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Review article

The impact of health information technology on organ transplant care: A systematic review

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ABSTRACT

Background: Health Information Technology (HIT) has a potential to promote transplant care. However, a systematic appraisal on how HIT application has so far affected transplant care is greatly missing from the literature. We systematically reviewed trials that evaluated HIT impact on process and patient outcomes as well as costs in organ transplant care.
Methods: A systematic search was conducted in OVID versions of MEDLINE, EMBASE, Cumulative Index to Nursing and Allied Health Literature (CINAHL), the Cochrane, and IEEE databases from January 1990 to December 2015. Studies were included if they: (i) evaluated HIT interventions; (ii) reported results for organ transplant population; (iii) reported quantitative data on process, patient, and cost outcomes; and (iv) used a randomized controlled trial or quasi-experimental study design.
Results: Primarily, 12,440 publications were identified; from which ten met inclusion criteria. Among HIT systems, uses of clinical decision support systems (CDSS) targeting different aspects of the complex organ transplant care were common. In terms of process outcomes, HIT positively impacted the timeliness of care, laboratory and medication management practices such as promoting therapeutic or diagnostic protocol compliance by clinicians, and reducing medication errors. Regarding patient outcomes, HIT demonstrated a beneficial impact on the percentage of post-transplant patients with normal lab values and decreasing immunosuppressive toxicity and also deviation from the predefined immunosuppressive therapeutic window. However, in terms of mortality, readmission, rejection, and antiviral resistance rates, the impact was not clearly established in the literature. Finally, these systems were associated with savings in the costs of transplant care in three studies.
Conclusion: This is the first study reviewing HIT impact on transplant care outcomes. CDSSs have mainly been reported to support transplant care in realizing the above-mentioned benefits. However, to make conclusions, more evidence with less risk of bias is warranted. Several gaps in the literature, including comparison of the impact of commercial systems in different transplant settings, was identified which can motivate future research.

1. Introduction

Transplant patients require expensive, long-term, and complex chronic care. From long before undergoing transplantation through frequent post-transplantation follow-up encounters, transplant patients are directly or indirectly cared for by a variety of healthcare providers including physicians, nurses, coordinators, pharmacists, and other medical professionals. The complex, lifelong care is centered around immunosuppressant and graft monitoring, as well as prevention and treatment of common complications such as infection, cardiovascular disease, malignancy, and hematological and bone disorders [1,2]. Despite the availability of comprehensive evidence-based clinical practice guidelines and recommendations for managing organ transplant patients (see for example [1–5]), care complications are prevalent among this high risk patient population [5–10]. Studies have shown that post transplant events and

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complications impose a major economic burden for healthcare systems [11–13].

A prerequisite for providing high quality care for the transplant patient population is the availability of rich and reliable clinical data. However, in a majority of transplant programs, the data and information required for transplant patient care is scattered over multiple inpatient and outpatient documents and systems. This situation constitutes a big challenge for the majority of transplant care programs [14,15]. To effectively meet their organizational and clinical requirements, transplant programs invest in costly data collection practices [16,17]. For many transplant programs, these practices heavily rely on paper-based data management systems despite their inherent limitations and shortcomings. A recent survey of US liver transplant programs showed that the use of paper-based manual processes for immunosuppressive monitoring is still dominant [18].

Health Information Technology (HIT) can play a pivotal role in supporting transplant care by managing data, information, and clinical workflow [19]. Early HIT developments in transplantation date back to 1988 when researchers at the University of Pittsburgh described their effort to develop a center-oriented transplant information management system [20,21]. Since then, similar reports on the design or use of systems for different aspects of transplant care have populated the literature (see for example [15,22–26]). These types of clinical systems have the potential to change the organization of care by redesigning care processes and improving efficiency, effectiveness, and quality of care [27]. However, the development and implementation of HIT is often expensive in terms of personnel, time and money. Moreover, unintended consequences may accompany the deployment of such systems [28]. Therefore, when planning to develop and implement HIT, policy makers, care providers, and healthcare organizations often inquire about an evidence-base impact of such systems on the processes of care, patient outcomes, and resource utilization.

To date, many published studies describe the design, implementation, and use of HIT in organ transplant settings [29]. However, a systematic appraisal on how HIT application has so far affected transplant care is greatly missing from the literature. Therefore, through this study, we aimed to systematically identify and synthesize trials that evaluated the effect of HIT on processes and patient outcomes as well as costs in organ transplant care. The result of our systematic review will enlighten transplant organizations, care providers, and researchers as to where and how to reap full benefits of such systems in providing the complex care for their transplant patients.

2. Methods

This review was conducted according to the Preferred Reporting Items for Systematic reviews and Meta-Analyses: the PRISMA statement [30].

2.1. Search strategy

A comprehensive literature search was conducted in OVID versions of MEDLINE, EMBASE Classic and EMBASE, Cumulative Index to Nursing and Allied Health Literature (CINAHL), the Cochrane Library and the IEEE database for English-language citations including full texts, abstracts, and reports published from January 1, 1990 to December 4, 2015. For this search, we developed a Boolean search strategy using key words and MeSH terms related to two areas of interest i.e.; the study setting or patient population (e.g.; transplantation OR transplant unit OR transplant center) AND the HIT intervention of interest (e.g.; computerized order entry system OR decision making; computerized OR alert system; medication OR therapy; computer-assisted OR diagnosis; computer-assisted; OR medical record systems; hospital information systems; and electronic health records; etc.). In order to not miss relevant studies of early HIT applications in the transplantation domain; we used a long time span. Appendix A in Supplementary material provides details of our search terms and search strategy in MEDLINE. Similar searches were conducted for each of the other databases used in this review. Electronic searches were supplemented by manual review of the reference lists of included studies.

