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Development And Validation Of A Predictive Model For Oncology Hospital-At-Home

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Development and Validation of a Predictive Model for Oncology Hospital-at-Home

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ABSRACT

Background:

Hospital-at-Home (HaH) is a unique care model that allows for the provision of inpatient level care in the patient's home. HaH has been used to facilitate early discharge from inpatient care or to substitute entirely for an inpatient admission. Hospital-at-Home has been shown to have similar clinical outcomes to inpatient care, while reducing cost and complications associated with inpatient admission. Application of the HaH model to patients with oncologic disease is a promising avenue to reduce healthcare costs while improving patients' quality of life by increasing time spent at home. A major challenge to implementing a Hospital-at-Home program for cancer patients is the lack of validated criteria to inform the selection of admissions most suitable for home-based hospital level care.

Methods and Results:

Admissions to the Yale New Haven Smilow Cancer Hospital's medical oncology floor in New Haven from Jan 2015- Jun 2019 were included in the analysis (N=3,322). The analysis focused entirely on patients with solid tumors hospitalized for unplanned admissions. The definition of suitability for HaH was based on a substitutive model and identified admissions that did not receive any services that would be difficult to deliver or were inconsistent with safe care in the home. Twenty-seven-point-three percent of admissions were identified as suitable for HaH, accounting for 908 admissions during the study period. Admissions that were suitable for HaH were shorter in duration (2.79 vs 6.41 days), more likely to result in discharge home rather than to other healthcare facility (87.5% vs 69.5%), and less likely to be readmitted in the following 30 days (25.3% vs 31.5%). A predictive logistic model constructed using a purposeful selection process identified 13 statistically significant predictors for suitability for HaH: Black/African American

race (vs all other), observation status, patient evaluated in the emergency department (ED) or oncology extended care center (vs admitted directly from clinic), primary admission diagnosis of secondary malignancy, primary admission diagnosis of fever, primary admission diagnosis of digestive diseases, oncology diagnosis of secondary or unknown malignancy, initial pre-admission respiratory rate >20 breaths/min, final pre-admission systolic blood pressure <100 mmHg, final pre-admission temperature >100^{o} F, Sodium < 135 mmol/L, hemoglobin <10 g/dL and ED visit in the previous 90 days. The predictive model had moderate discrimination (c-statistic 0.686) and was well calibrated in the validation cohort (Hosmer-Lemeshow P-value >0.05).

Conclusion:

We describe the first predictive model of suitability for Hospital-at-Home in oncology patients. This model serves as a starting point to creating selection criteria and can be further refined and tested in prospective validation and pilot studies. The modest discrimination of the model indicates that much of the variability that allows for accurate prediction is still unaccounted for and would benefit from larger studies and inclusion of clinician judgement.

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INTRODUCTION

With the rising prevalence of cancer the United States, treatment for cancer and its complications is becoming a larger part of healthcare and a significant contributor to costs [1,2]. A significant portion of that cost comes from inpatient care, with the cost of inpatient treatment for patients with cancer being 350% more expensive than similar patients without a cancer diagnosis [3]. Compared to those without a cancer diagnosis, patients with cancer are more likely to be admitted to the hospital after visiting the emergency department and have longer length of hospital stays [4–8]. Hospital-at-Home (HaH) is a care model designed to replace inpatient hospitalization for acute illnesses by providing the resources to care for patients in their homes [9]. HaH has been proposed as a way to reduce inpatient hospitalization for oncology patients [10]. One barrier to use of HaH in oncology patients is the lack of selection criteria to identify which admissions would potentially be safe for home-based hospital level care [10]. This study aims to inform the creation of such criteria by developing and validating a predictive model based on previous admissions to the medical oncology floor of Yale New Haven Hospital's Smilow Cancer Hospital.

History of Hospital-at-Home

Modern medical HaH programs have been around since the late 1980s and are starting to gain momentum in United States. In Australia, they have become an important part of the healthcare delivery apparatus [11]. A review of studies of HaH among medical patients shows that outcomes are comparable to inpatient admission [12]. Reductions in the total cost of care and decreased utilization of healthcare resources such as laboratory studies have been observed in multiple settings [13–15]. The potential to increase satisfaction and quality while reducing costs makes HaH a promising addition to the broader healthcare delivery system [16]. In the context of the larger healthcare system, HaH provides an avenue for better allocation of costly hospital resources

toward high risk patients, while allowing relatively stable patients to receive care in the home for their acute illness.

House calls and home care were common in healthcare until the 20th century when the rise of the hospital was fueled by the rapid advances in pharmacology and medical technology, the rise of multiple payors, and increased concerns about liability and accountability [17]. Early HaH models were developed and tested in Israel, England, and the United States [17–26]. Early successes led to expansion of models and continued scholarship, especially within public health systems and markets that had strong alignment between payors and providers. While there has been increasing interest in HaH in the United States, broad expansion has been limited by lack of a favorable funding mechanism [27].

Early studies in the 1990s established the feasibility of hospital at home and motivated interest around the world. The Edward Hines Jr VA in Chicago had developed a hospital-based home care program in 1971 and in 1992 they published a randomized trial comparing hospital and home care admission for terminally ill veterans. While in many aspects this was a study focusing on home-based hospice care, it was one of the first studies to show that home care could be used to replace hospital care for a broad range of diagnoses. This study reported an average reduction in 5.9 hospital days per patient leading to an 18% reduction in cost with no difference in clinical outcomes (survival, activities of daily living, and cognitive function) and significant improvement in patient and caregiver satisfaction [18]. From 1995-98, a series of randomized trials of HaH were published in the British Medical Journal. Taken together they showed that for many conditions, there was no significant difference in clinical outcomes between patients randomized to HaH verses inpatient care, with some improvements in patient satisfaction and significant patient preference for HaH. The studies showed mixed results when it came to cost analysis and length of

stay [22,23,28]. The clinical outcomes measured included mortality, readmission, Dartmouth Cooperative Functional Assessment Charts, SF-36 to measure mobility, COPD disease questionnaire, and Barthel Index for activities of daily living. The HaH programs implemented in these studies varied in their use of physician supervision, and whether the programs diverted patients from an inpatient admission or served as a pathway for early discharge. A common critique of the early hospital-at-home studies is that the heterogeneity of models makes it difficult to compare programs and differentiate them from home-based skilled nursing care or chronic ambulatory care [29,30]. There have been proposals to tighten the definition of HaH to those programs that substitute entirely for inpatient admission and provide around-the clock services similar to what is available in an inpatient setting [30]. Highlighting this distinction, separate Cochrane reviews are devoted to analyzing the evidence base for HaH programs that avoided inpatient admission (i.e., a "substitutive" model, 16 randomized trials with 1814 patients) verses those who focused on offering an avenue for early discharge (32 randomized trials with 4746 patients) [12,31].

Most early trials of HaH were conducted within single-payer health systems, limiting their applicability to the United States outside the VA. In 2005, a large multi-center quasi-experimental trial concluded that HaH was feasible, safe, and resulted in reduced length of stay and lower total costs [32]. The study focused on substitutive HaH for four medical illnesses (exacerbations of heart failure or COPD, pneumonia, and cellulitis) in elderly patients over 65. This was one of the first studies to show that patients in the HaH cohort had improvements in the functional status compared to traditionally-hospitalized patients, as measured by ability to complete instrumental activities of daily living and activities of daily living [33]. On cost analysis, they found significant cost savings for patients admitted for exacerbations of COPD and congestive heart failure but not

pneumonia nor cellulitis. For all diagnoses, the HaH cohort had significantly lower laboratory and procedure costs [14]. These results were validated by numerous models implemented across the country [15,27,34]. Since then, HaH programs have been created and studied at multiple large academic centers, including Johns Hopkins (Baltimore, MD), Mount Saini (New York City, NY), Presbyterian Health Services (New Mexico), and Brigham and Women's Hospital (Boston, MA) [13,15,35,36]. The most recent randomized trial of 91 patients from the Brigham and Women's Hospital showed cost savings of 38%, which included adjustment for demographics, patient education level, discharge diagnosis, and comorbidities. They found that patients hospitalized at home had fewer health interventions (labs, imaging, and consultations), were more active (less time sedentary or lying down), and had fewer re-admissions in 30 days [37].

Despite the growing body of literature that shows clear benefits with HaH programs, it has not been widely disseminated in the United States, mainly due to lack of codified reimbursement, especially from Medicare, in a fee for service environment [27]. To address this gap, proposals were submitted to the national Department of Health and Human Services Physician-Focused Payment Model Technical Advisory Committee (PTAC) by Mount Saini (New York City, NY) and Marshfield Clinic (Marshfield, WI) outlining potential payment structures for HaH under Medicare fee-for-service [38,39]. The Mount Saini model was initially developed using a $9.6 million grant from the Centers of Medicare and Medicaid Innovation to test bundle payment structures for HaH. While the Secretary of Health and Human Services chose not to implement either proposal at a national level, they indicated an interest in studying the concept further to create a sustainable payment mechanism [40]. In the absence of a national payment structure by Medicare fee-for-service, successful models have thrived in systems where incentives are aligned between payor and provider, such as Presbyterian Healthcare Services (New Mexico), whose

health plan covers 470,000 Medicare Advantage, Medicaid, and commercially insured patients [41]. The VA system offers Hospital-at-Home in 11 care sites and Cedars Sinai medical center in Los Angeles offers HaH for its managed care and accountable care organization patients [42]. A start-up called Medically Home (Boston, MA) hopes to implement HaH through a partnership with Atrius Health (MA), a non-profit health group with more than half million patients [43,44]. These developments show that HaH is poised for growth in the United States if the correct mix of reimbursement and health policy align to support its development.

