou et al. studied an e-prescription ecosystem that provided patients with an online prescription management account. The online account allowed patients to easily manage their prescriptions, view their prescription history, and refill their prescriptions automatically. Automatically dispensing prescriptions allows patients to obtain their refills without the risk of having gaps in therapy and without having to remember to do so. This type of service can combat one of the largest barriers to adherence—forgetfulness. Hill et al. provided simple verbal counselling at the time of the prescription and found that to have produced favourable gains in adherence.

In contrast, the studies in this review that concluded negative or no effects of e-prescribing on medication adherence did not use any extra component of health information technology or behavioural interventions. These studies focused on prescription abandonment, reversal, or failure to pick up medications from the pharmacy. Most of these studies highlighted that the implementation of e-prescriptions without necessary measures to educate the patient is often unsuccessful in improving adherence. In many cases, patients were unaware that a prescription had been generated and transmitted to the pharmacy. Interestingly, Ekedahl et al. reported that some patients had their unclaimed prescriptions filled after receiving an information letter, which is consistent with telephone reminders.

The patient's perceived knowledge of the importance of the prescribed medication is also a likely factor. In many cases, patients report that most unclaimed prescriptions are not needed. The

immediate increase in abandoned prescriptions after the implementation of e-prescribing could reflect the adaptation to a notable change in primary care practice for both providers and patients. Without explicit orientation to the new process, patient confusion may be expected. The lack of knowledge demonstrated by patients regarding the indication and dosing of their prescription could be an incidental finding, but it might also suggest that the new automated prescribing process improved a physician's efficiency at the cost of spoken patient communication. Another explanation might be that patients relied on handwritten prescriptions to obtain the indications and instructions for use, which points to the need for positive measures to educate patients.

In conclusion, this review emphasizes the importance of considering a comprehensive approach when implementing e-prescription systems to enhance adherence to prescribed medications. It suggests that the effectiveness of such systems is significantly bolstered when integrated into a broader ecosystem that encompasses both patients and healthcare providers. Moreover, this review highlights the significant role of self-management tools in promoting medication adherence by empowering patients with better information and autonomy over their treatment regimen. These insights emphasize the need for a multifaceted strategy that addresses both patient and provider perspectives to maximize the benefits of e-prescription systems in community settings.

Conflicts of Interest

Arun Keepanasseril is employed by McMaster University and has received research funding from Roche and Novo Nordisk, and grants from Canada's Drug Agency. Alfonso Iorio is employed by McMaster University and has received research funding from Bayer, Novo Nordisk, Sanofi, Roche, and Pfizer; holds patents or earns royalties from WAPPS-Hemo; and is a member of Florio's medical advisory board and the World Federation of Hemophilia's advisory board. No other authors have conflicts of interest to report.

Appendix A: Search Strategy

OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present

Sl No	Search terms
1	Electronic Prescribing/ or Clinical Pharmacy Information Systems/ or Medical Order Entry Systems/ or electronic prescri*.mp. or automat* prescri*.mp. or E-Rx.mp. or e-prescribing.mp
2	Medical Records Systems, Computerized/ or computer physician order entry/ or Decision Support Systems, Clinical/ or Ambulatory Care Information Systems/ or clinical decision support system*.mp. or "clinical Decision Support*".mp. or "computerized decision support tool*".mp. or "computer-assisted decision making".mp. or "computerized medical record system*".mp. or CDSS.mp.
3	exp medication adherence/ or exp patient compliance/ or (patient adj5 compliance).tw. or (patient adj5 adherence).tw. or (medication adj5 compliance).tw. or (medication adj5 adherence).mp. or (medication adj5 nonadherence).tw. or (patient adj5 compliance).tw. or (patient adj5 nonadherence).tw. or (patient adj5 non-adherence).tw. or (medication adj5 noncompliance).tw. or (medication adj5 nonadherence).tw. or (Medicat* adj5 non-fulfil).mp. or (Medicat adj5 fulfill).mp. or (Medicat* adj5 fill).mp. or (Unclaim* adj5 prescri*).mp. or (refill* adj5 prescri*).mp. or non-adherence events.mp. or formulary adherence.ti,ab.
4	clinical trial.mp. or clinical trial.pt. or random:.mp. or tu.xs. or search:.tw. or meta analysis.mp.pt. or review.pt. or di.xs. or associated.tw.
5	comparative study/ or Controlled Clinical Trial/ or quasiexperiment*.ti,ab. or quasi experiment.ti,ab. or quasiexperimental.ti,ab. or quasi experimental.ti,ab. or quasi-randomized.ti,ab. or natural experiment.ti,ab. or natural control.ti,ab. or Matched control.ti,ab. or (unobserved and heterogeneity).ti. or "interrupted time series".ti,ab. or difference studies.ti,ab. or two stage residual inclusion.ti,ab. or regression discontinuity.ti,ab. or non-randomized.ti,ab. or pretest-posttest.ti,ab. or exp cohort studies/ or cohort\$.tw. or controlled clinical trial.pt. or epidemiologic methods/ or exp cohort studies/ or cohort\$.tw. or controlled clinical trial.pt. or epidemiologic methods/ or exp case-control studies/ or (case\$ and control\$).tw. or (case\$ and series).tw. or case reports.pt. or (case\$ adj2 report\$).tw. or (case\$ adj2 stud\$).tw. or embedded mixed-methods study design.kw. or (Surveys and Questionnaires).kw. or retrospective observational study.ti,ab. or (retrospective* and analyzed).ti,ab.
6	1 or 2
7	4 or 5
8	3 and 6 and 7
9	(hospitals/ or Editorial/ or Letter/ or News/ or comment/ or Animals/) not (Animals/ and Humans/)
10	8 not 9