2.2. Inclusion and exclusion criteria

A study was included in this review if it met the following inclusion criteria: (1) the intervention of interest was an HIT system including an electronic medical record, computerized physician order entry system, clinical decision support system, or electronic communication system for data interchange between transplant care providers; (2) the control group used a handwritten or paper-based system, or was a less advanced system compared with an electronic system with a more advanced functionality, (3) the users of the system were transplant physicians, nurses, pharmacists and/or nurse coordinators, (4) the intervention (i.e. the HIT system of interest) was used to provide daily routine care, (5) the patient population concerned either (i) transplant candidates in the pre-transplant evaluation phase, (ii) hospitalized transplant patients in an inpatient setting to receive an organ transplant or care for transplant complications such as rejection or immunosuppressive toxicity, or (iii) post-transplant patients followed in an outpatient setting, (6) the study was an original research article, and (7) the study design was either a randomized controlled trial (RCT), non-randomized controlled trial (NRCT), controlled before-after (CBA) study, interrupted time series (ITS) or before-after trials.

We excluded hematopoietic stem cell transplant studies, lab and simulation studies, qualitative studies, HIT systems used merely for collecting data for research purposes, systematic reviews, commentaries, opinion papers, editorials, and articles describing theoretical or technical background without evaluating the HIT system.

2.3. Review procedures and data extraction

The combined search strategies identified 12,440 electronic records (after removing duplicates), which were screened for eligibility. Fig. 1 shows the flow diagram of our review procedure. ZN primarily screened all the titles and abstracts to find relevant studies based on this study's review objectives. A second reviewer (either HP or PRK) independently examined a random sample of these citations.

Among these citations, 66 potentially eligible publications were selected for full review. To retrieve original articles or to get more information, five authors were contacted of whom three responded [31–33]. An inquiry to access an unavailable study published in 1994 was unresponsive therefore the paper was excluded (Appendix B in Supplementary material). Another unresponded enquiry was for missing information in an included article. We referred to these missing points in Table 1. All full text articles were reviewed in detail for inclusion in the final review set according to our inclusion criteria mentioned earlier. Reasons for exclusion at this stage are given in Appendix B in Supplementary material.

Two authors (ZN and either HP or PRK) independently extracted the following main study characteristics from each paper in the final set of publications: general information (first author and the year of publication, country of origin), study objectives and outcomes measured (process outcomes, patient outcomes, or costs), study design, study setting, patient population (sample size, type of organ transplant), the intervention i.e., the HIT system in use

Table 1
HIT evaluation studies concerning inpatient and outpatient transplant care and their main findings.

Authors (publication year)[a]	Type of publication	Research method	Study objective	Clinical setting/country	Type of transplant	Phase of transplant care	Case numbers in control and experimental groups	The HIT system	Main study results[b]
Boon Falleur et al. [25]	Conference full paper	Before and after observational study	To evaluate the laboratory resource consumption with a rule based expert system	A pediatric liver disease unit in a university hospital in Brussels, Belgium	Pediatric liver transplant	Before and after transplantation assessment & immediate after transplantation care	For assessment protocol (control = 32 patients, experimental = 151 patients); for transplant protocol (control = 10 patients, experimental = 24 patients)	A rule based expert system for laboratory investigations management; the Liver Unit Management Protocol System (LUMPS) integrated with the Laboratory Information Systems and HIS; a homegrown program on a commercial system	• A 27% ↓ in laboratory resources consumption for transplant patients • A 44% ↓ in the percentage of requested "STAT" tests per patient • A 46% ↑ in the specialized diagnostic tests of special chemistry, serology, nuclear medicine, and bacteriology • A ↑ in the percentage of lab tests ordered per patient in agreement with the transplant monitoring protocols 33% before the introduction of the expert system to 45% when the system was used
Mekhjian et al. [33]	Journal article	Before and after observational study	To evaluating the impact of a CPOE system on order turnaround times, lengths of stay and cost[c]	Surgical organ transplant unit at The Ohio State University Medical Center	kidney, liver, pancreas, heart and lung[d]	Inpatient	For medication turnaround time (control = 46 orders, experimental = 70 orders); for radiology turnaround time (control = 11 orders, experimental 54 orders); for LOS (not documented)	A provider order entry (POE) system combined with an electronic medication administration record; a commercial system	• 64% ↓ in medication turnaround time ($p < 0.001$) • 43% ↓ in radiology order turnaround time ($p < 0.05$) • a statistically significant decrease in patient acuity adjusted length of stay following implementation of POE ($p = 0.002$) • a significant decrease in total costs for the organ transplant service ($p = 0.043$)
Staes et al. [32]	Journal article	Before and after observational study	To assess differences between the traditional result reporting related clinical processes that were dependent on faxes and printed documents, and improvements in quality of results reporting and timeliness of clinician responses after implementing computerized alert	The liver transplantation program at LDS Hospital in Salt Lake City, Utah, USA	Liver transplant	After transplantation follow up care	Control = 145 lab request, experimental = 2106 lab request	CDSS plus Intermountain EHR; a homegrown program on a commercial system	• After implementing computerized alerts: • ↑ in completeness of lab result reporting from 66% before to >99% after • ↑ in positive predictive value that a report included new information from 46 before to >99% after • a significant improvement in the timeliness of reporting and also clinicians' responses ($p < 0.001$) • ↓ in median times for clinicians to receive and complete actions from 33.4 h using the prior traditional reporting system to 9.2 h after implementing computerized alerts

Table 1 (*Continued*)