Globally, HaH has thrived in areas where payment structures support its growth. A prime example is the Australian state of Victoria, which includes the city of Melbourne. The state government's decision to reimburse HaH at the same rate as a hospital inpatient admission has led to the growth of a vast hospital-in-the home system, matching the capacity of a 500-bed hospital with over 32,000 admissions as year, representing 5% of all bed days in the state [11]. HaH is a complex multifaced intervention that requires appropriate patient selection, proper infrastructure, appropriate delivery of services, well-formed guidelines for patient monitoring and protocols in place to deal with deterioration in health. The success of the program in Victoria shows that HaH has the potential to be a potent tool to reduce the demand for beds in physical hospitals without compromising quality or patient satisfaction, while also providing cost savings to the system.

Favorable Outcomes and Reduced Complications in HaH

The last few decades have seen prolific scholarship on Hospital at Home, allowing for its efficacy to be tested across multiple health systems with a variety of different models. While there is much that remains unknown or unproven, there are multiple systematic reviews and meta-analyses examining feasibility and outcomes of the model. These reviews have found that outcomes for hospital at home are comparable to inpatient admission for a wide variety of diagnosis, there is

evidence of reduced patient harm, increased recovery, reduced mortality, and that treatment at home is both acceptable and even preferable for patients [12,45–48]. In properly selected patients, HaH has the potential to be applied to a wide variety of medical diagnosis and be comparable to an inpatient hospital admission, and may reduce some common complications seen in hospitalized patients. A meta-analysis of 61 randomized trials found a significant reduction in mortality, equivalent to one death prevented for every 50 patients admitted to HaH [47].

Hospital at Home has been validated in a wide variety of clinical diagnoses as being comparable to or even better than traditional hospitalization. For patients with acute exacerbation of heart failure, HaH showed no difference in cardiovascular mortality and led to improved quality of life, longer time to readmission and reduced costs [45]. HaH for COPD exacerbations showed significant reductions in readmission rates and a trend to toward reduced morality [46]. Treatment of deep vein thrombosis has been done in HaH programs, though data now suggests that outpatient treatment even without HaH is acceptable and reduces chances of recurrence compared to inpatient admission [11,49]. HaH has also been shown to be comparable to inpatient admission for selected cases of uncomplicated ischemic stroke, community acquired pneumonia, cellulitis, and for elderly patients with a broad range of medical diagnoses [12,48].

In addition to having comparable clinical outcomes to inpatient hospitalization, HaH has also been shown to reduce risk of some complications seen with inpatient hospitalization. Hospital at home patients tend to be more physically active and spend more time out of bed [15,37]. They tend to have lower instances of hospital acquired disability and improved function measured by IADLs and ADLs [15,33]. Elderly patients in Hospital at home are significantly less likely to develop delirium [32,50,51]. Patients are less likely to require the use of sedative medications and chemical restraints when treated at home [32]. Further studies may show that Hospital at Home is an

effective way of reducing many other complications associated with inpatient admission without compromising quality.

Oncology Hospital-at-Home

As hospital at home has expanded in the United States and abroad, it has been proposed as a potential avenue of treatment for oncologic patients [10]. HaH could allow the provision of selected inpatient cancer care to be transitioned to the home setting. In addition to benefits mentioned above, HaH could be particularly beneficial in increasing the time cancer patients spend at home during a particularly vulnerable time. Increasing "home days" at the end of life has been identified as an important patient centered quality metric, and is particularly relevant for patients battling cancer diagnosis [52,53]. Models for HaH for oncology patients have been studied outside the United States, including at institutions in France, Australia, and Switzerland [54–56]. In the United States, the Huntsman Cancer Institute (Salt Lake City, UT) announced a 3-year hospital-at-home trial starting in August 2018, and have enrolled 350 patients in the first year [57].

Cancer patients are often admitted to the hospital for planned administration of chemotherapy or for unplanned complications of their diseases [58]. In unplanned hospitalizations they commonly present to the emergency room with pain, respiratory complaints, gastrointestinal complaints, malaise, neurologic complaints, and fever [8]. There is a growing body of evidence that even complex chemotherapy regimens and autologous stem cell transplantation can be safely performed at home for selected patients [54,56,59–61]. Fewer studies focus on HaH as a substitute for unplanned hospitalizations of cancer patients [62,63].

Administration of intensive chemotherapy has been successfully implemented in the home setting. A group in Switzerland delivered 11 systemic chemotherapy regimens at home in 17 patients, resulting an increase in patient comfort and a 53% reduction in cost [56]. Outpatient autologous

stem-cell transplantation has also been successfully piloted with 14/21 patients not requiring any inpatient admission despite complications such as neutropenic fever being common [60]. A systemic review of 24 studies examining home hospitalization for cancer drug administration found increased patient satisfaction, a patient preference for home treatment and no evidence of safety risks [61]. The Centre L´eon B´erard in France conducted a non-randomized study of 82 patients and showed a cost savings of 34% for cancer patients receiving palliative care, while the savings for patients receiving chemotherapy was minor and not statistically significant [55]. The cost savings results of other studies across different countries show mixed results [61].

In addition to the Centre L´eon B´erard using home hospitalization for patients receiving palliative care, studies have examined the use of outpatient treatment of two common complications seen in cancer patients. Febrile neutropenia has been successfully treated at home with clinical outcomes equivalent to inpatient hospitalization [63]. In addition, studies referenced above treated febrile neutropenia at home as a complication of home administration of chemotherapy. Cancer associated venous thromboembolism, including pulmonary embolism has also been treated in the home with comparable clinical outcomes [62].

As outlined by Handley and Bekelman, challenges to widespread implementation of oncology HaH include inadequate tools for patient selections, lack of models for staffing, and resource allocation, and inadequate mechanisms of reimbursement [10]. The success of models created for general medical conditions in organizations like the VA and major academic medical centers in the United States shows that many of these challenges can be overcome. The ability to classify patients according to their risk of adverse events in HaH is critical to the development and success of a new HaH program. Due to the presence of certain specialized services, the Hospital will be a safer and more appropriate location of care for patients who are at risk of decompensation. On the

other hand, for patients who have a low risk of decompensation, the hospital may lead to unwanted complications or exposures. Developing tools to identify appropriate patients for oncology HaH is critical to its development and expansion. An examination of past cancer admissions allows for the preliminary development of such tools without putting patients at risk. These could be validated with prospective studies, similar to studies done to validate criteria for general hospital admissions [64]. Interest in innovative models of care delivery is growing within the field of oncology, and the changes in payment structures supports the development of such programs. The rise of the Oncology Care Model, an episode based payment structure created by Medicare that encourages cancer hospitals to take on risk, has caused cancer hospitals to think critically about the shift toward value based for cancer [65].

This thesis uses historical data from patients at the Yale New Haven Hospital's Smilow Cancer Hospital to create a predictive model that can be used to select appropriate patients for HaH consideration in a data-driven method. Yale New Haven Hospital (YNHH) has had a substantial growth of demand on its hospital beds and emergency rooms. This leads to longer wait times in the emergency department and extended boarding times in the emergency department as patients wait for an open bed. It has resulted in activations of the hospital's emergency management plans to cope with a "surge crises." This situation jeopardizes patient safety and quality of care [66]. This thesis aims to take preliminary steps toward developing a Hospital-at-Home program that could be part of the solution to reducing the demand for hospital beds. We focus on oncology admissions for two reasons: 1) The oncology care model is leading the way toward a value based payment structure that would incentivize programs like HaH, 2) Due to the potentially terminal nature of their diagnosis, giving patients with cancer more days at home could provide a valuable benefit to their quality of life [52].

This study focuses specifically on oncology patients admitted for complications or decompensations, since little is known about the potential for HaH to be applied to that population. It represents the first step in developing evidence-based selection criteria for oncology HaH and will enable programs to maximize the likelihood that patients selected for HaH will be successfully cared for within this model while reducing the risk of adverse events. To our knowledge, this is the first study creating a predictive model to identify which medical oncology patients could be successfully treated in a HaH model.

Statement of Purpose and Specific Aims

The purpose of this study to derive and internally validate a predictive model to inform optimal selection of patients who may be cared for in an oncologic Hospital-at-Home.

Aim 1: To identify the proportion of patients admitted to the oncologic floor that would have been suitable for hospital at home.

Aim 2: Describe any demographic and outcomes differences between patients who were identified as suitable for hospital-at-home vs those who were not suitable.

Aim 3: Develop and internally validate logistic prediction model based on a training cohort of index admissions to predict suitability using information available in the electronic medical record before the decision to admit the patient was made.

Aim 4: Develop an accessible calculator to classify a patient's suitability for hospital at home.

HYPOTHESIS

We hypothesized that there exists a subset of patients admitted to the Yale medical oncology service who do not require specialized hospital services and would be suitable for treatment at home.

We hypothesized that it would be possible to predict which subset of admissions would be least likely to require services only available in the hospital based on information available about the patient in the electronic health record prior to a physician's decision to admit the patient to the hospital. We hypothesized the admission diagnosis, vitals, and lab results would have the strongest association with a patient's potential eligibility for HaH. Based on previous HaH literature, we hypothesized that admission diagnosis of febrile neutropenia, infectious diseases, and cancer associated venous thromboembolism would predict higher eligibility for HaH compared to others. Respiratory distress, sepsis, and altered mental status have been shown to predict ICU admission and mortality in oncology admissions and we expected them to predict lower eligibility for hospital at home [7]. Tachycardia, tachypnea and low oxygen saturation have been shown to predict higher rates of rapid response team activation, and we predicted that they would also predict lower eligibility for hospital at home [67]. We expected anemia to predict lower suitability for HaH since concerns for Gastrointestinal hemorrhage could require specialist consultation and procedural intervention. We hypothesized that the type of cancer diagnosis and presence of metastatic disease would also be independent predictive factors.