Appendix B: Embase Search Strategy

Sl No	Search terms
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1	"Electronic Prescribing"/ or "Clinical Pharmacy Information Systems"/ or "Medical Order Entry Systems"/ or "electronic prescri*".mp. or "automat* prescri*".mp. or E-Rx.mp. or e-prescribing.mp.
2	"Medical Records Systems, Computerized"/ or "computer physician order entry"/ or "Decision Support Systems, Clinical"/ or "Ambulatory Care Information Systems"/ or "clinical decision support system*".mp. or "clinical Decision Support*".mp. or "computerized decision support tool*".mp. or "computer-assisted decision making".mp. or "computerized medical record system*".mp. or CDSS.mp.
3	exp "medication adherence"/ or exp "patient compliance"/ or (patient adj5 compliance).tw. or (patient adj5 adherence).tw. or (medication adj5 compliance).tw. or (medication adj5 adherence).mp. or (medication adj5 nonadherence).tw. or (patient adj5 compliance).tw. or (patient adj5 nonadherence).tw. or (patient adj5 non-adherence).tw. or (medication adj5 noncompliance).tw. or (medication adj5 nonadherence).tw. or (Medicat* adj5 non-fulfil).mp. or (Medicat adj5 fulfill).mp. or (Medicat* adj5 fill).mp. or (Unclaim* adj5 prescri*).mp. or (refill* adj5 prescri*).mp. or "non-adherence events".mp. or "formulary adherence".tw. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword heading word, floating subheading word, candidate term word]
4	random:.tw. or clinical trial:.mp. or exp health care quality/
5	di.fs. or predict:.tw. or specificity.tw. or comparative study/ or Controlled Clinical Trial/ or (quasiexperiment or "quasi experiment" or quasiexperimental or "quasi experimental" or quasi-randomized or "natural experiment" or "natural control" or "Matched control" or "interrupted time series" or "difference studies" or "two stage residual inclusion" or "regression discontinuity" or non-randomized or pretest-posttest).ti,ab. or (unobserved and heterogeneity).ti. or exp cohort analysis/ or exp longitudinal study/ or exp prospective study/ or exp follow up/ or cohort\$.ti,ab. or exp case control study/ or (case\$ and control\$).tw. or exp case study/ or (case\$ and series).tw. or case report/ or (case\$ adj2 report\$).ti,ab. or (case\$ adj2 stud\$).ti,ab.
6	1 or 2
7	4 or 5
8	3 and 6 and 7
9	hospitals/ or Editorial/ or Letter/ or News/ or comment/
10	8 not 9
11	Animals/ not (Animal/ and Human/)
12	10 not 11

Cochrane Database

Sl No	Search Hits
1	[mh ^"Electronic Prescribing"] OR [mh ^"Clinical Pharmacy Information Systems"] OR [mh ^"Medical Order Entry Systems"] OR (("electronic" NEXT prescri*):ti,ab,kw) OR ((automat* NEXT prescri*):ti,ab,kw) OR E-Rx:ti,ab,kw OR e-prescribing:ti,ab,kw
2	([mh ^"Medical Records Systems, Computerized"] OR [mh ^"computer physician order entry"] OR [mh ^"Decision Support Systems, Clinical"] OR [mh ^"Ambulatory Care Information Systems"]) OR ("clinical decision support" NEXT system*):ti,ab,kw OR ("clinical Decision" NEXT Support*):ti,ab,kw OR ("computerized decision

