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The Genesis of the CHAMP-Path: Pragmatic RCTs Methodology

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Abstract:

A clinical pathway is an evidence-based integrated plan of care within a pre-defined time frame by multidisciplinary health care professionals. There is conflicting evidence about the utility of clinical pathways in real life settings. The aim of the study is to determine if collaborative, clinical pathway-based care (PC) vs. Usual care (UC) will decrease the length of stay (LOS) across multiple medical diagnoses. CHAMP-Path is a pragmatic, parallel, single blind, and randomized controlled trial. Physicians will be randomized into two teams. Patient randomization will be computer-generated through permuted blocks in 1:1 ratio, and allocation to be concealed. Eligibility criteria is age ≥ fourteen years, hemodynamic stability, and pathway-specific inclusion and exclusion criteria. The intervention is PC compared to UC. The primary outcome is the reduction in LOS. The secondary outcomes are patient- centered outcomes, determinants of LOS, and 30-day re-admission rate. A sample of 512 patients is estimated (Venous Thromboembolism: 128, Asthma: 90, Heart Failure: 90, Community Acquired Pneumonia: 166, Acute kidney injury: 38) to provide 80% power, alpha of 5% and accounting for 20% attrition. Mean LOS ± SD, 95% CI, p-value will be performed for LOS and regression analysis to identify determinants of LOS.

Keywords: *Pragmatic clinical Trial, Randomized Controlled Trials, Healthcare providers, Clinical Pathways, integrated Health Care Systems*
Trial Registration: *ClinicalTrials.gov Identifier: NCT01561885*

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INTRODUCTION

There are several synonymous terms which characterize clinical pathways as time-based, evidence- informed, integrated care plans aiming to improve patient- centered outcomes, satisfaction, and optimizing organizational resources (Dobesh et al., 2006). Integrated care plans are developed to enhance the utilization of evidence-based guidelines, institutional best practices to facilitate communication, standardization of care among health care professionals, to improve quality of care and it is best utilized when developed by the multidisciplinary team involved in patient care (Campbell, Hotchkiss, Bradshaw, & Porteous, 1998; Durvasula et al., 2015; Steichen & Gregg, 2015). Therefore, clinical pathways have been proposed as a tool to optimize institutional resources, reduce delays in patient care, enhance patient safety, improve quality of care and subsequently reduce LOS and enhance patient-satisfaction ((EPA)).

Literature review

Patient flow problems exist universally and studies have demonstrated that a multidisciplinary approach facilitates early morning discharges and improves patient flow (Durvasula et al., 2015).

As clinical pathways are widely utilized, there remains inconsistent evidence about their effectiveness. A systematic review and meta-analysis conducted by (Thomas Rotter et al., 2008) included RCTs and non-RCTs to study the effects of clinical pathways on LOS, hospital costs, and patient outcomes. The overall conclusion was that the small number of studies involved provides insufficient evidence about the effectiveness of

clinical pathways in reducing LOS. There is insufficient evidence for reproducible strategies for pathways in general and their use may prove to be effective mainly in surgical care.

A subsequent Cochrane systematic review including 20 studies assessing the effect of clinical pathways versus usual care on professional practice and patient centered outcomes, LOS and hospital costs, has shown a reduction in the rate of in-hospital complication (Odds ratio (OR) 0.58 with a 95% CI (0.36-0.94) (T. Rotter et al., 2010). No statistically significant difference was reported for in-hospital mortality or readmission with a significantly reduced LOS in most of the trials, including invasive and non-invasive studies (stroke rehabilitation and pneumonia) and additional cost reduction. However, the review had a high heterogeneity for both outcomes due to different study designs and settings, which prevented statistical estimation of pooled effects and demonstrated knowledge gaps on effectiveness of clinical pathways across various medical diagnoses (Cruz-Flores, 2010).

Overcrowding and triage present a challenge in day-to- day emergency rooms and timely discharge from hospital is an indicator of quality of care with various ongoing resource management pressures at King Abdulaziz Medical City (KAMC), Jeddah. As a JCI accredited organization, clinical pathways have been proposed in our hospital as a tool to coordinate services aiming to improve quality of care in areas identified by organizational leadership. However, the effectiveness of clinical pathways in real life "pragmatic settings" has not been explored across multiple medical diagnoses, including asthma, community-acquired pneumonia (CAP), acute kidney injury (AKI), venous thromboembolism (VTE), and left ventricular heart failure (HF) were not addressed. Therefore, we hypothesized that designing and implementing clinical pathways to improve patient flow would reduce inpatient length of stay (LOS).