METHODS

Patient Selection

Records for all patients admitted to the medical oncology floor (North Pavilion 12) of the Yale Smilow Cancer Hospital between 1/1/2015 and 6/12/2019 were obtained from the electronic medical record system (EPIC©, Verona, WI). All admissions that were transfers from outside hospitals or other health facilities (including skilled nursing, hospice and psychiatric facilities) were excluded because these patients were not living at home prior to the admission and would therefore be unsuitable for a HaH program. All patients whose primary reason for admission was chemotherapy were excluded from the study in order to focus on unplanned admissions. North Pavilion 12 at Yale New Haven Hospital is traditionally a solid tumor oncology floor, though recent bed shortages have resulted in hematologic malignancy patients being admitted there. For uniformity across time, all patients with a hematologic malignancy were excluded. Only patients initially admitted to the medical oncology floor were considered for this study in order to avoid transfers from higher levels of care or post-surgical patients.

Defining Suitability for HaH

Suitability for HaH was defined as the lack of decompensation, lack of surgical intervention or any specialty consultation that could potentially lead to procedural intervention, and not utilizing any hospital services that would be difficult or unsafe to provide in the home during an acute illness. This definition was based on services provided by recently published HaH programs and consultation with experts at Yale [27,34,37]. Decompensation was defined as escalation of care (to step-down or ICU) and/or the use of rapid response/code teams for urgent evaluation and intervention. All patients who received a surgery or interventional procedure were considered unsuitable. The following consult teams were categorized as potentially leading to procedural

intervention: all surgical services, interventional radiology, gastroenterology, pulmonology, interventional pain, radiation oncology, and dermatology. These services are often consulted in the inpatient setting in order to evaluate the patient for specific interventional procedures, which may be more difficult to provide in a HaH program. Other HaH programs in the United States have arranged for telemedicine specialist consults, which would be appropriate for non-interventional services [37]. While it may be possible to transport HaH patients temporarily to an imaging center for advanced imaging, this would require extra infrastructure and therefore all patients who had CT scans or MRIs were considered unsuitable. The following interventions were defined as being difficult or unsafe to perform in HaH model: physical or chemical restraints, nasogastric tubes, cardiac telemetry, and transfusion. Chemical restraints were defined as the intravenous or intra-muscular prescription of any benzodiazepines or antipsychotics. Use of opioid analgesics was not a disqualifying factor since there exists precedence for the outpatient use of patient-controlled analgesia in patients with cancer [68,69]

Differences between admissions identified as suitable and unsuitable were compared in order to accomplish aim 2 of this study. Suitable and unsuitable admissions were compared by demographics, length of stay, disposition, and readmissions in 30 days. Common admission and oncologic diagnoses were identified for suitable and unsuitable admissions. We identified that admissions to the oncology floor originated from the emergency department (ED), Oncology Extended Care Center (ECC), or directly from outpatient clinics. Directly admitted patients were admitted directly to the medical oncology floor after evaluation in a clinic, transfusion center, or other outpatient location. As per the Smilow cancer center guidelines, patients could not be directly admitted from home following a phone consultation with a provider, an in person evaluation was

required. We compared the proportion of suitable admissions from each source and the most common reasons for unsuitability.

Data Preparation

Predictors prepared for potential use in the model included demographics (age, sex, race, ethnicity), route of admission (from ED/ECC or directly from clinic), admission categorized as observation, primary admission diagnosis, pre-admission vitals, pre-admission labs, oncologic diagnosis, and admissions to the hospital or ED in the previous 90 days. The categorization of an admission as observation is based on criteria developed by hospitals and payors to identify which admissions do not require inpatient level services.

Predictors that had lower than a 2% or higher than 98% prevalence in the derivation cohort were excluded in order to ensure an adequate number of observations for each characteristic. Predictors with greater than 20% missing data were excluded from analysis, as their clinical utility would be limited in future implementation efforts. We examined the missing data for associations with any known predictors in our data. Such an association would reject the assumption that our data is missing completely at random (MCAR), in favor of the assumption that it is missing at random (MAR) [70]. Under the assumption that our data would be missing at random, we planned to use multiple imputation to fill in missing values. As a secondary analysis we built a separate model with complete case analysis. Due to the large number of admissions and cancer diagnoses, the diagnosis ICD codes were grouped based on the multi-level clinical classification software (CCSR) developed by healthcare cost and utilization project (H-CUP) [71,72]. The classification groups ICD codes into CCSR groups based on similar pathology. For example, the ICD code for neutropenia (along with aplastic anemia and others) is grouped into the CCSR code for “diseases of white blood cells.” These CCSR codes are also grouped into larger disease categories. The

CCSR code for “diseases of white blood cells” is a group in the category of “disorders of blood.” Each CCSR code and category for admission and oncologic diagnosis were coded into binary indicator variables. Vitals and lab results were grouped into clinically relevant groupings, only categories with >2% prevalence in the sample were retained.

Separation of Training and Validation Cohorts

We included only the first admission for patients who had multiple admissions during the time period to avoid any interdependence of observations when using logistic regression. For the multiply imputed model, samples were divided into equal derivation and validation cohorts from all eligible patients. Characteristics of patients in the training and validation cohorts were compared using Pearson’s chi-squared test for categorical covariates and Wilcoxon rank-sum for continuous covariates in order to describe any significant differences between the two groups. Missing data were multiply imputed 20 times using chained equations [73]. For the complete case analysis patients with missing data for potential predictor covariates were removed from the study. The patient sample was randomly divided into equal sized validation and derivation cohorts and compared using the methods described above.

Predictive Model Construction

A multivariable logistic predictive model was built using a modified purposeful selection process described by Hosmer and Lemeshow [74,75]. Each model (complete case analysis and multiple imputation) followed similar model building steps outlined below.

Univariate logistic regression was done for each of the prediction covariates and examined for significance. The initial model was constructed with covariates that were significant predictors with a p value of 0.25 or less. All covariates with a p-value of 0.25 or less were checked for correlation with each other. Variables with high correlation (>|0.7|) were added separately to the

model and the model likelihood ratio and change c-statistic was compared to choose the covariate with a significant likelihood ratio that had the greatest increase in the c-statistic. Upon running a logistic regression model with all covariates selected from the univariate regression, non-significant covariates (p-value greater than 0.1) were removed in order of least significance. At each removal step, a likelihood ratio was used to compare the models to ensure the removed variable did not significantly contribute to the overall model. Confounding was evaluated as a change in the coefficients of any of the other significant covariates greater than 15% when compared to a model including the covariate in question. This process was repeated until the remaining model included all remaining covariates had a p-value less than 0.1 or were significant confounders. The Wald test was used to ensure that all covariates contributed significantly to the model. Any covariates not included in the original model with a p-value above 0.25 and were then added sequentially to the model. At each addition step, a likelihood ratio was used to compare whether the covariate added significantly to the model. Added variables were also checked for correlation with variables already in the model, and those that were highly correlated (>|0.7|) were excluded model in favor of the covariate already included. Once all variables in the second group were examined, the model was reduced iteratively using the same method used above, except only for covariates added in the second group. If they were found to be significant, admission and oncologic categories (groups of CCSR codes) were examined by code to see if major codes affected the model in the same direction (increased or decreased odds for suitability). If all major individual codes of a significant category affected the model in the same direction but were insignificant individually, the category was retained in the model. If a code was significant by itself, it was included independently, and the category was excluded to avoid problems with

collinearity. Categories with codes that spanned broad clinical syndromes (Signs and Symptoms) were not included in the model.

Assessment of the Predictive Models

The performance of the predictive models was assessed by measuring the area under the receiver operating curve for the model on both the training and validation cohorts. Hosmer-Lemeshow Goodness of fit testing was conducted using 10 groups [76]. The performance on training and validation cohorts was compared using chi-squared analysis of the area under the curve. The model created from the complete case analysis was compared with the model developed through multiple imputation using the c-statistic for derivation and validation cohorts. Significant covariates were compared between the models for direction of effect. In order to avoid bias caused by missing data, the model created through multiple imputation was used for further predictions [77–79]. The predicted suitability for HaH in the validation cohort was divided into quartiles and compared (using Hosmer-Lemeshow goodness of fit) to the observed suitability for HaH to assess the calibration of the model.

Creation of Clinical Calculator

A clinical calculator was created by multiplying all model coefficients by 10 and rounding to a whole number. The calculators scores were divided into quartiles based on predicted suitability used above for model calibration.

Author Contributions

The author of this thesis (Keval Desai) was involved in the conception, development and completion of this project along with mentors Dr. Kevin Chen and Dr. Sarwat Chaudhry. Dr. Kevin Chen was largely responsible for creating the purpose and objectives of the project and deciding the patient population. Data from EPIC was extracted by Soundari Sureshanand from the Yale

JDAT team, all subsequent patient selection and data preparation was completed by Keval Desai in coordination with Dr. Kevin Chen. The definition of suitability for HaH was developed in by both Keval Desai and Dr. Kevin Chen in collaboration with Dr. Kerin Adelson, Dr. Sarwat Chaudhry and Dr. Cary Gross. The statistical analysis and predictive model construction were done by Keval Desai, in consultation with Dr. Kevin Chen and Dr. Sarwat Chaudhry. All tables and figures and figures in this thesis were created by Keval Desai and are a result of work completed by him.