	support" NEXT tool*):ti,ab,kw OR "computer-assisted making":ti,ab,kw OR ("computerized record" NEXT system*):ti,ab,kw OR CDSS:ti,ab,kw)	decision medical
3	1 or 2	
4	[mh "medication adherence"] OR [mh "patient compliance"] OR (patient:ti,ab NEAR/5 compliance:ti,ab) OR (patient:ti,ab NEAR/5 adherence:ti,ab) OR (medication:ti,ab NEAR/5 compliance:ti,ab) OR (medication NEAR/5 adherence) OR (medication:ti,ab NEAR/5 nonadherence:ti,ab) OR (patient:ti,ab NEAR/5 compliance:ti,ab) OR (patient:ti,ab NEAR/5 nonadherence:ti,ab) OR (patient:ti,ab NEAR/5 non-adherence:ti,ab) OR (medication:ti,ab NEAR/5 noncompliance:ti,ab) OR (medication:ti,ab NEAR/5 nonadherence:ti,ab) OR (Medicat*:ti,ab,kw NEAR/5 non-fulfil:ti,ab,kw) OR (Medicat:ti,ab,kw NEAR/5 fulfill:ti,ab,kw) OR (Medicat*:ti,ab,kw NEAR/5 fill:ti,ab,kw) OR (Unclaim*:ti,ab,kw NEAR/5 prescri*:ti,ab,kw) OR (refill*:ti,ab,kw NEAR/5 prescri*:ti,ab,kw) OR "non-adherence events":ti,ab,kw OR "formulary adherence":ti,ab	
5	3 and 4	

Appendix B: Grey Literature Listing

Title	Country / Region of Focus	Preparing agency (if known)	Key take away
The perfect prescription: Obstacles and opportunities on the path to higher quality and lower costs (Ward-Charlerie et al., 2020).	USA	Surescripts	While 28 percent of paper prescriptions never make it from the physician's office to the pharmacy, e-prescribing increases first-fill medication adherence by 10 percent.iii The gains in administrative performance and clinical outcomes could generate between \$140 billion to \$240 billion in savings over ten years. When combined, electronic prescribing, prescription price transparency and electronic prior authorization can transform the prescription decision process and promote medication adherence. Prescribers

			and pharmacists benefit from a streamlined workflow and more time with patients, while patients benefit from lower costs and fewer surprises at the pharmacy
2019 impact report: Prescription Accuracy (Surescripts, 2019).	USA	Surescripts	Medication nonadherence creates up to \$300 billion in avoidable healthcare costs in the U.S. each year. A timeline of surescripts rollout is included in this document
2021 National progress report (Surescripts, 2021a).	USA	Surescripts	Eligibility brings clear information about a patient's prescription benefit coverage into workflows at the prescriber's office and at the pharmacy, where 90-day prescription pickup rates have found to be 2.7 percentage points higher for prescriptions informed by an Eligibility response. By the end of 2021, nearly half of U.S. prescribers were using Real-Time Prescription Benefit to access patient-specific benefit information, out-of-pocket costs, and more affordable medication alternatives. Significant growth gave even more clinicians the power to address cost concerns and boost adherence at the point of care. Mount Sinai Health System's population health team partnered with Surescripts to give care navigators proactive insight into medication adherence for thousands of patients with diabetes, hypertension, and high

			cholesterol by alerting them to medication-related events, including missed fills. Five months after implementation, their overall proportion of days covered (PDC) score had gone up nearly 60%
Investigating the Economic Impact of Mandatory Electronic Prescribing Requirements in the United States (Kent, 2017).	USA	Surescripts	Regulatory actions in the United States driving a shift in prescription channels to electronic prescribing have an initial short-term cost investment resulting in a long-term cost reduction for the overall healthcare system.
Blueprint for E-Prescribing: A Detailed Plan of Action for Implementing E-Prescribing (RxHub, 2008).	USA	Surescripts	An overview of e-prescription infrastructure, workflow, privacy and security issues, standards as well as a blueprint for implementation.
An Rx for America's Healthcare: Health IT and e-prescribing (Surescripts, 2012).	USA	Surescripts	When the prescription goes straight to the pharmacy instead of into the patient's pocket or purse, it is far more likely to be filled and taken. That means savings of as much as \$240 billion over the next 10 years through improved health outcomes.
Concept Series Paper on Electronic Prescribing (AMCP, 2019).	USA	Academy of Managed Pharmacy	Studies have demonstrated that drug costs may decrease and plan performance may improve because of better formulary adherence, better drug utilization review, and fewer errors when the prescription claim is adjudicated.
E-Prescribing Trends in the United States	USA	HealthIT.gov	This brief focuses on changes in rates of