Purpose

We aim to study if **C**ollaborative **H**ealthcare Professionals **A**pproach **in M**onitoring **of P**atient- Centered Outcomes through **Path**ways (CHAMP-Path) versus usual care will lead to a decrease in LOS across multiple medical diagnoses in pragmatic settings.

METHODS

Participants

All eligible patients for admission at KAMC, Jeddah will be screened in the Emergency Department. After obtaining written informed consent, patients will be randomized to either receive PC or UC. All enrolled patients will be blinded to their allocated arm. General eligibility criteria for all pathways are over14 years of age (institutional criteria for admission to adult medical wards), hemodynamic stability, and primary cause of admission is the medical diagnosis of interest. Additional criteria for patients with AKI will be serum creatinine more than 50% of baseline based on Acute Kidney Injury Network criteria (AKIN)(Mehta et al., 2007). General exclusion criteria include pregnancy, no re-enrollment for the same admitting diagnosis and ICU admission. Pathway-specific exclusion criteria for AKI were stage 4 and 5 chronic kidney disease, kidney allograft recipients, obstructive uropathy, glomerulonephritis and interstitial nephritis. For asthma, patients with chronic obstructive pulmonary diseases, Bronchiectasis, and severe asthma with peak expiratory flow rate of less than 40% will be excluded. Patients with heart failure, non-cardiogenic pulmonary edema, and those requiring inotropes will be excluded. Finally, for venous thromboembolism, patients with systolic blood pressure of less than 90 mmHg, massive pulmonary embolism and those with simplified Pulmonary Embolism Severity Index (sPESI) score ≥1 will be excluded (Konstantinides et al., 2014).

Intervention

Pathway-based care is defined as a multidisciplinary integrated plan of care within a pre-defined time frame integrated into a Computerized Provider Order Entry (CPOE) order set while Usual care is defined as current evidence-based practice. Pathway access will not be permitted for physicians allocated to UC. Deviation from PC will be allowed at the discretion of the treating physicians to address specific patient needs.

Study outcomes

The primary outcome is hospital length of stay (LOS), represented in a fraction of days and calculated from the time of inpatient admission until the time of hospital discharge, as reported by the hospital's electronic medical record system. The secondary outcomes include pathway- specific clinical outcomes, determinants of LOS, 30-day re-hospitalization rate for the same diagnosis, and patient satisfaction using a validated 46-item survey assessing the quality of care provided by physicians, nurses, pharmacists, patient educators, social workers, clinical nutritionists, and general hospital staff. The determinants of LOS identified for data collection and analysis are based on literature review and organizational experience.

Data collection

A Case Report Format (CRF) is created for each diagnosis and will be used by the research assistant. Variables include baseline patient characteristics such as age, weight and height, co-morbidities and admission history; the primary outcome (e.g. total LOS in days, hours, and minutes) and secondary outcomes such as 30- day readmission and the determinants of LOS which include admission and discharge factors (e.g. weekend admission, discharged against medical advice, and delays in discharge procedures); medical factors such as coexisting diseases, ability to ambulate, diagnosis-specific outcomes e.g. CURB-65 (Sharp et al., 2016) documented in the medical file for CAP, and whether dialysis is required for AKI; and hospital complication factors such as ICU transfer, hospital acquired infection, and adult cardiac arrest. Examples of pathway-specific outcomes to- be-studied include ultrasound within 24 hours of presentation for AKI; first dose of antibiotics administered within first 4 hours of presentation for CAP (Mandell et al., 2007); physician and pharmacist medication reconciliation within the first 24 hours of admission, and pharmacist discharge counseling ("ASHP Guidelines on the Pharmacist's Role in the Development, Implementation, and Assessment of Critical Pathways," 2004; Keeys et al., 2014).

Additionally, one of the co-investigators from the Quality Management Department will use a standard data collection spreadsheet to audit adherence and pathway- specific indicators (Vanhaecht, De Witte, Depreitere, & Sermeus, 2006). Source documents for data collection will be the patient medical records and responses of patient and/or caregivers to the Patient Satisfaction Survey.