Authors (publication year)[a]	Type of publication	Research method	Study objective	Clinical setting/country	Type of transplant	Phase of transplant care	Case numbers in control and experimental groups	The HIT system	Main study results[b]
Asberg et al. [38]	Journal article	A randomized prospective trial	To compare accuracy of Cyclosporine A therapeutic drug monitoring (TDM) performed by experienced clinicians with the dose suggestions from the Bayesian estimation computer model.	Oslo University Hospital, Norway	Adult kidney transplants	After transplantation and follow up care	Control = 20 patients, experimental = 20 patients	Stand alone CDSS; the computerized Bayesian forecasting model, utilizing nonlinear mixed effects modeling; a homegrown program on a commercial system	• The deviation from the predefined cyclosporine therapeutic window was significantly lower in the computerized group compared with the control group ($p = 0.042$). The average deviation was $9.9\% \pm 4.6\%$ and $12.6\% \pm 7.7\%$, respectively. • A deviation from the targeted blood concentration of more than 50% on at least one occasion was seen in 2 patients in the computerized group and 9 patients in the control group ($p = 0.015$).
Park et al. [36]	Journal article	A retrospective observational before and after study	To determine the clinical and cost effectiveness of an automated clinical management system for monitoring liver transplant patients on Tacrolimus therapy compared to the paper charting system	Liver Transplant Program at the University of Washington Medical Center, Seattle, USA	Liver transplant	After transplantation follow up care	Control = 301 patients, experimental = 127 patients	Specialized screens and forms in EHR to consolidate all clinical information to expedite immunosuppressive review integrated with LIS; a homegrown program on a commercial system	• A significant ↓ in rejection episodes from 22% of patients in the paper charting system to 6% in the automated system ($p < 0.01$) • A significant ↓ in Tacrolimus toxicity 31% of the patients in the paper charting system vs. 18% with the automated system ($p < 0.01$) • An average $1506 ↓ in costs per patient per year in the automated system ($1703 in the paper based system minus $197 in the automated system)
Polidori et al. [35]	Journal article	A retrospective observational before and after study	To measure the incidence and severity of potential DDIs and also to evaluate alert adherence before and after a mandatory acknowledgement function for alerts	ISMET, a 90 bed transplant hospital in Palermo, Italy	Not documented	Inpatient transplant settings	Not documented, clearly	CDSS on the Sunrise Eclipsys electronic medical record system; Commercial	• ↓ in the incidence of potential DDI from 42% to 39% • alert adherence: an increase of 25% in ICU, 54% in cardiothoracic surgery, 52.2% in abdominal surgery unit, 58% in step down unit, 67% in dialysis, 51% in endoscopy, 48% in the postanesthesia care unit

Table 1 (*Continued*)

Authors (publication year)[a]	Type of publication	Research method	Study objective	Clinical setting/country	Type of transplant	Phase of transplant care	Case numbers in control and experimental groups	The HIT system	Main study results[b]
Hooper et al. [37]	Journal article	Interrupted time series design	To evaluate the impact of a decision support monitoring program on treatment and control of dyslipidemia	The kidney transplant program at Cincinnati Children's Hospital Medical Center, Cincinnati, USA	Pediatric kidney transplant	Follow up	Control = 78 patients, experimental = 69 patients; among them 62 patients were before/after cohort	A decision support report automatically generated from an EMR integrated to LIS to (1) identify all kidney transplant recipients coming to clinic in the upcoming week, (2) assign 1 of the new 18 unique testing schedules to each patient according to dyslipidemia risk, and (3) report the most recent test results, whether additional testing was due, and the next due date for each test; a homegrown program on a commercial system	• ↑ in the proportion of visits in which cholesterol monitoring completed when indicated from 80% in the baseline period to 98% within 8 months after the intervention. This result was continued for more than one year • ↑ in the percentage of patients with cholesterol documented in the previous 12 months from 84% at the start of the project to 95% after that was continued for nearly 2 years • ↑ in the percentage of patients with dyslipidemia on statin therapy from 52% in the baseline period to 88% afterwards • ↑ in the percentage of patients with controlled LDL (<130 mg/dl) from 71% at the start of the project to 94% after a median follow up of 24 months ($p = 0.002$)
Hensler et al. [41]	Conference abstract	A retrospective observational before and after study	To assess the impact of an automated EMR based, pharmacist driven valganciclovir dose optimization program	Northwestern Memorial Hospital, Chicago, USA	Kidney, pancreas, and liver transplants	Follow up	Control = 388 patients, experimental = 346 patients	A CDSS program to automatically generate a list of patients with under or overdosing of valganciclovir based on estimated GFR on a EMR (OTTR Chronic Care Solutions, Omaha, NE); a homegrown program on a commercial system	• ↓ in the incidence of CMV replication ≥545 IU/mL or biopsy proven disease in transplant patients from 10.6% before to 5.8% after the intervention ($p = 0.02$)

Table 1 (*Continued*)

Authors (publication year)[a]	Type of publication	Research method	Study objective	Clinical setting/country	Type of transplant	Phase of transplant care	Case numbers in control and experimental groups	The HIT system	Main study results[b]
Wu et al. [40]	Conference abstract	A retrospective before and after study	To evaluate the effects of EPIC electronic health record (EHR) implementation in the before kidney transplantation process	Kidney transplant center, Thomas E. Starzl Transplantation Institute, University of Pittsburgh, USA	Kidney[c]	Before transplantation workup	Control = 114 patients, experimental = 209 patients	EPIC EHR; commercial	• a marked decrease in time from referral to appointment from mean 185 days (median = 99) before the intervention to mean 34 days (median = 28) after the intervention • a marked decrease in time from appointment to listing from mean 227 days (median = 197) before the intervention to mean 83 days (median = 63) after the intervention • The number of new patients listed at the center increased by 107%
Bonkowski et al. [39]	Journal article	A prospective observational before and after study	To evaluate the impact of a BCMA system on medication administration error rate	Solid organ transplant unit, The Ohio State University Wexner Medical Center, USA	Kidney, liver, and pancreas	Inpatient	control = 936 medication administration, experimental = 976 medication administration	BCMA integrated with a EMR; commercial	• a relative rate reduction of more than two thirds in the medication administration error rate (from 4.8% error rate before BCMA to 1.5% after the implementation ($p = 0.0001$) • wrong dose errors was the only error type with a significantly reduced rate ($p = 0.001$)