			physician e-prescribing, pharmacy capability to accept e-prescriptions, and the volume of e-prescriptions between 2008 and 2014. During that period, two important policies that promoted the use of e-prescribing were put into place.
Small steps drive big outcomes (Surescripts, 2021b).	USA	Surescripts	This white paper describes how eligibility and formulary and benefit data can be managed to improve patient safety, lower costs, and ensure quality care. The Surescripts study highlighted a 2.7% increase in adherence tied to eligibility use within 90 days of prescribing. Indeed, other studies have demonstrated that medication adherence is enhanced when decision support information, namely F&B data, is made available to the provider. Concerning chronic illness, studies have shown that e-prescriptions can enable patient adherence to medication, resulting in cost savings and enhancing patient health outcomes. However, if the provider does not trust the eligibility and formulary data and thus does not utilize it, this can hamper medication adherence. Studies have highlighted that ePrescribing in conjunction with eligibility and formulary information increased

			first-fill medication adherence by 20% and this process speeds up prescription refill requests. Patient adherence is boosted further when eligibility is checked, and a match is recorded.
Primary non-adherence to medication: new evidence from electronic health records (Pittell, 2020).	USA	Johns Hopkins (Thesis)	. Paper 1 examines the extent of such gaps in practice, quantifying the gaps in EHR data from many health systems. The latter papers use EHR data to examine primary non-adherence to medication, the share of prescriptions going unfilled. Paper 2 offers recent evidence on levels of primary non-adherence and delayed fills. Paper 3 examines the relationship between high deductibles and primary non-adherence.: Paper 1 finds EHR data offered an incomplete picture of office visits for 56% of the sample. Paper 2 finds 20% of prescriptions were unfilled. Among filled prescriptions, delays of over two weeks were uncommon (5% of fills). Paper 3 finds beneficiaries iii enrolled in high deductible plans had greater primary non-adherence than those enrolled in low deductible plans, especially among new users of medications with low generic uptake.
The association between electronic prescriptions and new prescription abandonment in the elderly (Forestal, 2018).	USA	University of the Sciences in Philadelphia (Thesis)	Understanding the impact of electronic prescriptions on new prescription abandonment is important, particularly in

			a poor elderly population that is prone to comorbidities. The results of this study indicate that electronic prescriptions may be associated with new prescription abandonment in the elderly. Moreover, these findings suggest that certain factors, such as out of pocket costs and patient location magnified this effect. Electronic prescription abandonment is concerning, given increased utilization of e-prescribing in the past decade. This study offers new insight, particularly as it focused on a poor elderly population that may be prone to polypharmacy and may not easily cope with the financial burden of drugs. This study aspires to support policy decisions aiming to reduce new prescription abandonment, but more research is needed to discern causes of abandonment of electronic prescriptions in the elderly.
Electronic Prescriptions An overview for dispensers (Australian Digital Health Agency, 2020).	Australia	Australian Digital Health Agency	A short primer on Australia's e-prescription workflow.
The ePrescription Initiative and Information Infrastructure in Norway (Hanseth et al., 2017).	Norway	Book section	A good description with case studies of Norway's healthcare system and e-prescription rollout, infrastructure, and implementation.
E-Prescribing in the Netherlands (Healthmanagement.org,	Netherlands	Healthmanagement.org	A good primer on early days of Netherland's e-prescription

2009).			implementation.
Electronic Prescribing in the United Kingdom and in the Netherlands (Villalba et al., 2011).	UK, Netherlands	AHRQ (USA)	This study provides an overview of the development of e-prescribing in the United Kingdom (UK) and the Netherlands (NL), with the aim of presenting evidence about how electronic prescribing (e-prescribing) has evolved in the two countries, how widely e-prescribing has been adopted, and most importantly, what type of policies have been put in place to foster adoption. The goal of this study is to provide information that could transfer lessons learnt to e-prescribing efforts in other countries. In particular, the objective is for the European experience to inform the implementation of e-prescribing in the United States. Implementation in both countries has become more difficult, however, when more functionality was desired. For example, the EVS, which aimed to improve adherence to prescribing guidelines as part of existing e-prescribing systems, was not as widely adopted by Dutch GPs as initially foreseen. This was partly due to difficulties with the diagnosis-driven model of prescribing that EVS (a prescription support module) used and to its incompatibility with some of the existing GP IT systems.
National Standard on	Ireland	Health Information	HIQA has developed