Randomization sequence generation

Practices in Internal Medicine Clinical Teaching Units (CTU) will be randomized in 1:1 ratio to pathway based care versus usual care in February 2012. The biostatistician developed the patient randomization sequence using central computerized software in permuted blocks of different sizes.

Allocation concealment

Allocation will be concealed via opaque sealed envelopes to be located in the Emergency Department (ED) Pharmacy, accessible to the on-call residents after obtaining a written informed consent in ED.

Implementation of randomization

After randomization, the practicing physicians will not be allowed to cross over to the other team.

Recruitment

To standardize the enrollment process, periodical orientation sessions will be conducted and handouts on the steps for screening, recruitment and the use of clinical pathways integrated into CPOE will be distributed. A specific referral form is developed to enhance communication among various healthcare providers upon enrollment of PC patients, and to be emailed thereafter, by the ED nurse to the CHAMP-Path group. Additional sessions will be organized for obtaining informed consent for medical residents. Similar sessions will be coordinated for nurses, pharmacists, quality management specialists, nutritionists, health educators, and social workers to facilitate the process of pathway implementation.

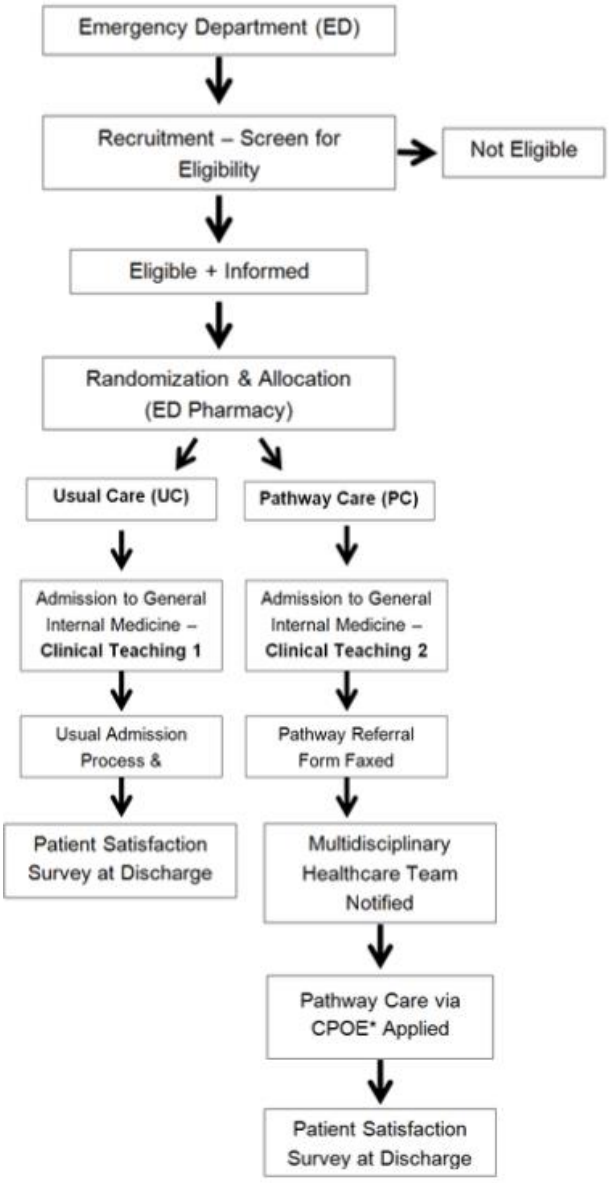

Figure 1. CHAMP-Path participants' enrollment flow diagram.
*CPOE: Computerized Provider Order Entry

Blinding

Patients will be masked to the allocated arm; however blinding healthcare providers delivering direct patient care or outcome assessors is not feasible. Figure 1 presents CHAMP-Path participants' enrollment flow diagram.

Null hypothesis

There is no difference between clinical pathway based care versus usual care in terms of LOS.

Expected Duration of Study

Three years.

Sample size

To detect a reduction in LOS by two days based on published reports (with standard deviation for each medical diagnosis (Caprini et al., 2005; Chertow, Burdick, Honour, Bonventre, & Bates, 2005; Hauptman, Swindle, Burroughs, & Schnitzler, 2008; Usui, Kage, Soda, Noda, & Ishihara, 2004) using a two-sided hypothesis, 5% level of significance, and a power of 80%, a sample of 512 patients was estimated as 166, 90, 38, 128, 90 respectively for community acquired pneumonia, heart failure, acute kidney injury, venous thromboembolism, and asthma accounting for 20% attrition rate.