RESULTS

Suitability for HaH

There were 6,852 patient admissions to the medical oncology floor of the Smilow Cancer hospital during the period of the interest. 3,322 admissions met the study inclusion criteria, of which 908 (27.33%) were found to be suitable for HaH. The average length of stay for patients who were suitable for HaH was 2.79 vs 6.41 for patients who were unsuitable. 87.5% of patients identified as suitable for HaH were discharged home, a majority (56.2%) of them without services. In comparison, 69.5% of admissions identified as unsuitable resulted in discharge to home, with most of the rest being discharged to skilled nursing facilities, hospice facilities, or expired during their stay (Table 1). Only three patients identified as suitable expired during their hospital stay, compared to 125 deaths in patients identified as unsuitable. Admissions deemed suitable were significantly less likely to be readmitted with 30 days (25.3% vs 31.5%). ED visits in the 30 days following the episode were similar between both groups.

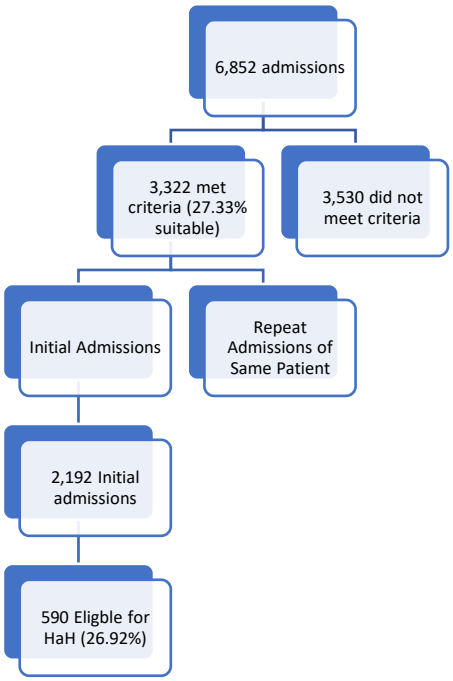


Figure 1: Flowchart of patient admissions to the Medical Oncology Floor Showing the number of Index admissions considered suitable for HaH based on source of admission

Table 1: Demographics, length of stay and disposition of admissions identified as unsuitable and suitable for HaH. This data includes all admissions included in study (including duplicate admissions of the same patient). P-values in bold are significant to the 0.05 level.

	Unsuitable for HaH	Suitable for HaH	P-value
	N=2,414	N=908	
AGE	62.28 (12.86)	62.28 (12.62)	1.00
SEX			0.064
Female	1,145 (47.4%)	398 (43.8%)	
Male	1,269 (52.6%)	510 (56.2%)	

Race			0.22
White or Caucasian	1,985 (82.2%)	729 (80.3%)	
Black or African American	218 (9.0%)	100 (11.0%)	
Other	211 (8.7%)	79 (8.7%)	
ETHNICITY			**0.035**
Hispanic or Latino	149 (6.2%)	77 (8.5%)	
Non-Hispanic	2,249 (93.2%)	828 (91.2%)	
Unknown	16 (0.7%)	3 (0.3%)	
Admission Source			**<0.001**
Direct Admit	899 (37.2%)	243 (26.8%)	
From ED/ECC	1,515 (62.8%)	665 (73.2%)	
Length of Stay	6.41 (5.79)	2.79 (2.09)	**<0.001**
Disposition			**<0.001**
Expired	125 (5.2%)	3 (0.3%)	
Home or Self Care	795 (32.9%)	510 (56.2%)	
Home-Health Care Svc	882 (36.5%)	284 (31.3%)	
Hospice/Home	106 (4.4%)	26 (2.9%)	
Hospice/Medical Facility	171 (7.1%)	28 (3.1%)	
Skilled Nursing Facility	291 (12.1%)	44 (4.8%)	
Other	44 (1.8%)	13 (1.4%)	
ED visit 30-day post discharge	613 (25.4%)	229 (25.2%)	0.92
Readmission 30-day post discharge	761 (31.5%)	230 (25.3%)	**<0.001**

The two most common primary admission diagnoses were abdominal pain and respiratory complaints (Table 2). The most common oncologic diagnoses were lung, pancreatic, colorectal, and breast cancers (Table 3). The proportion of admissions with certain diagnoses varied based on suitability for HaH, with statistically significant differences seen in abdominal pain, secondary malignancy, fever, and nervous system signs & symptoms. Abdominal pain and fever were more common in the suitable patients, while secondary malignancy and nervous system signs were less common in the suitable group. The proportion of admissions with colorectal cancer and secondary malignancies were statistically different between suitable and unsuitable admissions. The

proportion of colorectal cancer was higher among suitable patients while the proportion of secondary malignancy was lower.

Table 2: Admission Diagnosis with greater than 2% cumulative prevalence separated by suitability for HaH. P-values in bold are significant to the 0.05 level.

Primary Admission Diagnosis	Unsuitable for HaH	Suitable for HaH	Total	P-value
	N=2,414	N=908	N=3,322	
Abdominal pain and other digestive/abdominal pain	151 (6.3%)	90 (9.9%)	241 (7.3%)	**<0.001**
Respiratory signs and symptoms	141 (5.8%)	58 (6.4%)	199 (6.0%)	0.55
Secondary malignancies	161 (6.7%)	19 (2.1%)	180 (5.4%)	**<0.001**
Fever	86 (3.6%)	65 (7.2%)	151 (4.5%)	**<0.001**
Fluid and electrolyte disorders	110 (4.6%)	40 (4.4%)	150 (4.5%)	0.85
Nausea and vomiting	88 (3.6%)	36 (4.0%)	124 (3.7%)	0.67
Diseases of white blood cells	65 (2.7%)	34 (3.7%)	99 (3.0%)	0.11
Conditions due to neoplasm or the treatment of neoplasm	67 (2.8%)	31 (3.4%)	98 (3.0%)	0.33
Other general signs and symptoms	69 (2.9%)	21 (2.3%)	90 (2.7%)	0.39
Nervous system signs and symptoms	70 (2.9%)	7 (0.8%)	77 (2.3%)	**<0.001**
Acute and unspecified renal failure	58 (2.4%)	17 (1.9%)	75 (2.3%)	0.36
Respiratory cancers	59 (2.4%)	16 (1.8%)	75 (2.3%)	0.24
Malaise and fatigue	49 (2.0%)	24 (2.6%)	73 (2.2%)	0.28
Bacterial infections	50 (2.1%)	22 (2.4%)	72 (2.2%)	0.54
Endocrine system cancers - pancreas	59 (2.4%)	13 (1.4%)	72 (2.2%)	0.074
Pneumonia (except TB)	51 (2.1%)	21 (2.3%)	72 (2.2%)	0.72

Table 3: Primary Oncologic for all admissions separated by suitability for HaH. P-values in bold are significant to the 0.05 level.

Primary Oncologic Diagnosis	Unsuitable for HaH	Suitable for HaH	Total	p-value
	N=2,414	N=908	N=3,322	
Respiratory cancers	445 (18.4%)	168 (18.5%)	613 (18.5%)	0.96
Endocrine system cancers - pancreas	240 (9.9%)	97 (10.7%)	337 (10.1%)	0.53
Gastrointestinal cancers - colorectal	211 (8.7%)	114 (12.6%)	325 (9.8%)	**<0.001**

Breast cancer - all other types	221 (9.2%)	95 (10.5%)	316 (9.5%)	0.25
Urinary system cancers - kidney	118 (4.9%)	46 (5.1%)	164 (4.9%)	0.83
Skin cancers - melanoma	113 (4.7%)	41 (4.5%)	154 (4.6%)	0.84
Gastrointestinal cancers - stomach	84 (3.5%)	32 (3.5%)	116 (3.5%)	0.95
Urinary system cancers - bladder	85 (3.5%)	24 (2.6%)	109 (3.3%)	0.21
Male reproductive system cancers - prostrate	78 (3.2%)	25 (2.8%)	103 (3.1%)	0.48
Gastrointestinal cancers - esophagus	57 (2.4%)	24 (2.6%)	81 (2.4%)	0.64
Secondary malignancies	55 (2.3%)	11 (1.2%)	66 (2.0%)	**0.050**

The most common reasons for unsuitability for HaH were consult to a procedural service, use of chemical restrains, and use of advanced imaging. The frequency of these were statistically different based on route of admission (Table 4). More patients who were evaluated in the ED/ECC were suitable for HaH compared to admissions directly admitted from outpatient clinics. Admissions directly from clinic were significantly more likely to be unsuitable due to the use of interventional consults, chemical restraints, and advanced imaging.

Table 4: Reasons for unsuitability for HaH in total and separated by route of admission. P-values in bold are significant to the 0.05 level.

