2014

Impact evaluation of international multidisciplinary tumor boards

BOSTON UNIVERSITY

SCHOOL OF MEDICINE

Thesis

IMPACT EVALUATION OF INTERNATIONAL MULTIDISCIPLINARY TUMOR BOARDS

by

JASON A. SREEDHAR

B. S., University of California Berkeley, 2012

Submitted in partial fulfillment of the

requirements for the degree of

Master of Science

2014

Approved By

First Reader_____

Karen Symes, Ph.D.
Assistant Dean of Student Affairs
Associate Professor of Biochemistry

Second Reader _____

Ami S. Bhatt, M.D., Ph.D.
Assistant Professor of Medicine and Genetics,
Stanford University

DEDICATION

For my father, Kannan:

“No matter how long the night is, the day is sure to come.”

--African Proverb

ACKNOWLEDGEMENTS

I would like to acknowledge Dr. Karen Symes and Dr. Ami Bhatt for their advising during the writing process, your commentary has been crucial in compiling my research and creating this document. I would also like to thank Dr. Bhatt, Dr. Franklin Huang, and all parties related with the Global Oncology Initiative, for allowing me to work on such and amazing and innovative project. I thank the staff of Boston University's Department of Medical Sciences, for helping me throughout my course of study there. Lastly, I would like to thank my parents, Kannan and Sue, for their everlasting support.

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ABSTRACT

Over the last 20 years, cancer clinicians have begun to improve the efficacy of cancer care through tumor boards, meetings of multidisciplinary patient care teams used to educate attendees and align treatment plans. In addition to the potential for collaboration between different disciplines, these meetings allow for the incorporation of information from peer-reviewed literature. Despite their use, very little research has been done on the effect of tumor boards on treatment efficacy. Within this small body of work, the indicators used are often inherently biased, and little concern is given to their confounding effects. This document will discuss alternative metrics that provide a less biased estimate of the impact of tumor boards.

Given their educational aspects, tumor boards are beginning to be used in an international context to support clinicians in developing nations. Despite the relative lack of evidence supporting use of tumor boards, they provide a low-cost method for improving clinician education in a setting where treatment protocols vary greatly. Moreover, international tumor boards provide a way for low-resource hospitals to tap into facilities of high-resource hospitals, receive resource-sensitive guidelines for future practice, and collaborate with clinicians from other hospitals. However, there are serious barriers to implementing international tumor boards, including technological, logistical, linguistic, and oversight issues. This document outlines potential issues and methods to

circumvent them, as well as benefits of international tumor boards (including future collaboration).

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LIST OF ABBREVIATIONS AND ACRONYMS

ALS: Amyotrophic Lateral Sclerosis

Before-and-after: An evaluation tool outlining how tumor boards discussion changed patient management (diagnosis, staging, treatment)

HIV: Human Immunodeficiency Virus

HPV: Human Papillomavirus

ITB: International Tumor Board, often involving a collaboration between a resource-rich hospital and a resource-limited hospital

LMCs: Low- and Middle-income Countries

MCC: Multidisciplinary Cancer Conference, also "Tumor Board"

N=: Sample size of

Path.: pathological

Mgmt.: management

TB: Tumor Board, synonymous with "Multidisciplinary Cancer Conference"

INTRODUCTION

In the development of better care of cancer patients, the involvement of multidisciplinary cancer conferences (MCCs), otherwise known as "tumor boards" (TBs), has become commonplace in may parts of the world.[1, 50] These conferences, which aim to improve patient care by enhancing clinician education and collaboration, bring clinicians of many specialties (radiology, pathology, radiation oncology, medical oncology, surgery) together for discussion of patient cases.[36] These meetings enable collaboration of practitioners, culminating in their provision of a multimodal consensus treatment supported by peer-reviewed literature.[30] The main objectives of these meetings are to improve patient care, further educate trainees and faculty, and standardize treatments of a given disease.[12] Moreover, TBs allow for multidisciplinary collaboration in order to improve integration of multiple components patient care (nursing, psychosocial care, social work, etc).

