NON-PARTICIPATION BIAS IN HEALTH SERVICES RESEARCH USING DATA FROM AN INTEGRATED ELECTRONIC PRESCRIBING PROJECT: THE ROLE OF INFORMED CONSENT

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Abstract: Electronic prescribing potentially reduces adverse outcomes and provides critical information for drug safety research but studies may be distorted by non-participation bias. 52,507 patients and 28 physicians were evaluated to determine characteristics associated with consent status in an electronic prescribing project. Physicians with less technology proficiency, seeing more patients, and having patients with higher fragmentation of care were less likely to obtain consent. Older patients with complex health status, higher income, and more visits to the study physician were more likely to consent. These systematic differences could result in significant non-participation bias for research conducted only with consenting patients.

Keywords: informed consent, non-participation bias, electronic prescribing, primary care physicians, prescription medication

SESGO POR FALTA DE PARTICIPACIÓN EN LA INVESTIGACIÓN DE LOS SERVICIOS DE SALUD AL USAR DATOS DE UN PROYECTO INTEGRADO DE PRESCRIPCIÓN ELECTRÓNICA: EL PAPEL DEL CONSENTIMIENTO INFORMADO

Resumen: La prescripción electrónica reduce, potencialmente, los resultados adversos. y proporciona información crítica para una investigación segura en drogas, pero los estudios pueden ser distorsionados por un sesgo por falta de participación. Se evaluó a 52.505 pacientes y a 28 médicos para determinar características asociadas con el estatus del consentimiento en un proyecto de prescripción electrónica. Los médicos con menor eficiencia tecnológica, con más cantidad de pacientes que, además, mostraban mayor fragmentación en su atención, presentaban menor opción de obtener consentimiento. Los pacientes de más edad, con estatus de salud complejo, mayor ingreso y con más visitas al médico a cargo, manifestaban mayor disposición a consentir. Estas diferencias sistemáticas podrían desembocar en un sesgo significativo por falta de participación en la investigación llevada a cabo sólo con pacientes con consentimiento.

Palabras clave: consentimiento informado, sesgo por falta de consentimiento, prescripción electrónica, médicos de atención primaria, medicación por prescripción

SESGO PELA FALTA DE PARTICIPAÇÃO NA PESQUISA DOS SERVIÇOS DE SAÚDE AO USAR DADOS DE UM PROJETO INTEGRADO DE PRESCRIÇÃO ELETRÔNICA: O PAPEL DO CONSENTIMENTO INFORMADO

Resumo: A prescrição eletrônica reduz potencialmente os resultados adversos e proporciona informação crítica para uma pesquisa segura em drogas, porém os estudos podem ser destorcidos por um sesgo por falta de participação. Avaliou-se 52.505 pacientes e a 28 médicos para determinar características associadas com o estatus do consentimento num projeto de prescrição eletrônica. Os médicos com menor eficiência tecnológica, com mais quantidade de pacientes que os outros, mostravam maior fragmentação em sua atenção, apresentavam menos opção para conseguir o consentimento. Os pacientes mais idosos, com estudos de saúde maiôs complexos, maiores salários e com mais visitas ao médico, manifestavam maior disposição de consentir. Estas diferenças sistemáticas poderiam desembocar num erro significativo por falta de participação na pesquisa levada a cabo somente com pacientes que consentiram.

Palavras chave: consentimento informado; erro por falta de consentimento; prescrição eletrônica; médicos de atenção primária; medicação por prescrição.

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Introduction

In our current era of expanding utilization of technology in health care, information from health care encounters is increasingly being recorded electronically*(1,2)*. Integrated electronic prescribing systems provide a new set of tools that allow timely information to be used to improve the safety and effectiveness of prescribing decisions*(3-8)*. An advantage of integrated prescribing systems compared to traditional methods is that information is readily available to health professionals as patients enter and re-enter the health care system. In addition, these systems provide decision support, alerts and reminders for care options that improve prescribing choices and patient care*(9-11)*. Medical conditions that pose a health danger can be permanently flagged in an electronic environment to greatly reduce or eliminate medical errors*(5, 8, 11-14)*.