Abbreviations: HIS, Hospital Information Systems; POE, Provider Order Entry; CDSS, Clinical Decision Support System; EMR, Electronic Medical Record; EHR, Electronic Health Record; LIS, Laboratory Information Systems; BCMA, Barcode-Assisted Medication Administration; DDI, Drug–Drug Interaction; ICU, Intensive Care Unit; LDL, Low Density Lipoprotein; CMV, Cytomegalovirus; USA, United States of America; STAT, From the Latin word statum, meaning 'immediately'; IU/mL, International Unit/milliliter.

[a] In the chronological order of publication year.

[b] Whenever a p values is not provided, it was not in the referenced article.

[c] Only the section of the study relevant to the transplant service was provided here.

[d] Provided by the authors upon request.

[e] In contrast to the title of the publication, the data analysis included only kidney transplant patients.

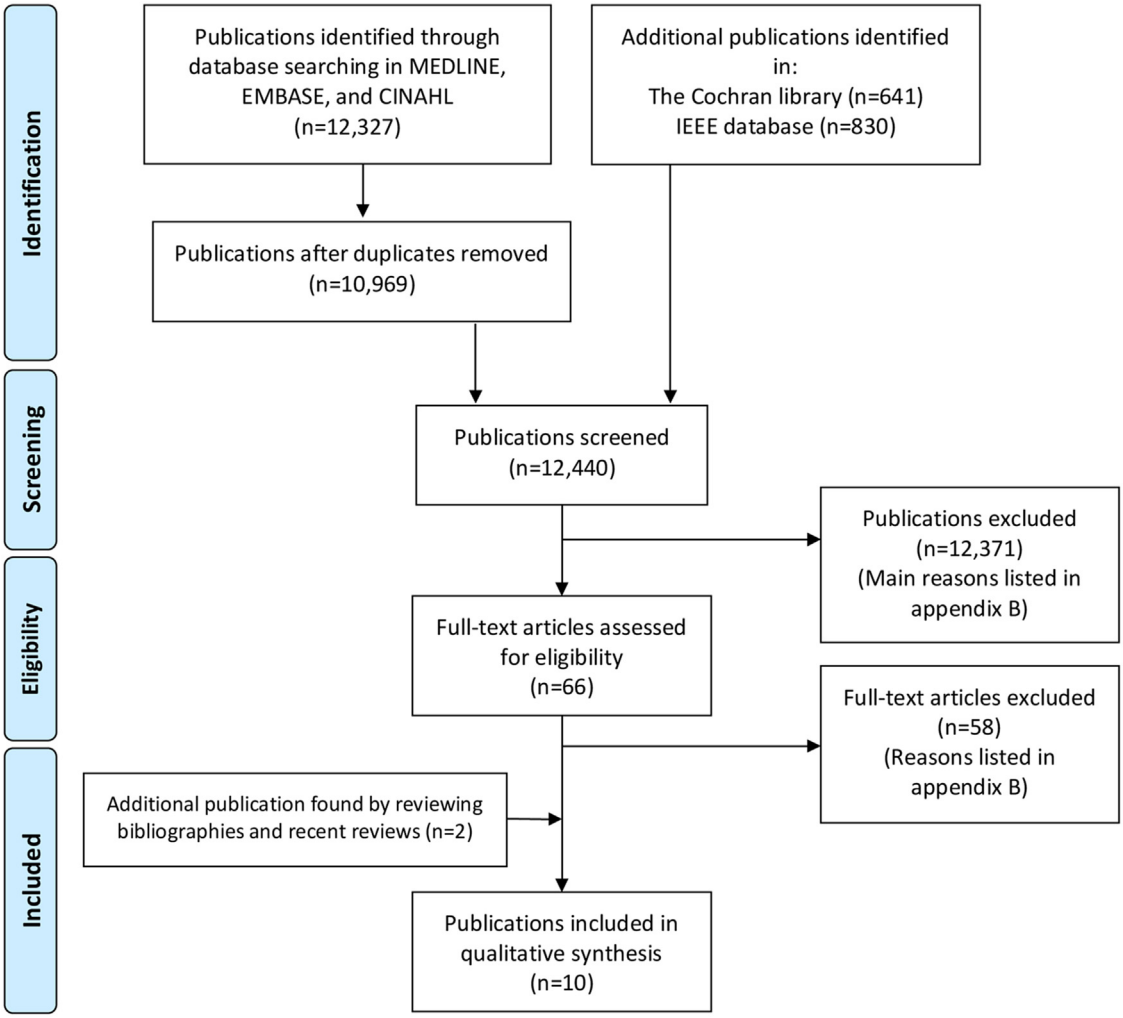

Fig. 1. Flow diagram of study selection (1990–2015).

(description of the information system and its integration to other systems, users of the system, type of the system in terms of home-grown or commercial), the phase of transplant care studies (donor-recipient matching, pre-transplant workup, inpatient hospitalization, post-transplant follow up), study in real world or simulation, and the main study results in terms of the outcomes of interest in this review (see Section 2.6. for categorization of study outcomes). The extracted data were checked for consistency among the authors during multiple meetings and disagreement was solved by discussion. Endnote version XI was used to manage citations.