Reason for Unsuitability	Direct Admit	ED/ECC	Total	P-value
	N=1,142	N=2,180	N=3,322	
Escalation of Care	42 (3.7%)	58 (2.7%)	100 (3.0%)	0.10
Rapid Response	24 (2.1%)	42 (1.9%)	66 (2.0%)	0.73
Code Blue	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Surgery	148 (13.0%)	248 (11.4%)	396 (11.9%)	0.18
Consult to Procedural Service	484 (42.4%)	807 (37.0%)	1,291 (38.9%)	0.003
Physical restraints	9 (0.8%)	22 (1.0%)	31 (0.9%)	0.53
Chem restraints	350 (30.6%)	456 (20.9%)	806 (24.3%)	**<0.001**
Nasogastric Tube	27 (2.4%)	31 (1.4%)	58 (1.7%)	**0.049**
Telemetry	5 (0.4%)	7 (0.3%)	12 (0.4%)	0.59
Transfusion	230 (20.1%)	421 (19.3%)	651 (19.6%)	0.57

Advanced Imaging	603 (52.8%)	962 (44.1%)	1,565 (47.1%)	**<0.001**
Suitable for HaH	243 (21.3%)	665 (30.5%)	908 (27.3%)	**<0.001**

Creation of Derivation and Validation Cohorts

Of the 3,322 admissions, 1,130 were repeat admissions during our time period of interest, the remaining 2,192 were used for model construction. Missing values were most common in lab and vitals, with direct admissions having a greater number of missing (Table 5). Measures with >20% missing values in the entire cohort were dropped from the multiple imputation model. Missing values for oncology diagnosis were not imputed since the oncology diagnosis was separated into a series of binary variables for each CCSR code. Multiple imputation using demographic and clinical predictors (in addition to suitability for HaH) was conducted 20 times for the reaming laboratory and vital sign values. 1,538 of the admissions had complete vitals and laboratory data prior to admission and were used to construct the complete case analysis model predictive model.

Table 5: Missing values for the predictors missing >5% of values. Absolute neutrophil count, chloride and potassium were dropped from analysis due to >20% missing in the entire sample.

	Admissions through ED/ECC			Direct Admissions		
Value	**N Missing**	**N Complete**	**% Missing**	**N Missing**	**N Complete**	**% Missing**
Absolute Neutrophil count	352	1,087	24.46%	205	548	27.22%
Potassium	246	1,193	17.10%	204	549	27.09%
Bicarbonate	222	1,217	15.43%	203	550	26.96%
Sodium	233	1,206	16.19%	202	551	26.83%
Chloride	259	1,180	18.00%	202	551	26.83%
BUN	234	1,205	16.26%	202	551	26.83%
White Blood Cell	234	1,205	16.26%	198	555	26.29%
Hemoglobin	233	1,206	16.19%	198	555	26.29%
Platelets	235	1,204	16.33%	198	555	26.29%
Final RR	65	1,374	4.52%	95	658	12.62%
Initial RR	64	1,375	4.45%	94	659	12.48%
Final Temperature	79	1,360	5.49%	91	662	12.08%
Initial Temperature	81	1,358	5.63%	90	663	11.95%

Final Blood pressure	49	1,390	3.41%	89	664	11.82%
Initial Blood Pressure	47	1,392	3.27%	88	665	11.69%
Initial HR	48	1,391	3.34%	87	666	11.55%
Final HR	49	1,390	3.41%	87	666	11.55%
Oncology Diagnosis	84	1,355	5.84%	58	695	7.70%

The entire cohort of 2,192 were divided randomly into derivation and validation cohorts. The characteristics of patients in the derivation and validation cohorts were similar in terms of demographics, reason for admission and oncologic diagnosis (Table 6). For the complete case analysis, the derivation and validation cohorts were constructed using the 1,538 complete cases, with random allocation done using the same random seed. Data for complete case analysis is presented in the appendix.

Table 6: Training and Validation cohorts compared on a variety of patient and admission factors. Categorical variables were compared using Parsons's chi2 and continuous variables using Wilcox Rank Sum. Data presented as N (percentage) for categorical and mean (SD) for continuous measures.

Covariate	Derivation	Validation	p-value
	N=1,096	N=1,096	
Age	63.41 (12.81)	63.56 (12.32)	0.78
Sex			0.49
Female	535 (48.8%)	519 (47.4%)	
Male	561 (51.2%)	577 (52.6%)	
Race			0.54
White or Caucasian	896 (81.8%)	896 (81.8%)	
Black or African American	114 (10.4%)	103 (9.4%)	
Other	86 (7.8%)	97 (8.9%)	
Ethnicity			0.53
Hispanic or Latino	58 (5.3%)	68 (6.2%)	
Non-Hispanic	1,028 (93.8%)	1,022 (93.2%)	
Primary Admission Diagnosis category			0.52
Blood Disorders	48 (4.4%)	66 (6.0%)	
Circulatory Disorders	48 (4.4%)	38 (3.5%)	
Digestive Disorders	97 (8.9%)	90 (8.2%)	
Endocrine Disorders	76 (7.0%)	71 (6.5%)	
Genitourinary Disorders	49 (4.5%)	42 (3.8%)	

Infections	31 (2.8%)	29 (2.7%)	
Musculoskeletal Disorders	30 (2.7%)	26 (2.4%)	
Neoplasm	252 (23.1%)	228 (20.9%)	
Nervous System Disorders	20 (1.8%)	39 (3.6%)	
Respiratory System Disorders	51 (4.7%)	49 (4.5%)	
SYM	341 (31.2%)	361 (33.1%)	
Oncologic Category			0.86
Breast	107 (10.6%)	112 (11.0%)	
Endocrine	108 (10.7%)	120 (11.7%)	
Gastrointestinal	221 (21.9%)	205 (20.1%)	
Head & Neck	79 (7.8%)	61 (6.0%)	
Male Reproductive	42 (4.2%)	44 (4.3%)	
Respiratory/Cardiac	211 (20.9%)	231 (22.6%)	
Secondary/Ill-defined Site	49 (4.8%)	42 (4.1%)	
Skin	54 (5.3%)	56 (5.5%)	
Urologic	83 (8.2%)	84 (8.2%)	
Comorbidities			
History of Myocardial Infarction	105 (9.6%)	94 (8.6%)	0.41
Congestive Heart failure	148 (13.5%)	122 (11.1%)	0.091
Peripheral Vascular Disease	195 (17.8%)	192 (17.5%)	0.87
History of Cerebral Vascular Accident	181 (16.5%)	191 (17.4%)	0.57
Dementia	28 (2.6%)	18 (1.6%)	0.14
Pulmonary Disease	407 (37.1%)	409 (37.3%)	0.93
Rheumatic Disease	40 (3.6%)	47 (4.3%)	0.44
Peptic Ulcer Disease	69 (6.3%)	74 (6.8%)	0.67
Liver Disease	405 (37.0%)	435 (39.7%)	0.19
Diabetes	274 (25.0%)	275 (25.1%)	0.96
Metastatic Cancer	990 (90.3%)	985 (89.9%)	0.72
Evaluated in ED/ECC	710 (64.8%)	729 (66.5%)	0.39
Length of Stay	5.42 (5.37)	5.37 (5.01)	0.82
Suitable for HaH	295 (26.9%)	295 (26.9%)	1.00

Predictive Model Creation

For the Multiple Imputation model, 19 predictors were included in the initial model based on their individual significance. The final model contained 13 predictors (Figure 2). Predictors of suitability for HaH (OR,p-value): observation status (10.15,0.000), admission for fever (3.21, 0.000), final pre-admission temperature >100^{o} F (1.79,0.015), admitted via ED/ECC (1.64,0.003),

sodium >135 mEq/L (1.64,0.007), African American Race (1.61, 0.051). Predictors of unsuitability for HaH (OR, p-value): oncology diagnosis of secondary or unknown malignancy (0.32, 0.024), initial pre-admission respiratory rate >20/min (0.38,0.032), admission for secondary malignancy (0.40,0.032), final pre-admission systolic blood pressure <100 (0.42,0.007), hemoglobin <10 (0.51,0.001), admission category of digestive disorders (0.57, 0.052), and previous ED visit in previous 90 days (0.68,0.015).