As well, integrated electronic prescribing systems provide a wealth of information from diverse sources including administrative records, private community pharmacy records and the electronic prescribing application database*(4, 9)*. Clinical, health services and population health research, which normally relies on painstaking data collection on samples of the population to address questions that are crucial in defining optimal therapeutic treatment, adverse drug reactions and evidence-based decision making, can benefit greatly from improved access to this data*(1, 14, 15)*. While the computerization and coding of prescription and health information is an important resource for researchers as well as clinicians, the realization of the benefits of such a system will be restricted to those patients who consent to their prescription records being released to their treating physician. If a patient does not provide this consent, either because they truly do not want to release their records or they are not offered the opportunity to participate by the physician, then these «non-consenting» patients will not experience direct benefits from the system. Furthermore, any research that is restricted to the data collected on the consenting patients will include a certain amount of bias due to non-participation. The degree and magnitude of this bias will depend on whether participants are significantly different from non-participants*(16)*.

Studies of bias introduced by authorization for the secondary use of information from electronic health records provide some insight into the type and magnitude of bias that may be introduced by the informed consent process. In Minnesota, legislation was passed in 1977 that required a signed general authorization to release medical records for research purposes (Minnesota Statute 144.335: «Patient Consent to Release Records»). Studies of the impact of this legislation found higher refusal rates for some sub-groups, such as middle aged or younger patients, women and patients with mental health concerns*(17, 18)*. When the potential effects of authorization bias were studied in a Mayo Clinic, researchers found a refusal rate of 20.7% with higher rates for younger women and patients with sensitive diagnoses*(18)*. These findings have been substantiated in urban family practice centers*(19)* and hospital settings where researchers determined that more severely ill patients are more likely to refuse or not be approached about consent*(20)*. Other studies examining the role of socioeconomic status and patient education indicate that the informed consent process may be limiting research to more affluent or better educated patients*(21-23)*.

Another factor that may play a role in obtaining patient consent includes the role of the physician*(21, 22, 24, 25)*. For example, the availability of an extensive prescription drug profile may cause physicians to preferentially enroll patients that they see on a regular basis or

for whom records are available (i.e. publicly insured patients whose records are provided by the administrative database and are more complete). Physicians may also be unwilling to offer patients the opportunity to participate if they do not see themselves as the «responsible» physician for the drug management*(11)*. This has been illustrated in a Dutch study, in which physicians varied in their perception of responsibility for their patients' treatment regimens*(26)*. This variation in responsibility will likely have an impact on the effort made by the physicians when recruiting patients. Obtaining informed consent from a patient often places a significant burden on physicians and this may be a critical factor in determining how many patients are even approached by the physician*(21,24,25)*. This appears to be particularly true for the case of single, acute consultations*(21)*.

To date, a detailed investigation of the characteristics of patients who consent versus those who do not for projects that involve the use of information technology has not been conducted. No study that we know of has simultaneously investigated the role of both physicians and patients in obtaining consent. The objective of this study was to evaluate the characteristics of patients, physicians and their relationship that determines participation in a research project utilizing an integrated electronic prescribing system.

Methods

The MOXXI System

The Medical Office of the Twenty First Century (MOXXI), a prototype for a fully integrated electronic prescription system, links information from primary care physicians and retail pharmacies for patients in a geographically circumscribed area in Montreal, Canada. Physicians are equipped with wireless mobile personal digital assistants (PDA) and given the MOXXI system with access to complete prescription information for consenting patients. This provides a significant added value to physicians as 40% of prescriptions are written by other physicians (data provided by IMS Canada, 1999)*(27)*. Patient information is retrieved by real-time integration with the beneficiary, prescription and medical services claims files of the provincial health insurance board and with private pharmacy computer networks.

Study Design & Population

This study was conducted with family physicians who agreed to participate in the MOXXI III trial. Eligible physicians were 30 years of age or older, in full-time, community based fee-for-service practice. Patient consent documents and brochures were delivered to the 28 participating physicians starting in June, 2002. The date the documents were delivered was considered the beginning of the enrollment period and the end of the enrollment period was September 1, 2003. The physician's practice population was defined using medical services claims and thus potentially eligible patients who could grant access to prescription information were identified. Eligible patients were persons who had made at least one visit to the study physician during the enrollment period. As the MOXXI integrated electronic prescribing systems uses information from Quebec provincial administrative databases as well as pharmacies and community based physicians, access was granted to denominalized patient information by the provincial Privacy Commissioner *(Commission d'accès à l'information)*. Consenting patients were assigned to the participating physician to whom they gave the first consent and the date of the consent was recorded electronically. Non-consenting patients were assigned using medical billing information to determine the first participating physician visited after the

beginning of the enrollment period. For non-consenting patients within a physician's practice, prescription and medical services information from administrative databases were available in a de-identified format. Ethics approval for the study was provided by the McGill Faculty of Medicine Institutional Review Board.