Statistical analysis

Descriptive statistics (Mean ± SD, median (IQR) and proportions) will be used to report patient demographic characteristics and for 46-items validated survey. Unpaired two-tailed t- test is planned to report the difference in LOS (P-value <0.05, 95% CI) using intention to treat (ITT) analysis. For secondary outcomes, Chi-square test will be applied to compare 30-day readmission rates and multiple linear regression analysis for determinants of LOS. All analyses will be conducted using STATA version 13.

Institutional Review Board Approval

The study is a grant-Recipient of King Abdullah International Medical Research Center (RC 10/134/J) in October 2011. A pilot phase was conducted for six months, from March 2012 until September 2012. The study has stopped enrollment in February 2016 and data analysis is ongoing.

DISCUSSION

We decided to use a pragmatic design, known to assess the effectiveness of interventions in real life settings (Elder & Munk, 2014; Zwarenstein et al., 2008) in reducing LOS across multiple medical diagnoses identified as the top admitting diagnoses (accounting for (80%) of hospitalization in our medical wards). Furthermore, we could not perform a cluster RCT as clinical pathways integrate locally agreed best evidence practice and detailed institutional integrated care, which make it challenging to run the study in different institutions or sites within our organization. Additionally, a historical control observational design was improper due to temporal effects and the dynamic changes in medical practice.

On the other hand, the pragmatic studies have the advantage of using broad inclusion criteria to include patients with the disease of interest in comparison to explanatory studies, which add further restriction on inclusion and exclusion criteria for participants' selection based on adherence, risk for achieving the primary outcome or other safety concerns (Thorpe et al., 2009). Although specific details were provided regarding dosing schedule, selection of drugs and timed-plan for care delivery through order set, pragmatic studies, are characterized by flexible implementation of the intervention across the spectrum of clinical expertise's of physicians from residents to specialists vis-a`-vis the impact of the PC vs. UC in real life settings (Roland & Torgerson, 1998; Thorpe et al., 2009).

Although assessing adherence of patients or practitioners to the intervention is not required in pragmatic studies (Thorpe et al., 2009), adherence can be enhanced if clinical pathways are readily available at the time of making the decision (Kitchiner & Bundred, 1998); hence, we integrated clinical pathways into CPOE to facilitate its use (Hyde & Murphy, 2012). This process was steered by clinical pharmacists (Dobesh et al., 2006; Kirk et al., 1996), according to published reports ("ASHP Guidelines on the Pharmacist's Role in the Development, Implementation, and Assessment of Critical Pathways," 2004) and Institute of Safe Medication Practice (ISMP) Guidelines for order sets, in collaboration with multidisciplinary health care professionals and the IT team.

Limitations

We acknowledge several limitations of our selection of the pragmatic design (1) challenges of enrollment and admission rates, (2) feasibility of recruiting patients by on- call residents and possible contamination, therefore we aimed to provide continuous training in clinical research skills and daily phone reminders for residents, (3) the development of new guidelines and institutional polices during the study period, hence we aimed to

update pathway based care on a frequent basis, and, (4) cost effectiveness of clinical pathways is not assessed in our study.

Strengths

The strengths of CHAMP-Path studies include: (1) Randomization, (2) planned ITT analysis, (3) Integrated pathways into CPOE, (4) the selection of LOS as an objective outcome for assessment of effectiveness of clinical pathways in a pragmatic setting and (5) the choice of 30 day readmission as a secondary outcome, to avoid possible Hawthorne effects since the primary caring physician was not blinded to the type of care.

In conclusion, we propose that our CHAMP-Path Pragmatic RCT robust methodology can serve as pioneering studies in demonstrating whether integrated patient-centered clinical pathways are truly effective in real life settings to improve clinical outcomes.

Implications for practice

Our results are likely to provide our organization with data driven management tools to establish and promote patient-centeredness while improving patient flow. Additionally, it should inform decisions of health care administrators in improving the quality of care across various medical diagnoses.

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Conflict of interest and financial disclosure

The authors followed the International Committee or Journal of Medical Journals Editors (ICMJE) form for disclosure of potential conflicts of interest. All listed authors concur with the submission of the manuscript, the final version has been approved by all authors. The authors have no financial or personal conflicts of interest.

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