Tumor boards are generally structured to involve both case-based discussion of diagnoses and treatments (both prospective and retrospective cases) and evidence-based teaching sessions to familiarize attendees with the literature surrounding a given topic.[35] Through the use of both didactic teaching and interactive case discussions, the information shared during the tumor board regarding a specific cancer type is reinforced multiple times. Attendees of TBs should come from multiple different oncology-related specialties, thus allowing improved education and integration across all aspects of cancer care. This list can include physicians in radiation oncology, surgical oncology, medical oncology, internal medicine or

pediatrics (with subspecialization in the neoplastic organ being discussed), pathology, and radiology. This group of physicians should be supplemented by specialist nurses, social workers, medical trainees, psychologists, and other members of the care team as needed. Having multiple specialties and training levels present at a TB allows for a more holistic discussion of how to proceed with the patient's care, as well as continuation of this collaborative methodology through incorporation of trainees.[28]

At present, there is only a small amount of published literature regarding tumor boards.[30] Despite the Calman-Hine ruling of 1995, which mandated the use of TBs across the United Kingdom, very few studies on the effectiveness of TBs have been conducted since this ruling.[45] Most of the existing literature use "before and after" metrics, which measure what effect the TB had on the proposed diagnosis and treatment, rather than patient outcomes.[11] While valuable, this metric is not a stand-alone metric given the countless biases that are inherent within its measurement and analysis, and therefore should be used only in conjunction with other measures. Thus, use of an indicator containing such biases leads to the inherent limitation in scope of current TB effectiveness literature. Despite the push for increased use of TBs to coordinate care, evaluation of TBs has not been carried out in a scientifically rigorous manner.

Another threat to the validity of TB effectiveness literature is that a set structure or constitution for tumor boards does not exist, causing high levels of variation between different TBs. Croke et al. make note of variations between TBs, such as available technological and therapeutic resources, and how this creates

variation in the projected impact of different TBs. [11] As a result, the existing data on TB effectiveness remains both small in size as well as highly variable.

As low- and middle-income countries look for ways to improve their quality of care, tumor boards present a method for advancement through coordination of care and generation of resource-sensitive care models. Despite the lack of valid effectiveness research on TBs, these conferences provide a method for collaborating with clinicians from the developed world in order to improve training and education levels within their own staff. Given that there are significantly fewer physicians as well as training programs in the developing world, care-givers are often less sub-specialized than their developed world counterparts, leading to frequent variation in treatment regimens between physicians.[14] Additionally, as financial challenges may arise in purchasing frontline diagnostics and drugs, physicians in resource-limited settings are often faced with uncertainty when selecting alternative therapies, for which little data exist.[52] Through collaborative international tumor boards, hospitals of undeveloped nations can pair with those of more developed nations in order to provide more post-graduate training, standardize care via resource-sensitive guidelines, and identify the most effective alternative therapies as outlined by peer-reviewed literature.[13] In this way, international tumor boards (ITBs) provide a collaborative platform for improving international cancer care.

TBs are projected to be highly effective in improving the quality of patient care, as shown by a number of previous studies. According to Wright et al., these conferences are "integral to patient process and patient outcomes", improving patient

outcomes, physician education, and patient satisfaction in addition to other indicators.[51] While this does provide a great avenue for improving the quality of care, more rigorous quantitative analysis must be used to ensure that the expected progress is in fact being made. As with any other intervention, data-driven statistical approaches and more quantitatively-focused outcome analysis are needed to prove that tumor boards are improving cancer care, both in regards to patient care and physician education.[11] This thesis serves to discuss the methods whereby we may more appropriately measure the impact of tumor boards, as well as the implementation of tumor boards and effective impact evaluation in the resource-limited context of low- and middle-income countries. Specific attention will be given to the structure of TBs, the hypothetical attendees, the methodology for measuring the impact of TBs on patient care, and potential issues that would arise when implementing and evaluating TBs in the developing world.