Measurement

Physician characteristics included factors that may place constraints on the physicians' time (number of practice settings, number of patients seen in a day) as well as the physicians' facility with the electronic prescribing system (ease of use, intentions to use the system, familiarity with computers). The number of practice settings was measured using codes from the medical billing databases, *patient volume* measured as the number of patients with a medical visit divided by number of distinct days with at least one billing for a medical visit. Computer efficacy was measured by a physician's ease of use with the system, *intention to use* the system, and general *computer self-efficacy*. Ease of use with the MOXXI system was based on the time the physician took to complete a standardized task performed two weeks after the physician started using the system. For this task the physician was required to write three new prescriptions using the electronic pad. The intention to use the system and computer self-efficacy (familiarity and comfort using computers) was measured using questions from the Technology Acceptance Model*(28,29)* rated using a 5-point Likert scale with opinion descriptors («1» for strongly disagree and «5» for strongly agree). The questionnaire was available on-line through the personal digital assistants (PDA), and study physicians completed the questionnaire after a 3-hour training session.

Patient-physician relationship characteristics were measured to identify mutual characteristics that might influence consent status. In Quebec, there are two official languages, French and English. To measure potential communications difficulties, a physician and a patient with the same primary language preference (French-French or English-English) were considered to have *concordance of primary language. Concordance for gender* was also assessed based on the sex of the study physician and their patients.

Patient characteristics that might influence consent included demographic variables (age and socioeconomic status), health status (comorbidities, severity of illness), continuity of care (how often the patient visited other family physicians), and summaries of prescription medication use (counts of unique medications as well as medications used to treat mental health problems or medications with a potential for misuse/abuse). Age was measured categorically (to protect patient identification no date of birth was available for non-consenting patients) and postal codes were used to obtain census approximations for *household income(30)*. Co-morbidity and severity of illness were assessed 6 months before the start of the enrollment period using diagnostic codes recorded in medical service claims and hospitalization discharge records to determine the *Charlson comorbidity index(31-33), number of specialists visited* and t*he number of emergency room visits*. Continuity of care was measured by the *number of non-participating family physician visits* made by the eligible patients using algorithms developed by the co-investigators *(34)*. For patients with continuous public drug insurance, information on prescription medication use was summarized. This included a count of the *number unique medications dispensed* from all prescribing physicians during the enrollment period and whether a patient was dispensed a *medication of potential abuse/misuse or a medication used to treat a mental health problem(35,36)*.

Medications of potential abuse and/or misuse included opioids (narcotics), barbiturates, benzodiazepines and amphetamines as classified using the American Hospital Formulary (AHF codes 28:08:08; 28:08:12; 28:12:04; 28:12:08; 28:20). Medications used to treat mental health problems included anti-depressants, anti-psychotics and lithium (AHF codes 28:16:04; 28:16:08; 28:28).

Data Sources

Three data sources were used to assess potential predictors of consent. First, the provincial health insurance board *(Régie de l'assurance maladie du Québec: RAMQ)* and the Ministry of Health administrative databases were used to assess service use and beneficiary characteristics. The validity of these databases has been previously established for healthcare research*(37-39)*. The RAMQ *beneficiary demographic database* provided data on age, sex, postal-code linked data on income and education based on 2001 Statistics Canada enumeration area mapping*(30)*, patient language preference and prescription drug insurance status. The *medical services claims database provided* information on the beneficiary, date, type, provider, and location of service delivery (e.g. inpatient, emergency, clinic) for all medical services remunerated on a fee-for-service basis (approximately 86% of all services)*(40)*. The *hospitalization database* provided admitting and discharge diagnoses for all acute care hospitalizations in Quebec based on medical archivist review and coding of the hospital record. The *prescription claims database* and *retail pharmacy* data provided information on each drug dispensed including the drug name, quantity, date and duration for each prescription, the prescribing physician, and the dispensing pharmacy. Second, data on consent status and physician responses to on-line questionnaires was retrieved from the MOXXI server. Data from all sources are linked by an encrypted health insurance number (RAMQ number), a unique identifier for each Quebec resident, with a look-up table for all consenting patients. Finally, physician demographics were provided by RAMQ and the Quebec College of Physicians *(Collège des Médecins du Québec)* and include sex, language preference, location of graduating medical school, year of graduation, and medical specialty. Physician data was linked through the medical license number. The occurrence of visits to the study physician during the study period was determined by information retrieved from medical services claims database. The existence of one or more prescriptions during follow-up was determined from the pharmacy records retrieved for each patient daily from the RAMQ and retail pharmacies.