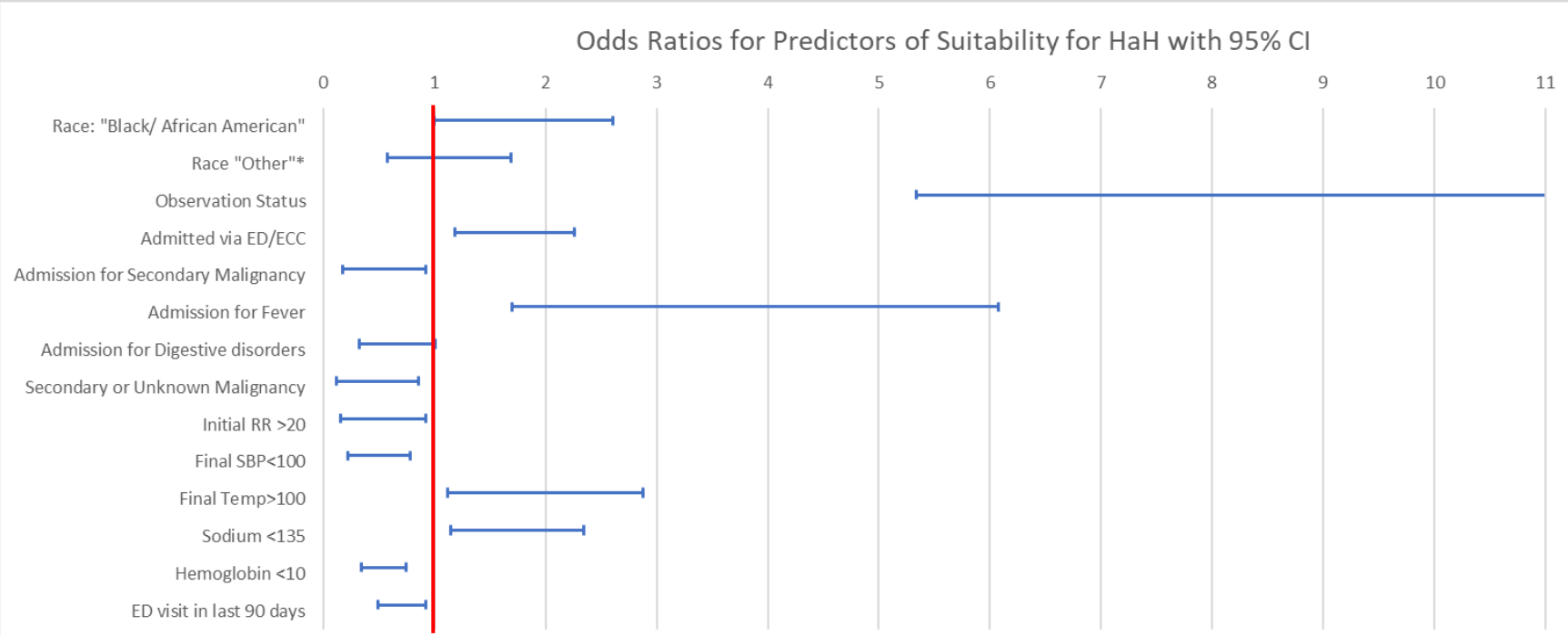
All major codes in the CCSR category of "admission for digestive diseases" were not significant individually, but all were trending toward decreased suitability. The four most common (with N>10 each in derivation group) CCSR codes in the digestive disorders' category were intestinal obstruction/ileus, noninfectious gastroenteritis, biliary tract disease and gastrointestinal hemorrhage. Codes for GI symptoms such as abdominal pain, nausea & vomiting, and diarrhea are not included in the digestive disorders' category and were found to not be significant in the multiple imputation model. Oncology diagnosis category of secondary or unknown malignancy included only three CCSR codes, which were individually insignificant but all trending in the direction of decreased suitability. The three codes included unspecified malignant neoplasm, neoplasm of unspecified nature/uncertain origin, and secondary malignancy. There was no correlation between oncologic diagnosis of secondary malignancy and admission for secondary malignancy. On chart review, admission for secondary malignancy described patients who admitted for complications of metastatic solid tumors such as peritoneal carcinomatosis. African American race was significant compared to White/Caucasian race, other racial categories such as Asian or Native American did not meet the 2% prevalence cutoff and were grouped into "Other". The "Other" category was not significant compared to "White/Caucasian" with an odds ratio of

0.98 (p value of 0.953). The choice of final vs initial value for each vital sign included in the model was based on which was more significant when added in separately (due to high correlation).

The complete case analysis model (detailed in appendix) contained 13 significant predictors, of which 9 matched predictors in the multiply imputed model. The direction of effect and odds ratios for the covariates in common were similar.

Figure 2: Odds Ratios for significant predictors included after averaging analysis of 20 imputed data sets. The blue bars indicate 95% CI, with Odds Ratios listed in table below. The 95% CI for Observation status extends beyond the range of the graph. For predictors in which one category occurred at less than 2% prevalence (RR<10, SBP >180, Hgb>18 & Sodium >145) the category was merged into the normal value.

** The "Other" category within race contains race identified as "other" or "unknown" as well as Asian and Native American. The other category was not significant and is only included since it is a subcategory of race, of which "Black/African American" was significant.*

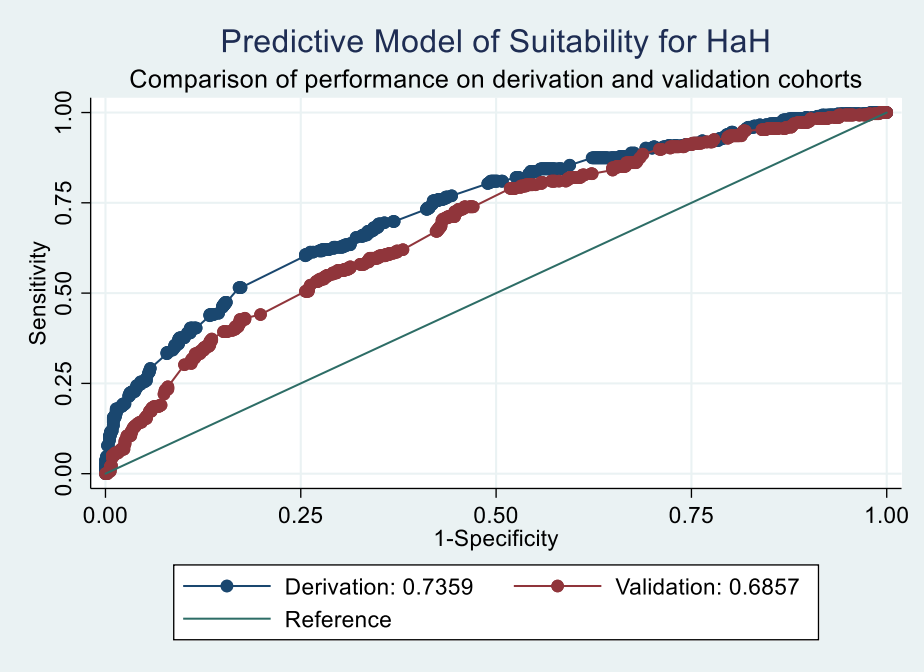


	ED visit in last 90 days	Hemoglobin <10	Sodium <135	Final Temp>100	Final SBP<100	Initial RR >20	Secondary or Unknown Malignancy	Admission for Digestive disorders	Admission for Fever	Admission for Secondary Malignancy	Admitted via ED/ECC	Observation Status	Race "Other"*	Race: "Black/ African American"
Odds Ratio	0.68	0.51	1.64	1.79	0.42	0.38	0.32	0.57	3.21	0.40	1.64	10.15	0.98	1.61
p>z	0.015	0.001	0.007	0.015	0.007	0.032	0.024	0.052	0.000	0.032	0.003	0.000	0.953	0.051

Assessment of the Predictive Model

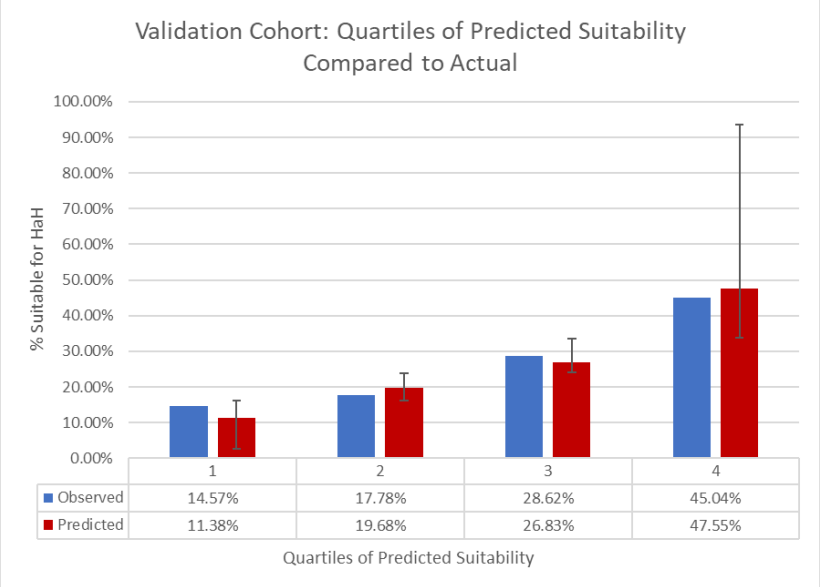
Receiver Operating Curves (ROC) of the model showed moderate discrimination with c-statistics of 0.736 on derivation, and 0.686 on validation (Figure 3). The performance of the complete case analysis model was similar with c-statistics of 0.757 on derivation, and 0.683 on validation (Figure 5 in appendix). There was a significant loss of model discrimination between the derivation and validation cohorts (p-value 0.044). Hosmer-Lemeshow goodness of fit on the validation cohort showed good calibration with a p-value of 0.19 (10 groups). Quartiles of predicted suitability for HaH closely tracked actual proportion of suitable admissions for the validation cohort (Figure 4). The Hosmer-Lemeshow goodness of fit test for these four categories confirmed appropriate calibration (P-value 0.14).

Figure 3: Receiver Operating Curve (ROC) of predictive model for suitability for HaH on derivation and validation cohorts. Chi2 analysis used to compare area under the curve (c-statistic) between derivation and validation cohorts.



Cohort	N	C-statistic	std. error	[95% Conf.	Interval]
Derivation	1096	0.7359	0.0173	0.70203	0.7697
Validation	1096	0.6857	0.018	0.65054	0.72091
	Ho:	area(0) =	area(1)		
	chi2(1)	= 4.05		Prob>chi2	= 0.0441

Figure 4: Quartiles of predicted suitability for HaH compared to actual proportion of suitable admissions in the validation cohort. Bars on predicted values show full range of predicted probabilities within that quartile.



Creation of Clinical Calculator

A clinical calculator was created by multiply all model coefficients by 10 and rounding to a whole number. The quartiles were based on quartile ranges determined above during model calibration.