information requirements for national community-based ePrescribing (Health Information and Quality Authority, 2018).		and Quality Authority	information requirements for community-based ePrescribing and dispensing. ePrescribing can deliver significant benefits for patients, prescribers, pharmacists, and others involved in the process. Information requirements are a minimum set of data items that are recommended for implementation in information systems that create and transfer information to support the delivery of safe and quality care to patients. The inclusion of data items in the minimum set of data is determined by the clinical relevancy of the data item and the potential for the data item to improve patient safety in integrated care. The information requirements presented in this document have been developed in conjunction with eHealth Standards Advisory Group.
A Comparative Review of Electronic Prescription Systems: Lessons Learned from Developed Countries (Samadbeik et al., 2017).	Denmark, Finland, Sweden, England, and the United States		This review study aimed to compare the electronic prescription systems in five selected countries (Denmark, Finland, Sweden, England, and the United States)
European e-Prescriptions: Benefits and Success Factors	Estonia, the United Kingdom, Denmark, and Sweden	Oxford University	This paper examines the economic, health, and social benefits of e-prescriptions, as well as their realisation within different time frames of policy implementation. Based on previous evidence and expert interviews for case studies

			of Estonia, the United Kingdom, Denmark, and Sweden, this work analyses to what extent existing models of e-prescription implementation can determine implications for their wider utilisation across Europe. The findings confirm some economic benefits, such as efficiency gains for prescribers and dispensers, savings arising from transparency, fraud reduction, and reduced printing costs; health benefits such as reduced medication errors, better accessibility of medicines, increased monitoring of adherence to physician recommendations, and aggregate analysis of health data; and social benefits around patient satisfaction with the health system, financial relief for society, and social care for the elderly.
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Appendix C: List of studies, e-prescription data as an adherence measure

Citation	Summary
Pill count, self-report, and pharmacy claims data to measure medication adherence in the elderly (Grymonpre et al., 1998).	When calculated from self-report or manual or electronic prescription claims data, mean percent adherence by drug was high and not statistically different ($95.8\% \pm 17.1\%$, $107.6\% \pm 40.3\%$, and $94.6\% \pm 24.0\%$, respectively), whereas the pill count adherence was significantly lower at $74.0\% \pm 41.5\%$ ($p < 0.0001$). An unexpected finding was that the pill count technique used in this study of elderly clients using chronic, repeat medications appeared to

	underestimate medication adherence. Numerous other limitations of pill count, self-report, and a province-wide prescription claims database in estimating medication adherence are presented. When using medication adherence as a process measure, the researcher and practitioner should be aware of the limitations unique to the data source they choose and interpret data cautiously.
Validation of the electronic prescription as a method for measuring treatment adherence in hypertension (Márquez-Contreras et al., 2018).	This prospective study initially included 120 patients treated for hypertension in primary care centers. Adherence was measured using the gold standard, the medication event monitoring system (MEMS), versus the index test, the e-prescription program, at baseline and at 6, 12, 18 and 24 months. This prospective study initially included 120 patients treated for hypertension in primary care centers. Adherence was measured using the gold standard, the medication event monitoring system (MEMS), versus the index test, the e-prescription program, at baseline and at 6, 12, 18 and 24 months. If patients are included in an e-prescription program for at least 2 years, e-prescription is an inexpensive method to measure adherence in hypertension.
A computational framework to identify patients with poor adherence to blood pressure lowering medication (Mabotuwana et al., 2009).	The observed adherence levels indicate that a substantial proportion of patients classified with hypertension and diabetes have poor adherence, associated with poorer rates of blood pressure control, that can be detected through analysis of electronic prescribing.
Validation of patient reports, automated pharmacy records, and pill counts with electronic monitoring of adherence to antihypertensive therapy (Choo et al., 1999).	Adherence levels determined from pill counts and pharmacy dispensing records correlate more closely with quantity than with timing of doses. Nonadherence reported by patients can serve as a qualitative indicator and predictor of reduced adherence.
Congruence of self-reported medications with pharmacy prescription records in low-income older adults (Caskie & Willis, 2004).	This study examined the congruence of self-reported medications with computerized pharmacy records. The percentage of individuals with perfect agreement between self-reports and pharmacy records varied from

	49% for major drug classes to 81% for specific cardiovascular and central nervous system drugs. Self-reported medications are most likely to be congruent with pharmacy records for drugs prescribed for more serious conditions, for more specific classes of drugs, and for healthier individuals.
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