Statistical Analyses

Frequency distributions of physician and patient characteristics were determined and the means, standard deviations (sd) and ranges were reported for continuous variables (p-values were not reported as the large sample size would make even minor differences statistically significant). Multivariate logistic generalized estimating equations (GEE) were used to investigate whether patient or physician characteristics increased the probability of consenting to participate. Patients were clustered within physicians with an exchangeable correlation structure. The unit of analysis was the patient (with positive consent status as the outcome of interest). Statistical analyses were conducted using SAS 9.1.

Results

During the enrollment period, the study physicians saw 52,444 distinct patients. Patients who were seen only in locations other than the

community-based office were excluded, and 52,507 patients were eligible to be enrolled in the MOXXI study and 11,954 (26.9%) consented to participate. Almost half of the participating physicians were female (46.4%) and 78.5% indicated that their primary language preference was French. Table 1 presents the characteristics and description of practice settings for the study physicians. Enrolment rates varied greatly among the physicians, from 8.8% to almost 75% with the length of the enrollment period lasting an average of one and a half years. Other locations where the physicians might practice besides the community-based office included drop-in clinics, emergency rooms, hospital out-patient clinics and nursing homes.

Table 1. Description of the characteristics and practice setting for study physicians (N=28) during the enrollment period (starting June 2002 to August 2003).

	Mean (sd)	Median	Range
Practice Setting Characteristics			
Number of practice settings	1.8 (1.1)	1.5	1 - 5
Total number of unique patients with a clinic visit	2,472.8 (1340.4)	2,216.5	650-4,770
Nº of patients seen by physician per clinic day*	23.7 (5.9)	23.6	13.4-36.1
Technology Efficacy			
Nº of minutes to complete standardized task	2.0 (0.97)	1.7	0.4 - 4.5
Intention to Use the MOXXI System†	4.3 (0.8)	5	2 - 5
Computer Self-Efficacy†	4.0 (0.8)	4	2 - 5
Consent Rates			
% unique patients who signed a consent form	26.9 (18.9)	18.6	8.8 - 75.3
Length of enrollment period in days	411.6 (71.2)	438	203 - 448

* A clinic day is counted if the physician billed for at least one clinic visit for that day.

† Self-report questionnaire measured on a 5-point scale where «5» indicates «Strongly Agree» and «1» indicates «Strongly Disagree».

Table 2 presents the characteristics of patients who consented and patients who were not approached or who refused to consent. Consenting patients tended to be older, have a higher household income, have a higher severity of illness and have greater continuity of care. On average, patients who consented saw their study physician almost two and a half times as often compared to non-consenting patients (mean of 4.2 visit days versus 2.0, $p>0.0001$) and had almost twice as many comorbidities (Charlson Comorbidity Index of 0.68 versus 0.34, $p>.0001$). The majority of patients were primarily French-speaking (69.8% of consenting patients and 74.6% of non-participating patients) and over half were female (60.1% and 54.7%, consenting and non-participating respectively).

Table 2. Patients' characteristics (N= 52,507) in relationship to consent status.