Predictors	Calculator Score
Admitted as Observation	+23
Admission for Fever	+12
Black/African American Race	+5
Admitted via ED/ECC	+5
Sodium <135 mEq/L	+5
Final Temperature >100º F	+3
ED visit in last 90 days	-4
Admission for Digestive Diseases	-6
Hemoglobin <10 g/dl	-7
Final Systolic Blood Pressure <100 mmHg	-9
Admission for (complications of) Secondary Malignancy	-9
Oncology diagnosis of Secondary/Unknown Malignancy	-11
Quartile Cutoffs	Predicted% Suitability
≤ -4	14.5%
-3 to 0	17.8%
1 to 5	28.6%
≥ 6	45.0%

DISCUSSION

In a contemporary sample of patients hospitalized for oncologic disease at Yale New-Haven Hospital, we found that, 27% of admissions to the medical oncology floor were potentially suitable for HaH. The predictive model identified 13 significant predictors that combined to have a moderate discrimination (c-statistic of 0.69 on validation). The model was well calibrated to identify 4 quartiles of suitability for HaH, with the lowest quartile having a predicted suitability of 12%, and the highest having a predicted suitability of 48%. A notable challenge to implementing a hospital at home program for oncology patients is identifying subsets of patients who are most likely to be suitable for care at home [10]. This predictive model has the potential to be used as a starting point to identifying subsets of oncology patients who could be treated in a substitutive hospital at home program. To our knowledge this is the first predictive model created for oncology patients to identify admissions suitable for HaH. While a few oncology HaH programs have been developed and studied around the world, there is limited literature on selection criteria for oncology patients admitted with acute illness related to their cancer or its treatment [54–56,61]. Admissions for acute illness and decompensation form a significant part of the total inpatient admissions in cancer patients, and can affect the patient's quality of life, as well as total cost of care [4,6,8,58,72,80,81].

Our work advances the development of oncologic hospital at home by beginning to address the challenge of patient selection [10]. For a HaH program to be successful it is important to select appropriate patients that would not require services difficult to deliver in the home. While HaH aims to deliver hospital level care in the home, it lacks the direct proximity to specialized care that is available in most hospitals. Intensive care units, rapid response teams, round the clock in-house

physician and nursing coverage, quick access to advanced imaging, and a full suite of consultants are unique to hospitals and cannot be replicated in a home. We attempted to create a model that would predict which patients do not require these hospital-specific services. Our results show that it is possible to group admissions by levels of suitability based on information available in the electronic medical record at the time of admission. Further studies can be done to prospectively validate the model and create a pilot HaH program for oncology patients.

Our criteria for suitability were based on the conceptual framework of substitutive HaH [14,30,82]. Patients who at any point during their hospital admission required a service deemed difficult to provide at home were considered unsuitable, without considering the possibility of early discharge to HaH. Our criteria identified 908 admissions to the medical oncology floor during our time period of interest. This equates to a little over 200 admissions and 562 bed-days per year, enough to support a dedicated HaH team [83]. Patient admissions identified as suitable for HaH with our criteria had significantly lower length of hospital stays, were more likely to result in discharge to home, and less likely to be readmitted within 30 days. These statistically significant differences support the hypothesis that our definition of suitability identified patients who had a lower complexity of medical illness and better outcomes. The propensity of these patients to be safely discharged home after their hospital admission supports the possibility of them being cared for through a HaH program.

Our predictive model showed moderate discrimination to predict suitability and was well calibrated across quartiles in our validation cohort. There were 13 significant predictors, 6 predicted increased suitability, and 7 predicted unsuitability. Predictors of suitability for HaH: observation status, admission for fever, final temperature >100^{o} F, admitted via ED/ECC, sodium >135 mmol/L, African American Race. Predictors of unsuitability for HaH: oncology diagnosis of

secondary or unknown malignancy, initial respiratory rate >20 /min, admission for secondary malignancy, final systolic blood pressure <100 mmHg, hemoglobin <10 g/dL, admission category of digestive disorders, and previous ED visit in previous 90 days. The predictor with the strongest odds ratio was observation status, which applied to only a small proportion of admissions (5.4%). Observation status is defined through criteria by Medicare and other payors and is used to classify admissions that do not require inpatient level care, which supports its relevance in our model.

While age and sex were not significant predictors, we were surprised to find that race was a significant predicator. Since suitability for HaH is based on the complexity of medical care required during an admission, this result seems to indicate that with other significant predictors held constant, Black/African American cancer patients utilize less complex medical care during their admissions to the medical oncology floor. Racial disparities in healthcare in the United States are prevalent and can be observed through the higher un-insurance rates, lower access to care, and delaying of care due to cost amongst minority groups, especially African Americans [84]. Black cancer patients have higher mortality rates and shorter survival times [85]. In the context of our model, African American race may be correlated with decreased access to healthcare in an outpatient setting, resulting in more admissions for conditions that could have been cared for as an outpatient.

At baseline, patients evaluated in the ED or ECC were more likely to be suitable for HaH compared to patients admitted directly from clinic. The reasons for this are likely to be multifactorial but can be partially explained by the increased use of advanced imaging and interventional consults after admission among patients admitted directly from clinic. These patients were admitted directly to the medical oncology floor after evaluation in a clinic, transfusion center, or other outpatient location. These locations may lack the easy access to consults and advanced imaging available in

the ED/ECC, delaying their use for these patients until they are admitted to the hospital. It is possible that patients admitted through the ED/ECC likely received relevant imaging and consults as part of their evaluation prior to admission. Since these actions occurred before admission, they were not considered when determining suitability for HaH, potentially contributing to the higher proportion of suitable admissions within the ED/ECC group.

The primary admission diagnosis and cancer diagnosis of the patient contributed four significant predictors. Our model found that both admission for secondary malignancy and oncology diagnosis of secondary/unknown malignancy predicted lower suitability. The oncology diagnosis category for secondary/unknown malignancy was usually applied to patients whose tumors were diagnosed as metastatic or of unknown primary. The admission diagnosis of secondary malignancy applied to patients who were suffering from complications of metastatic disease (even with a known primary site). On further examination we found no correlation and almost no overlap between the two categories (only 0.3% admissions had both). Advanced stage cancer is common among cancer patients needing ICU admission and is associated with increased mortality [86]. In line with our hypothesis, admission for fever was predictive of increased suitability. While fever is a common reason for admission amongst cancer patients, it is not associated with increased risk for ICU admission or hospital mortality [7]. Admissions included under the category of "digestive disorders," such as intestinal obstruction and biliary disease, are often evaluated by a variety of imaging modalities, especially CT scans. Increased use of advanced imaging in this group could be contributing to their decreased suitability.

Vital signs and laboratory findings contributed five predictors to the model. Tachypnea with a respiratory rate >20 was predictive of lower suitability, similar to previous studies showing that cancer patients admitted with respiratory distress are more likely to require ICU care [7]. Final

pre-admission systolic blood pressure less than 100 was predictive of unsuitability. This is in line with a previous data showing that both increased respiratory rate and decreased systolic blood pressure measured in the ED before admission are strong predictors of ICU admissions and in-hospital mortality [87]. Increased suitability associated with hyponatremia (sodium <135) could be due to admissions for complications such as fluid and electrolyte abnormalities or dehydration that do not pose high risk for decompensation. Since transfusion was a criterion for unsuitability, it was unsurprising that anemia was a strong predictor of unsuitability.

ED admissions in the previous 90 days were predictive of unsuitability, likely a marker of the patient's overall health status. Interestingly, hospital admissions in the last 90 days were significant on univariate analysis but was removed from the predictive models due to lack of significance once other factors were considered. This may be related to the intentional decision to use index admissions only, which may artificially limit the number of previous hospitalizations seen in our cohort. Any admission in which the patient was admitted to medical oncology in the past 90 days was excluded from analysis in favor of the earlier admission.

There are some important limitations to our study that must considered. First, this study focuses on only one center, and may not reflect the patient population and treatment protocols at other cancer centers. Second, we only included admissions to the medical oncology floor, which limits the number and type of admissions. For a variety of reasons (such as bed availability, chief complaint, and severity of disease), cancer patients are often admitted to other parts of the hospital, including the general medicine ward. A more comprehensive study would examine the admissions of cancer patients to any hospital service. Third, in order to avoid confounding, we choose to include only the first admission for each patient within our time period. This decision excluded 34% of the admissions during our time period of interest, thus reducing the power of our study.

Using the first admission for each patient may bias the sample toward admissions that occur are earlier on in the progression of a patient's disease and are therefore less prone to complications that would limit suitability. Fourth, our definition of suitability was based only on clinical criteria. HaH programs also must include socioeconomic and convenience factors in defining suitability. Examples include distance of patient's home to the hospital, layout of home, supportive home and family environment, patient frailty, mobility, and support of the patient's family/caretakers. Fifth, the moderate discrimination of both models (c-statistic <0.7 on validation) means that a significant portion of the variability in suitability remains unexplained by our current model. If implemented in its current form, the model poses a significant risk of misalignment, where a substantial proportion of patients selected to be cared for through HaH may be unsuitable and could suffer adverse outcomes. While patients identified as unsuitable after admission to HaH could be transferred back to the hospital, it could still jeopardize or substantially delay appropriate patient care. This model could be improved through further studies in order to reduce the risk of misalignment. Further studies could consider the clinical judgement of the admitting physician, patient frailty, and functional status.

Future models may also re-evaluate our definition of suitability, which was based on previous HaH programs in medical patients. It is possible that HaH programs developed for patients with oncology diagnosis may provide more services for this population. We discussed this possibility with leadership at the Smilow Cancer Hospital and identified three possible services that would be important for this patient group that are not included in many HaH programs: advanced imaging, telemedicine consultation with specialists, and in-home transfusion. Due to the frequent use of CT scans in population, a HaH program that could arrange for transport to the hospital for advanced imaging would be able to treat more patients. Telemedicine for expert consultation would allow

patients who need specialist care to also be part of a HaH program. For some patients, transfusions can be performed in the outpatient setting, and including that capacity in a HaH would be important to treat complications of chemotherapy. A HaH program with these capabilities would be able to provide more services than the one we envisioned when defining suitability, potentially increasing the pool of eligible patients.