Specific Aims and Objectives

1. Outline how tumor boards work: structure, function, attendees

2. Identify the metrics that are currently used in local tumor boards, including rationale and confounding variables

3. Discuss how different tumor boards have performed on these scales

4. Examine the potential benefits and drawbacks of applying tumor board construct on an international scale

5. Identify the problems faced by low- and middle-income countries and how these problems could alter the aforementioned metrics

6. Generate a new set of metrics that should be used for international TBs: define metrics, identify the underlying constructs being measured, examine possible confounding factors

OVERVIEW OF TUMOR BOARDS

As stated by De Guzman, the main objective of TBs is to utilize literature-based discussions as well as patient cases in order to improve the quality of care.[12] This is done via the use of both retrospective and prospective case discussions as well as short teaching sessions outlining existing research, diagnostics, and therapeutics for a given cancer subtype.[35] Through the discussion of appropriate diagnostic methodology and therapeutic approaches in patient care, these conferences aim to improve the quality of care by improving clinician knowledge of appropriate clinical care protocols and algorithms for a given cancer or developing such guidelines.[12]

Attendance and Structure

In his discussion of the attendees of a tumor board, Jazieh explains that the objective of having physicians of multiple disciplines and treatment modalities present is to improve the knowledge base present within the room; ideally, the multidisciplinary collaboration would allows the multiple aspects of cancer care to work together in a more cohesive manner, leading to better patient care.[28] To this end, Jazieh suggests involving physicians from many different specialties, who should be joined by other clinical staff when appropriate.[28] Participation from trainees and junior physicians should be particularly emphasized in view of the need for training. Incorporating as many aspects of patient care as possible allows for greater cross-talk between care providers. Furthermore, Jazieh suggests that multiple clinicians be present from each discipline, allowing for educational mini-discussions regarding a given field by multiple physicians trained in that field.[28] Furthermore,

Jazieh suggests that multiple clinicians of each discipline be present.[28] Having multiple clinicians from a given discipline allows for cross-talk between peers, enhancing the quality of the discussion by providing multiple perspectives regarding treatment protocols, patient management, etc.[28] Lastly, in addition to the aforementioned attendees, an additional participant should serve as the tumor board leader, who facilitates discussion surrounding the cases and encourages participation from all parties.[26, 28] Ideally, the physician caring for the patient would fill this role, but this does not have to be the case.

As previously mentioned, the main function of tumor boards is to discuss how/when to apply existing treatment protocols to cases, or to develop new protocols should they not exist for a certain case. Thus, TBs should be structured in such a way that facilitates this knowledge transfer. The main components of tumor boards include introductions (when attendees do not know each other), didactic teaching sessions, discussion of the patient's initial presentation, analysis of diagnostics (including pathology and radiology), review of the patients treatment regimens, and concluding remarks on the case. Other components can be added, but these are the essential aspects of a TB.

In order to prepare attendees for a TB, Halsted et al. mention the need for 10-page written reports, including radiology and pathology images, to be disbursed one week before the date of the TB. This policy allows all participants to have some previous knowledge of the case and better prepare for the TB, and results in better participation.[24] The didactic teaching component of the TB should rely heavily on

published quantitative data (in addition to qualitative measures) in order to provide background for the cases being discussed.[23] The ensuing case studies should then serve as a means to discuss the implementation of the didactic material.[43] Case discussions should include an review of the initial presentation by the covering physician (including all tests and diagnostic procedures), a discussion by the radiologist and pathologist of all images and slides (including the criteria on which the diagnosis was made), and a discussion of what treatment options have been explored by the surgeon, radiation oncologist, and medical oncologist.[28] The input of the pathologist and radiologist is crucial here, given their highly important role in establishing an accurate diagnosis.