	Consented (%) n=11,954	Not Approached or Refused to Consent (%) n=40,553
Relationship to Study Physician		
Concordance for primary language*	9,350 (78.2%)	30,158 (74.3%)
Concordance for gender	6,853 (57.3%)	21,137 (52.1%)
Demographics Age (years):		
≤ 18 years	477 (3.9%)	11,281 (27.8%)
19-43 years	2,696 (22.5%)	15,166 (37.3%)
44-63 years	5,117 (42.8%)	10,325 (25.4%)
≥ 64 years	3,664 (30.6%)	3,781 (9.3%)
Household Income (CND $)†:		
≤ 41,276	2,583 (21,6%)	10,594 (26.1%)
41,277 - 51,574	2,535 (21,2%)	10,641 (26.3%)
51,575 - 62,296	3,240 (27,1%)	9,788 (24.1%)
≥ 62,297	3,596 (30,1%)	9,530 (23.5%)
Opportunities for Consent and Potential Benefit of Electronic Drug Management		
Visits to study physician during enrollment:		
1	1,740 (14.5%)	23,275 (57.3%)
2 - 3	4,168 (34.8%)	12,107 (29.8%)
≥ 4	6,046 (50.5%)	5,171 (12.7%)
Public drug insurance coverage:‡	5,787 (48.4%)	15,280 (37.7%)
Comorbidity and Severity of Illness		
Charlson Comorbidity Index > 0.5‡	4,324 (36.1%)	8,957 (22.0%)
No. of specialists visited: ‡		
0	5,842 (48.8%)	26,177 (64.5%)
1-2	5,007 (41.8%)	12,828 (31.6%)
≥ 3	1,105 (9.2%)	1,548 (3.8%)
No. of emergency room visits: ‡		
0	10,775 (90.1%)	36,862 (90.8%)
1-2	549 (4.5%)	2,169 (5.3%)
≥ 3	630 (5.2%)	1,522 (3.7%)
Continuity of Care		
No. of visits to non-study physicians: ‡		
0	8,222 (68.7%)	24,333 (60.0%)
1-2	3,171 (26.5%)	13,543 (33.3%)
≥ 3	561 (4.6%)	2,677 (6.6%)

* Patient's and physicians' language preference is determined from administrative records that indicate the preferred language of communication: English or French. Concordance occurs when the stated language preference is the same for the physician and the patient.

† Household income is (Canadian $) based on census track information for 6-digit postal code.

‡ Measured for the 6 months prior to the start of the enrollment period for the patient's study physician.

Table 3 presents the adjusted likelihood (odds ratios with 95% confidence intervals) for patient and physician characteristics that may have influenced whether patients consented to participate. All characteristics included in the model that adjusted for clustering among physicians were significant; however, status of public drug insurance was collinear with patient age and was removed from the model. The main characteristics that positively influenced consent were patient age with a 13-fold increase in probability, patient household income (up to 32% increase), the number of opportunities for consent with an 11-fold increase in probability, the physician's intention to use the

system (74% increase) and severity of illness for the patient (10% - 47% increase). The main characteristics that negatively influenced consent were an increase in the number of patients seen by the study physician per clinic day, with an increase of 5 patients decreasing the probability of consenting by 30% and poor continuity of care with more than 3 visits to other family physicians before the enrollment period decreasing the probability of consent by over 60%. A decrease in proficiency with the MOXXI system as measured by the completion of a standardized task also significantly decreased the likelihood of obtaining consent from a patient by 13%.

Table 3. The association between patient and physician characteristics and likelihood of consenting: multivariate logistic regression analysis.

	Likelihood of Consent (Odds Ratios)	95% Confidence Intervals
Practice Setting Characteristics		
Practicing in more than one setting†	1.08	1.01 - 1.15
Per 5 additional patients seen per clinic day	0.72	0.70 - 0.74
Physician's Technology Efficacy		
No. of minutes to complete standardized task	0.86	0.84 - 0.89
Intention to Use the MOXXI System‡	1.20	1.13 - 1.25
Computer Self-Efficacy‡	1.04	0.99 - 1.14
Patient Relationship to Study Physician		
Concordance for primary language	1.22	1.15 - 1.30
Concordance for gender	1.12	1.07 - 1.18
Patient Demographics		
Age (years): ≤ 18	reference	-
19-43	3.62	3.26 - 4.02
44-63	7.83	7.08 - 8.66
≥ 64	11.19	10.03 - 12.47
Household Income (CND $): ≤ 41,276	reference	-
41,277 - 51,574	1.09	1.02 - 1.17
51,574 - 62,296	1.26	1.17 - 1.35
≥ 62,297	1.33	1.23 - 1.43
Opportunities for Consent		
Visits to study physician during enrollment: 1	reference	-
2 - 3	3.92	3.68 - 4.18
≥ 4	11.08	10.37 - 11.84
Patient Comorbidity and Severity of Illness		
Charlson Comorbidity Index > 0.5	1.10	1.04 - 1.17
No. of specialists visited: 0	reference	-
1-2	1.28	1.22 - 1.35
≥ 3	1.31	1.18 - 1.46
No. of emergency room visits: 0	reference	-
1-2	1.20	1.07 - 1.36
≥ 3	1.46	1.27 - 1.67
Patient Continuity of Care		
No. of visits to non-study physicians: ‡ 0	reference	-
1-2	0.64	0.60 - 0.68
≥ 3	0.39	0.34 - 0.44