With these limitations, to the best of our knowledge, this study is the first to attempt to create guidelines for patient selection of oncologic hospital-at-home using a predictive model. The methods described here can be validated in other cancer centers to see if the significant predictors are similar across centers. Future work can focus on prospective validation of the model at Yale New Haven and refining the model to include clinician perception of suitability. Expansion of the model to all admissions of cancer patients, including general medicine floors could allow for a more comprehensive picture. The selection criteria can be further refined alongside development of a HaH system to better match the capabilities and services of the program being developed.

APPENDIX:
Complete Case Analysis Model:

Table 7: Training and Validation cohorts compared on a variety of patient and admission factors. Categorical variables were compared using Parsons's chi2 and continuous variables using Wilcox Rank Sum. Data presented as N (percentage) for categorical and mean (SD) for continuous measures.

Covariate	Derivation	Validation	p-value
	N=769	N=769	
Age	63.20 (12.22)	63.97 (12.62)	0.22
SEX			0.88
Female	379 (49.3%)	382 (49.7%)	
Male	390 (50.7%)	387 (50.3%)	
PRIMARYRACE			0.90
Black or African American	74 (9.6%)	81 (10.5%)	
Other	27 (3.5%)	23 (3.0%)	
Other/Not Listed	20 (2.6%)	15 (2.0%)	
White or Caucasian	630 (81.9%)	626 (81.4%)	
ETHNICITY			0.11
Hispanic or Latino	58 (7.5%)	37 (4.8%)	
Non-Hispanic	706 (91.8%)	728 (94.7%)	
Patient Refused	1 (0.1%)	2 (0.3%)	
Unknown	4 (0.5%)	2 (0.3%)	
Primary Admission Diagnosis Organ system			0.40
Blood	41 (5.3%)	34 (4.4%)	
Circulatory	31 (4.0%)	27 (3.5%)	
Digestive	77 (10.0%)	67 (8.7%)	
Endocrine	58 (7.6%)	52 (6.8%)	
Genitourinary	24 (3.1%)	38 (5.0%)	
Infectious	21 (2.7%)	22 (2.9%)	
Injury	11 (1.4%)	17 (2.2%)	
Musculoskeletal	14 (1.8%)	22 (2.9%)	
Neoplastic	155 (20.2%)	163 (21.3%)	
Nervous system	19 (2.5%)	18 (2.3%)	
Respiratory	27 (3.5%)	44 (5.7%)	
Skin	16 (2.1%)	10 (1.3%)	
Constitutional Signs & Symptoms	265 (34.5%)	245 (31.9%)	
Oncologic Diagnosis Category			0.64
Breast	81 (10.6%)	89 (11.7%)	
Endocrine	86 (11.2%)	94 (12.4%)	
Gastrointestinal	188 (24.6%)	151 (19.9%)	
Gynecologic	8 (1.0%)	6 (0.8%)	
Head & Neck	49 (6.4%)	42 (5.5%)	
Male Reproductive	29 (3.8%)	28 (3.7%)	

Respiratory/Cardiac	164 (21.4%)	173 (22.8%)	
Secondary/Ill-defined Site	35 (4.6%)	34 (4.5%)	
Skin	27 (3.5%)	43 (5.7%)	
Urologic	59 (7.7%)	65 (8.6%)	
Comorbidities:			
MI	80 (10.4%)	74 (9.6%)	0.61
CHF	101 (13.1%)	90 (11.7%)	0.40
Peripheral vascular disease	150 (19.5%)	136 (17.7%)	0.36
Cerebrovascular accident	129 (16.8%)	129 (16.8%)	1.00
Dementia	11 (1.4%)	19 (2.5%)	0.14
Pulmonary disease	282 (36.7%)	281 (36.5%)	0.96
Rheum	41 (5.3%)	26 (3.4%)	0.061
Peptic Ulcer Disease	45 (5.9%)	50 (6.5%)	0.60
Liver Disease	296 (38.5%)	306 (39.8%)	0.60
Diabetes	202 (26.3%)	190 (24.7%)	0.48
Metastatic Cancer	701 (91.2%)	705 (91.7%)	0.72
Admission in prior 90 days			0.83
0	497 (64.6%)	507 (65.9%)	
1	191 (24.8%)	181 (23.5%)	
2	81 (10.5%)	81 (10.5%)	
ED admissions in prior 90 days			0.93
0	480 (62.4%)	482 (62.7%)	
1	183 (23.8%)	186 (24.2%)	
2	106 (13.8%)	101 (13.1%)	
Seen in ED/ECC	522 (67.9%)	530 (68.9%)	0.66
Length of Stay	5.49 (5.35)	5.37 (5.02)	0.67
Suitable for HaH	220 (28.6%)	221 (28.7%)	0.96

Table 8: Final Predictive logistic model for complete case analysis containing 13 significant predictors. For predictors in which one category occurred at less than 2% prevalence (HR<50, RR<10, Hgb>18 & Sodium >145) the category was merged into the normal value.

Predictor	Odds Ratio	P>z	[95% Conf.	Interval]
Admitted as Observation	8.469375	0.000	4.016268	17.85995
Admitted via ED/ECC	2.092021	0.000	1.405821	3.113163
Admission for complications of Secondary Malignancy	0.318486	0.021	0.12014	0.844293
Admission for Fever	2.768015	0.004	1.387331	5.522765
Admission for Nausea and Vomiting	2.529777	0.023	1.133531	5.645876
Admission for Diseases of White Blood Cells	2.440641	0.043	1.029571	5.785642
Secondary or Unknown Malignancy	0.249061	0.028	0.071993	0.861628
History of MI	1.840362	0.024	1.084262	3.123721
Initial HR >100	1.383503	0.080	0.961411	1.990908

Initial RR>20	0.32007	0.049	0.102803	0.996519
Sodium <135	1.77694	0.002	1.233508	2.559787
Hgb < 10	0.318116	0.000	0.202105	0.50072
ED admission in last 90 days	0.584995	0.005	0.403481	0.848167

The area under the curve (AUC) in the receiver operating curve for the model was 0.7313 for derivation cohort and 0.6769 for the validation cohort (figure 2). Pearson's Chi2 comparison between the two AUC curves showed that the model performed better for the derivation as compared to the validation cohort (Table 1). Visual comparison of kernel density plots for suitable and unsuitable patients shows similar density distributions in both derivation and validation cohorts (figure 3).

Figure 5: Comparison of receiver operating curves for the model on derivation and validation cohorts for complete case analysis model

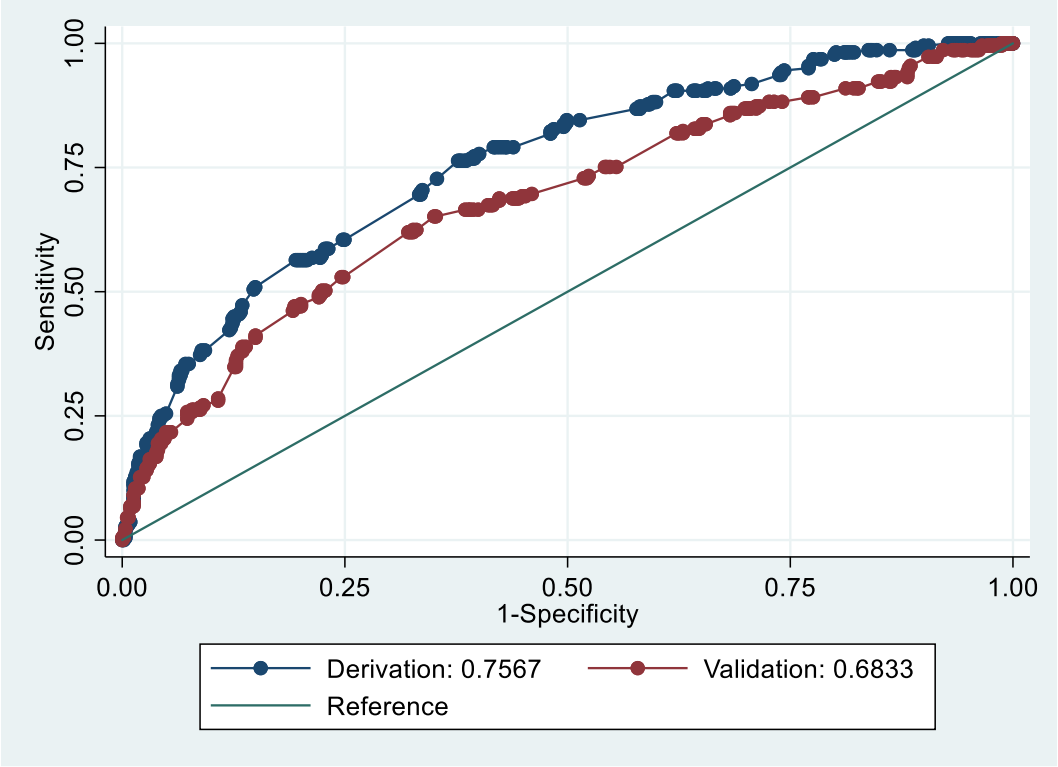


Table 9: Comparison of the area under the curve for model on derivation and validation cohorts. Area compared using Pearson Chi2 test.

Group	Obs	Area	Std. Err.	[95% Conf.	Interval]
Derivation (0)	769	0.7567	0.0190	0.71943	0.79402
Validation (1)	769	0.6833	0.0218	0.64052	0.72610
Ho:	area(0) = area(1)				
	chi2(1) = 6.43	Prob>chi2 = 0.0112			

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