2.4. Methodological and reporting quality

Studies that met the inclusion criteria were further assessed for their quality. We used the Cochrane Collaboration's tool for assessing risk of bias for randomized trials and the Newcastle-Ottawa Score for observational studies. For reporting quality, we used STAtement on Reporting of Evaluation studies in Health Informatics (STARE-HI) [34].

2.5. Data synthesis

Several limitations precluded us from conducting a formal meta-analysis. These limitations included a paucity of randomized controlled trials (RCTs) among the articles reviewed, inconsistent outcomes measurement, and varying information systems being evaluated. Thus, we only provide a narrative description of the results.

2.6. Categorization of interventions and study outcomes

We categorized system use based on the phases of transplant care in which a system was deployed and the outcome of interest studied. The outcomes of interest in this review were in turn categorized as process outcomes (such as adherence to recommended guidelines, order turnaround time, drug–drug interaction, drug-lab interaction, time spent on patient care, and quality of patient records), patient outcomes (such as transplant rejection rate, graft survival rate, hospital lengths of stay, readmission rate, mortality, quality of life, adverse drug events, and post-transplant follow-up lab tests or other patient monitoring such as vaccination rate), and cost-effectiveness including resource utilization.

3. Results

3.1. Description of the studies

A total of ten publications including seven journal articles [32,33,35–39] and three conference papers and abstracts [25,40,41] met our inclusion criteria. Table 1 shows the main characteristics of the included publications. The type of transplant populations varied, including kidney [37,38,40], liver [25,32,36], and mixed

organs i.e., kidney, pancreas, liver [35,39,41] and kidney, liver, pancreas, heart and lung [33] transplants. The phase of transplant care being evaluated were pre-transplant [40], inpatient transplant [33,35,39], follow up [32,36–38,41] and two combined phases of pre-transplant and follow-up [25]. All studies used observational before-after design, except one interrupted time series [37] and one randomized trial [38]. The system in use in the majority of settings was composed of a decision support system integrated with a hospital information system (HIS), computerized provider order entry system (CPOE) or an electronic health/medical record (EHR/EMR) with the exception of one stand-alone clinical decision support system (CDSS) [38] and a barcode-assisted medication administration system integrated with an EMR [39]. CDSS capabilities were mainly reported to support medication process [33,35,36,38,41] and lab tests [25,32,37] ordering and managements. The majority of studies evaluated a homegrown tool integrated with an existing HIS or EHR/EMR system. Only four commercial systems were assessed [33,35,39,40]. The majority of studies were conducted in the USA. The number of evaluation articles increased over time.

3.2. Effectiveness of interventions

In this section, we categorized study findings on the basis of process outcomes, patient outcomes, and cost-effectiveness or resource utilization.

3.2.1. Impact on the processes of transplant care

Studies that reported outcomes regarding timeliness of care, efficiency in medication management, protocol compliance by providers (provider performance), and document quality is presented here.

3.2.1.1. Impact on timeliness of patient care processes. Three studies reported outcomes for timeliness in the processes of transplant care with HIT systems [32,33,40]. In a before-after study of computerized alerts for lab result monitoring at the liver transplantation program of LDS hospital, Staes et al. [32] found a significant decrease in the reporting and response time for both creatinine and tacrolimus results favoring computerized alerts: using the alerts, the nurses received, reviewed, and completed actions faster than their traditional way of reporting by faxes, printouts and mailed reports (median 9.2 h vs. 33.4 h, respectively, $p < 0.001$). A study of a CPOE system combined with an electronic medication administration record at The Ohio State University Medical Center showed significant reductions in both medication and radiology order turnaround times [33]. After the implementation of EPIC EHR in the pre-kidney transplant process of Thomas E. Starzl Transplantation Institute, a study by Wu et al. [40] reported that the mean (median) time of referral to appointment decreased from 185 (99) days to 34 (28) days following the EHR implementation. Moreover, the mean (median) days from appointment to listing decreased from 227 (197) days to 83 (63) days.

3.2.1.2. Impact on transplant medication management. Four studies provided information on medication management with HIT interventions. In a kidney transplant program at Cincinnati Children's Hospital Medical Center, Hooper et al. [37] evaluated a quality improvement initiative including the use of an EMR with an embedded, transplant-specific protocol-based, decision support system. In this study, the later component was the main intervention that was evaluated. This decision support aimed at monitoring 12 lab tests including cholesterol monitoring to improve the treatment and control of dyslipidemia individualized by dyslipidemia risk. The study results revealed that only 52% of patients with dyslipidemia received statin therapy at the initiation of the project, while over the next 3 years after the intervention, this rate increased to 88% of patients with dyslipidemia. The increase in statin therapy was translated into an improvement in patient outcomes (see Section 3.2.2 for patient outcomes for details). In another study, Polidori et al. [35] evaluated the impact of mandatory acknowledgement of drug–drug interactions (DDIs) alerts of a computerized physician order entry system in a 90-bed transplant hospital in Italy. In the first period of study (before the mandatory acknowledgement of DDI alerts), clinician adherence to alerts was 38% (ranging from 10% to 70% in different units). After requiring mandatory reading of alerts by physicians, adherence to alerts markedly improved to 82% (ranging from 30% to 96%). This study also evaluated DDIs before and after the above-mentioned intervention. The results showed a positive trend (a reduction of potential-DDIs) in only four out of eight study units. The authors attributed this finding to the greater adherence to warning systems in these units. In the next study, the use of a barcode-assisted medication administration (BCMA) system in an academic solid organ transplant unit was associated with a significant reduction in medication administration error rate (from 4.8% error rate before BCMA to 1.5% after the implementation, $p = 0.0001$) [39]. Finally, in a study by Hensler et al. [41], the impact of an automated EMR-based decision support program developed in the transplant center of Northwestern Memorial Hospital was evaluated. This program facilitated reviewing and adjusting the prophylactic dose of valganciclovir (valGCV) by generating a list of patients with under or overdosing to be reviewed by pharmacists on a weekly basis [41]. This study found that 10% of patients reviewed by the help of the computerized program required dose adjustments. The implementation of the system was accompanied by improved patient outcomes (see Section 3.2.2 for patient outcome).