* Adjusted for physician level clustering using multivariate GEE modeling, values greater than one indicate increased likelihood.
† Other practice locations include emergency rooms, community drop in clinics (salaried physicians), and nursing homes.
‡ Responses were dichotomized into high and low groups (high response = 4 or 5).

To determine if specific patients might refuse consent due to confidentiality issues or a desire to withhold information, a secondary analysis was performed on patients who had medication information available (publicly insured). Patients were included in this analysis if they filled at least one prescription at a community-based pharmacy. Selected characteristics for these 15,004 publicly insured patients are reported in Table 4 and include the number of unique medications dispensed and whether the patient had ever been dispensed a medication to treat mental health problem or a medication with a potential for misuse or abuse. The consent rate for these patients was 31.5% (4,756 patients). Consenting patients were dispensed an average of 48.5 unique medications during the enrollment period compared to 25.3 unique medications for non-participating patients ($p<0.0001$). Being dispensed two or more unique medications significantly increased the probability of consenting to participate by 40%.

Table 4. Description and association of patients' characteristics and consent status for patients with continuous public drug insurance during enrollment (N=15,004).

Characteristics*	Consented (%) n=4,756	Not Approached or Refused to Consent (%) n=10,248	Odds Ratios**	95% Confidence Interval
Patients dispensed at least one medication of potential abuse/misuse during enrollment†	351 (7.4%)	652 (6.4%)	0.86	0.73 - 1.02
Patients dispensed at least one medication used to treat mental health problems during enrollment‡	33 (0.7%)	66 (0.6%)	0.69	0.42 - 1.12
The number of unique medications dispensed during enrollment:††				
1	132 (2.8%)	1,180 (11.5%)	reference	-
2 - 6	443 (9.3%)	2,929 (28.6%)	0.97	0.76 - 1.23
7 - 18	756 (15.9%)	2,315 (22.6%)	1.40	1.10 - 1.77
>18	3,425 (72.0%)	3,824 (37.3%)	1.95	1.55 - 2.45

* Measured during the enrollment period.

† Medications of intentional abuse/misuse included opioids (narcotics), barbiturates, benzodiazepines and amphetamines.

‡ Medications used to treat mental health problems included anti-depressants, anti-psychotics and lithium.

†† A medication was counted as one unique prescription as long as the drug and dose remained the same (i.e. 12 refills for 10 mg tablets of Lipitor (r) would only be counted as one medication).

** Adjusted using multivariate GEE modeling for all patient, patient-physician and physician characteristics included in the initial analysis (Table 3) except drug insurance status. The magnitude and significance of all the odds ratios in the initial analyses remained similar except the Charlson Comorbidity Index which became non-significant (OR 0.93; 95% CI 0.85-1.03).

Discussion

This study was a unique opportunity to compare physician characteristics in concert with the characteristics of both participating and non-participating patients. We found that higher consent rates were obtained by physicians who saw fewer patients per day (patient flow) and who were more proficient utilizing the technology. Consenting patients were older, sicker, lived in areas with higher household income levels and visited the study physician on a more regular basis. These patients were also more likely to be the same gender as their

physicians and have the same language preference. These findings appear to support the hypothesis that physicians enroll patients when they perceive there to be value-added benefits to patient management, i.e. older patients with more complex prescription drug histories. The strongest predictor of consent was the number of visits the patient made to the study physician. This emphasizes the physician's role in providing the opportunity for patients to consent as well as the physician's perception of their role as the physician most responsible for the care of that patient*(26,41,42)*. Physicians who saw more patients in a day and were not as proficient in utilizing the technology were less likely to obtain consent from their patients. Thus, the importance of the role of the physician in obtaining patient consent is apparent particularly when the range of consent rates is examined by individual physician (9 to 75%, Table 1).