3.2.1.3. Impact on transplant laboratory monitoring practices. We found three studies in this category: two reported results regarding protocol compliance for laboratory tests by clinicians and one on quality of transplant laboratory result reporting. In the first study, Boon Falleur et al. [25] embedded protocols for clinical laboratory investigation management in a rule-based expert system and evaluated its impact on protocol compliance in a pediatric liver transplantation unit in Brussels. After one year, the percentage of lab tests ordered in agreement with the transplant monitoring protocols (i.e., compliance with chemistry testing suggestions) increased from 33% before the introduction of the expert system to 45% when the system was used. The second study in this category assessed the impact of a protocol-based decision support system to monitor 12 lab tests including cholesterol monitoring [37]. The results revealed that the percentage of patients with cholesterol monitoring documented in the previous 12 months increased from 84% at baseline to 95% after the intervention. According to the authors, this improvement was continued even for nearly 2 years during the study time. Regarding the quality of transplant laboratory result reporting, the third study [32] evaluated the impact of alerts for new and overdue results for creatinine tests and immunosuppression levels and found that completeness of reporting increased from 66% to >99%, as did positive predictive value that a report included new information from 46% to >99% after the implementation.

3.2.2. Impact on patient outcomes

Studies in this category evaluated patient outcomes such as drug concentration levels, drug toxicity or resistance, rejection rates, readmission rate, mortality, and patients' normal laboratory values.

Three studies evaluated the impact of HIT systems on transplant patient's drug related patient outcomes i.e., predefined therapeutic drug concentration levels/ranges [38], drug toxicity [36] and drug resistance [41]. A single center randomized trial in adult kidney transplant recipients compared the performance of

a computer-based therapeutic drug monitoring (TDM) aimed at calculating the required Cyclosporine doses to the standard TDM routine [38]. This study found that the deviation from the predefined therapeutic window for Cyclosporine was significantly lower in the computerized group (9.9% ± 4.6%) compared to the control group (12.6% ± 7.7%) ($p = 0.042$). However, the overall percentage of whole-blood concentrations within the therapeutic window was not different between the two groups (36.6% ± 17.0% in the computerized group vs. 32.8% ± 15.4% in the control group, $p = 0.57$). Park et al. [36] studied the impact of using an automated clinical management system for immunosuppressive review during follow-up care of liver transplant patients and found that Tacrolimus toxicity significantly decreased from 31% of patients managed using the paper charting system to 18% of patients managed using the automated system ($p < 0.01$). Regarding drug resistance, a study found a decrease in the rate of valganciclovir-resistant cytomegalovirus (CMV) after the implementation of a computerized program, although it was non-significant (0% versus 0.5%, $p = 0.5$) [41]. This study also revealed that the incidence of CMV replication ≥545 IU/mL or biopsy proven disease significantly decreased from 10.6% during the control period to 5.8% during the intervention period ($p = 0.02$).

One of the other patient outcomes assessed in the included studies was the percentage of pediatrics kidney recipients having their low density lipoprotein (LDL) cholesterol value in normal range (an LDL <130 mg/dL (3.3 mmol/L)) before and after the implementation of a protocol-based decision support system [37]. In this study, using the system significantly increased the percentages of patients with a normal LDL level from 71% pre-implementation to 94% post-implementation after a median follow-up of 24 months ($p = 0.002$). The next patient outcome assessed was rejection episodes after using an automated system for immunosuppressive review during liver transplant follow-up care [36]. The study found a significant decrease in rejection episodes during the one year post-implementation period compared to the pre-implementation period (6% vs. 17%, respectively; $p < 0.01$). Also, in this study, in a multivariable analysis with 10 factors including the automated system, patient care with the automated clinical management system produced lower odds of a rejection episode than management with the paper charting system (OR = 0.20; $p < 0.01$). However, the decrease found in the readmission rate and mortality after the implementation of the system was not significant ($p = 0.5$ and $p = 0.08$, respectively) [36]. After implementing a CPOE system at the Ohio State University Medical Center, a statistically significant decrease was documented in patient acuity-adjusted length of stay in organ transplant service (pre-CPOE, 4.71 days; post-CPOE, 4.02 days; $p = 0.002$) [33]. In a randomized trial of a computer-based CDSS calculating the individualized Cyclosporine doses by Asberg et al. [38], no difference was found in biopsy-proven acute rejection episodes when compared to routine care.

3.2.3. Impact on cost-effectiveness of transplant care

We found three studies that compared the cost effectiveness of and resource utilization with computerized systems to that of paper based systems. The first study conducted a formal cost-effective analysis of an automated clinical management system targeting the follow-up of immunosuppressive care for one liver transplant patient/year by nurses and compared it to the costs of the paper charting system before the intervention [36]. The analysis showed that the automated system was more cost-effective than the paper charting system, saving on average US$1506 per patient per year ($1703 in the paper charting system minus $197 in the automated system, costs standardized for the year 2008). The authors calculated that with this cost saving, the automated system's cost of development was recovered in following 6–12 patients for one year. Regarding total projected one-year cost saving of $150,600 (range 136,700–188,000) in this study, the automated system would save between 1.1–1.6 nursing equivalents per year after the initial year. Another study evaluated laboratory resource consumption in transplant monitoring tests in a pediatric liver transplantation unit after implementing a protocol-based laboratory test decision support system [25]. After one year, they observed a 27% reduction in the mean number of tests requested per patient (from 1047 mean number of tests/patient to 768). However, there was a 13% increase in the total number of tests requested per patient in the pre- and post-transplant assessment patients, where the authors attributed this finding to requesting of more specialized diagnostic tests per patient in this phase. In the third study, implementation of a CPOE system was associated with a significant saving in total costs for the organ transplant service (pre-CPOE, $8382; post-CPOE, $7711; p = 0.043) [33].

3.3. Methodological quality: study and reporting quality

Appendix C in Supplementary material provides information on methodological quality of studies included in this review. It shows that with few exceptions, risk of bias in study design was high. Also, we noticed that according to the STARE-HI guidelines important items such as clinical settings and features of HIT systems (as the main intervention) were briefly reported in published literature.

4. Discussion

To the best of our knowledge, this is the first systematic review exclusively dedicated to the impact of HIT use on transplant care. Through a comprehensive search strategy, our review identified ten publications that provided quantitative data related to HIT impact on processes and costs of transplant care and patient outcomes. One predominant HIT application in organ transplant settings has been CDSS capabilities for medication and/or lab management. Our review of the outcomes related to the processes of transplant care showed that HIT systems have had a positive impact on the timeliness of transplant care as well as on laboratory and medication management practices such as promoting protocol compliance by clinicians for therapy or laboratory requests, reducing medication errors, and improving data completeness and timely data access. Moreover, regarding patient outcomes, these systems have demonstrated a beneficial impact in terms of improving the percentage of post-transplant patients with normal lab values, a non significant effect on reducing mortality and readmission rate, and a mixed impact on rejection episodes (positive in one study and no effect in another). HIT systems have also helped in decreasing deviation from the predefined immunosuppressive therapeutic window, immunosuppressive toxicity and antiviral resistance in patients. Finally, these systems have been associated with savings in the costs of immunosuppressive management practices as well as decreased resource utilization, particularly concerning laboratory tests.

4.1. Impact on process and patient outcomes

The positive impact of HIT systems on quality and efficiency of health care delivery is well documented in the literature [27,42]. However, this does not guarantee that such interventions are extensively implemented and used in acute or chronic care settings [43,44]. Our review suggests that this finding is also valid in the transplant care domain. Studies have reported that transplant specialized HIT systems are not in routine use even in developed countries [18,45]. This is especially true when it comes to support the entire continuum of transplant care. In fact, comprehensive transplant-oriented HIT systems application is yet to be realized, and current systems only support limited aspects of transplant

care [29]; though, they appear to be valuable as shown by the present review. In this regard, the study by Park et al. documented the value of having a consolidated individualized immunosuppressive information overview enabled by HIT to have better outcomes [36]. Other studies demonstrated the favorable impact of a protocol based CDSS on transplant practitioner performance and patient outcomes [25,37]. These findings are in line with the results of other studies embedding guidelines in HIT systems to affect quality and efficiency of inpatient and outpatient care [46,47]. Yet, routine use of HIT systems covering all phases and aspects of transplant care based on comprehensive transplant care protocols is greatly lacking. This gap in practice emphasizes the need for the "next-generation long-term transplant clinics" in which HIT enables an orchestrated, evidence based, teamwork of multiple distributed stakeholders including patients and providers [48]. Thus, organ transplant organizations ought to consider such HIT enabled model for transplant care.

From our review, it becomes evident that CPOE and/or CDSS have come to play a role in improving the efficiency of transplant care and overcoming some of the hurdles in transplant medication management and lab monitoring practices including multiple dose adjustments and identifying the DDIs or other interactions between drugs and patient's current laboratory values or underlying diseases [32,33,35–38,41]. For CPOE and CDSS to support specialized transplant care their knowledge base should be relevant, current and up-to-date and their underlying workflow models should match those of transplant care. Scholars highlighted that the hospital-wide general systems do not always accommodate transplantation needs and requirements [45]. A case study that reported the consequences of using a vendor supplied CDSS tool for this high risk patient population explained how a potential adverse drug error occurred when a significant immunosuppressant interaction alert was omitted [49]. This particular case prompted the institution to review its CDSS and customize it by downgrading and upgrading the severity of a number of potential immunosuppressive DDI alerts to address specialized transplant patient needs. Another study also detected a number of clinically significant medication errors in an inpatient kidney transplant setting even after a hospital wide CPOE system was well adopted [50]. Such reports call transplant programs to closely monitor the application of their HIT systems and their knowledge bases through well-designed systematic evaluation studies.

Timeliness of care is one of the priority areas for improving quality of health care as established by the Institute of Medicine [51]. Among advantages of HIT systems in clinical workflow is promoting timeliness of care by removing many administrative tasks such as looking for necessary data in multiple records and also quicker communicating of orders, lab results, or patient information between care providers [42,46]. In our review, two studies showed time savings with HIT systems both in pre-transplantation assessment phase and post-transplant lab result monitoring practices [32,40]. Moreover, in line with the results of other inpatient settings [42], CPOE was shown to contribute to care timeliness in terms of shorter medication and radiology order turn-around times in transplant services [33].