For the patients who did not consent, we are unable to determine if the patient was approached by the physician to obtain consent and declined, or whether the patient was never approached. However, a time and motion study completed by one of the authors (LP) provided evidence that physicians were preferentially selecting patients to approach regarding participation in the project. This study was conducted among 14 physicians participating in the MOXXI project to estimate the time and method by which an integrated drug management system would be used in their clinical practice. Available data on 315 patient-physician encounters indicate that only 45% of the patients were asked to participate in the research project. Of these, 6% refused and 18% requested that the physician ask them again at a later date. The average duration of a clinic visit was 13.9 minutes (sd 8.8 minutes) and approaching patients for consent to participate in the study required, on average, 1.5 minutes (sd 1.3 minutes). Excluding patients who were already participating in the study, a total of 48% of patients were not asked to consent. Anecdotal evidence from physicians indicate that they recruit patients «who are our regular patients» supporting previous expectations that physicians do not seek consent for patients who receive more fragmented care*(26,41,42)*. While a preliminary analysis of the data from the time and motion study indicated that there was no clear association between mean *duration* of the clinical encounters and patient recruitment rates for physicians, our findings indicate that an increase in the *patient flow* (number of patients seen in a day) significantly decreases the probability of obtaining consent (odds ratio 0.72 per 5 additional patients; 95% CI 0.70-0.74).

We attempted to determine whether the use of medications for mental health problems or those that have the potential for abuse or misuse play a role in determining patient consent. From previous studies by Jacobsen et al.*(18)* and Yawn et al.*(17)* that found patients with more sensitive diagnosis or mental health problems were less likely to consent, we expected to find a difference in rate of medication use between consenting and non-consenting patients. However, our study did not have enough patients who were dispensed these types of medications to allow for clinical or statistical significance. Ideally, to examine the role of medications with the potential for misuse or abuse in determining participation, the patterns of use should be evaluated to identify excessive or escalating use over time*(35, 43, 44)*. This would require a far larger sample accrued over a longer period of time than was available for this study. A larger sample would also be necessary to evaluate the medications used to treat mental health problems. In our study, only 88 patients (0,6 %) with public drug insurance were dispensed an anti-depressant, an anti-psychotic or a prescription for lithium. These relatively low rates may be due to the age of

the insured population who were mostly greater than 65 years old as well as the geographical location of the pilot study, a suburban area of a large metropolitan city with relatively high socioeconomic status*(45)*. The MOXXI project is currently expanding to include additional physicians and patients from more geographically diverse areas with lower socioeconomic levels. This expansion will allow us to further investigate what, if any, role these medications play in determining patient participation.

Based on the findings of our study, physician and patient characteristics play an important role in determining the probability of patient consent to participate in an electronic prescribing project. More importantly, patients who consent to participate are significantly and systematically different than patients who are not approached or who refuse consent. These non-trivial differences that are often related to important health outcomes would introduce serious bias in any research that was restricted to consenting patients.

While informed consent plays a critical role in the protection of a patient's rights to privacy and confidentiality, there is considerable debate centered on how to best inform patients with respect to the potential use of their data and whether patients must, need or want to provide explicit consent for both clinical care and health care research*(46-51)*. This is a critical issue for public health as adverse drug events are estimated to be the sixth leading cause of mortality in the United States*(52)*. This has created an urgent need for rigorous and systematic post-market surveillance for prescription medications*(53,54)*. Integrated electronic prescribing systems offer an unprecedented opportunity to capture timely information regarding drug safety and quality to address this issue. However this process may be biased if obtaining informed patient consent is required for the use of this patient-specific data. Furthermore, if certain physician characteristics are pivotal in acquiring informed consent, as suggested by our findings, we run the risk of obtaining a technically informed but uneducated consent*(51)*. Future research should focus on new models of patient consent that balance the rights of individuals for privacy and confidentiality with the requirements of public health research.

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