4.2. Cost effectiveness

Organ transplantation has been shown to be more cost effective than treating end stage organ disease. Yet, the economic aftermath of transplantation and post-transplant events per se is also notable. In this regard, multiple studies have been conducted to assess the economic burden of post-renal-transplant events including studies in European countries [52–57]. These studies have estimated a cost from minimum € 4204 per patient per year to a maximum of € 44,540 for events such as hospital stays, delayed graft function, outpatient appointments, laboratory tests, anemia, hypertension, dyslipidemia, and infections (without considering immunosuppressant drug costs). The immunosuppressive treatments may itself account for around 23% of total post-transplant costs [58]. Furthermore, costs can greatly increase in the occurrence of care process events (e.g., communication breakdowns and medication errors) or other adverse events such as rejection [11–13]. By supporting multiple aspects of care such as preventing adverse events, HIT systems have been contemplated to contribute in healthcare cost containment. But this claim has not been the subject for thorough evaluation as highlighted in systematic reviews [59,60]. In our review, only two studies evaluated cost and cost-effectiveness issue and both showed that HIT systems were associated with reductions in resource utilization and costs of care [25,36]. This is in accordance with the result of other studies when there is supporting evidence [61]. In our review, the beneficial impacts on process and patient outcomes may support the view that by decreasing post-transplant events such as rejections, infections, or drug toxicity and resistance, HIT contributes to the overall cost-effectiveness of transplant care. However to make any definite conclusions, high quality economic evidence is warranted.

4.3. Limitations of the review

This review has limitations. First of all, mainly due to a small number of available quantitative studies in each outcome category, higher risk of bias in trials, and limited description of settings and HIT systems, the generalizability of the effects to other settings or HIT systems is limited. Second, given that our review only focused on HIT systems, it does not address the larger systems influences on care improvements that have been taken place during the time period of our review. It is noteworthy that the systems improvements have meanwhile been unmeasured but confounding variables. Third, the objective of our study does not address organ transplant registries. We excluded this literature because both national and international registries such as The Global Database on Donation and Transplantation, Collaborative Transplant Study (CTS), Organ Procurement and Transplantation Network/Scientific Registry of Transplant Recipients (OPTN/SRTR) [62–64] are seen as solely research tools for transplant outcome analysis and not used prospectively by *care providers* in providing *real-time, routine* transplant care. Forth, our review objective focused on the care of transplant recipients and not on donors'. That should be the focus of another review.

4.4. Implications for further research

Our review suggests several important future directions for research. First, much literature published on the subject had qualitative and descriptive nature (see Appendix B in Supplementary material). This method of sharing experiences is necessary for and valuable in advancing the development of HIT systems. However, the paucity of quantitative studies in literature highlights that the use and impact of HIT systems themselves have generally not been the subject of systematic evaluations [65]; and when being evaluated, the risk of bias was high with few exceptions (see Appendix C in Supplementary material). In fact, in a number of studies, these systems were mainly approached as research tools to provide structured data for clinically focused studies (for example [66–68]). Second, although health and care needs of transplant patients partly overlap with other chronic patients', these patients have other unique and complex care needs such as frequent monitoring of immunosuppressive drugs. On the one hand, these needs may totally not be supported if general hospital-wide HIT systems such as EMRs are implemented in transplant units [45]. On the other hand, development of transplant focused HIT systems for trans-

plant care is not an option for many transplant programs due to the lack of necessary monetary investment, expertise, and time issues. Therefore, when general hospital-wide systems such as EMRs are implemented in transplant units, their use and impact in these units should be evaluated with well-designed studies and shared with others. This will enable getting insights into the ways that such systems should be customized according to transplant needs. Third, it will also be fruitful if future studies compare the impact of similar systems such as commercial CPOE and CDSS implemented in different organ transplant settings. Fourth, the reviewed studies were mainly from kidney, liver, and pancreas transplant settings. HIT deployment in other transplant settings (e.g., for heart, lung, and intestine transplantation) is also required to strengthen the evidence base of our knowledge on the subject. Fifth, in the majority of the included studies, limited numbers of outcome measures were assessed and the focus of evaluations was on relatively short-term effects. These systems are considered socio-technical systems and evolve through time during use, so their impact might be altered through time as well [69]. To monitor the intended use and impact of such systems, longer-term effects should also be the focus of future research.

5. Conclusions

This review summarized current knowledge on the impact of HIT systems in inpatient and outpatient transplant settings. Among HIT systems, those with CDSSs were reported supporting the complex aspects of organ transplant care. The findings of this review provide insight for transplant programs on how to reap the full benefits of HIT systems in providing patients with a higher quality care. Furthermore, it highlights the gaps in the literature which can motivate and direct future studies.

Summary point

What was already known on the topic

- Health Information Technology (HIT) has a potential to promote chronic care including complex organ transplant care.
- Many published studies have described the design, implementation, and use of HIT in organ transplant settings.
- A systematic appraisal on how HIT application has so far affected organ transplant care is greatly missing from the literature.

What this study added to our knowledge

- Despite a comprehensive search, we found only limited number of quantitative studies on the subject. This points out that the use of HIT itself has so far not been the subject of systematic evaluations in organ transplant care.
- The qualitative analysis of existing evidence shows beneficial impact of HIT in organ transplant care. However, to make conclusion more studies with higher quality are warranted.
- The use and impact of commercial systems in transplant units should be evaluated with well-designed studies and shared with others.

Conflict of interest

None.

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Author's contribution

ZN and HP designed the study and conducted the search. ZN, HP and PRK selected articles for inclusion according to the inclusion/exclusion criteria. All authors contributed in the review, extraction and analysis of data from the included articles. ZN drafted the manuscript and revised its different versions according to the other authors' comments. All authors approved the final version. HP scientifically supervised the work.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.ijmedinf.2017.01.015.

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