Given the teaching objective of TBs, participation from junior staff should be encouraged throughout the conference. Trainees and junior physicians should be expected to present cases as well as head didactic sessions during the TBs. Doing so provides residents and fellows with a sense of ownership and responsibility over the material presented while limiting the preparation time required of senior staff.[23]

Objectives and Effectiveness

Despite a small body of research on TBs, a subset of literature utilizing before-and-after metrics for TBs has shown that TBs may improve patient management and quality of patient care (Table 1). Newman et al. reported that a breast cancer TB based out of the University of Michigan (N=149) resulted in changes in surgical management in 32% of patients, and chances in pathological diagnosis in 29% of cases; these results imply an improved level of care due to the

literature survey and multidisciplinary case review.[35] Many other studies have been employing the same "before-and-after" indicators, which identify the percentage change in diagnosis, staging, or treatment plan of cancers as a result of tumor boards. Most of these studies show that TBs change the management of a significant number of cases in one of these criteria, suggesting that these changes may allow for a higher level of care as a direct result of multidisciplinary collaboration. Van Hagen et al. mention an upper GI tumor board discussions causing treatment plan changes in 34% of cases (N=171), while Wheless et al. noted a head and neck TB (N=120) encourage care-givers to alter 25% of diagnosis/staging decisions and 18% of treatment plans.[47, 49] Similarly, Chang et al. mention that in a breast tumor board held by the University of Pennsylvania, 43% of proposed therapeutic plans presented (N=77) were disputed between physicians.[8] Similar results are echoed by countless other articles. All of these studies show higher numbers of cases facing stricter scrutiny and analysis as a result of TBs, implying that enhanced discussion allows for better care. Moreover, these studies point to variability in care between physicians and the need for standardization guided by literature, a service provided by TBs.

Table 1: Studies of TB Efficacy Utilizing "Before-and-After" Indicators			
Authors	**Type of Cancer**	**Study Size**	**Main Findings**
Newman et al.	Breast	149	32% change in surgical mgmt. 29% change in path. diagnosis
Van Hagen et. al	Upper GI	171	34% change in treatment plans
Wheless et al.	Head/Neck	120	25% change in diagnosis/staging 18% change in treatment plans
Chang et al.	Breast	77	43% of therapy plans disputed
Ganesan et al.	Ovarian	108	37% change in path. grade of tumor 52% change in diagnosis 22% change in overall mgmt.
Gatcliffe et al.	Multiple types	153	18% change in diagnosis 26% need further discussion
Pawlik et al.	Pancreatic	203	23% change in overall mgmt. 25% change in treatment
Wright et al.	Multiple types	Unknown	7-43% change in overall mgmt.

While most studies have utilized "before-and-after" indicators to measure the impact of tumor boards, few have used patient outcomes (the ultimate goal of TBs) to evaluate the efficacy of TBs (Table 2). Stephens et al. reported that an esophageal TB (N=54) decreased operative mortality from 26% to 5.7% while increasing 5-year survival from 10% to 52%.[43] In a study of non-small cell lung cancer, Forrest et al. showed that TBs (N=243) doubled patient life expectancy to from 3.2 months to 6.6 months.[19] Junor et al. reported that patients presented at a multidisciplinary TB (N=479) were more than twice as likely to get the appropriate treatment (platinum treatment) for their ovarian cancers.[29] Outside of the field of oncology, Traynor et al. mention a multidisciplinary clinic for ALS patients (N=344) causing a 30% decrease in mortality and a 7.5-month increase in lifespan for patients.[46] This body of work

shows that a multidisciplinary approach to disease, specifically to cancer, can extend the lives of patients.

Table 2: Studies of Tumor Board Efficacy Utilizing Patient Outcome Indicators

Authors	Type of Cancer	Study Size	Main Findings
Stephens et al.	Esophageal	54	20.3% drop in operative mortality 42% increase in 5-year survival
Forrest et al.	Lung (non-small cell)	243	106% increase in life expectancy
Junor et al.	Ovarian	479	100% more likely to receive appropriate treatment
Traynor et al.	ALS (non-cancerous)	344	30% decrease in 1-year mortality

Drawbacks

One of the major issues with existing tumor board literature is the variability between physicians, hospital systems, and tumor boards themselves. Speaking on this subject, Croke address the relative weakness of existing data in saying, "available data are weakened by the heterogeneity and vagueness of the studies and their ill-defined endpoints and large number of confounding variables…As a result, firm conclusions can not be drawn".[11] While many tumor boards do report positive outcomes as a result of their discussions, an equally large number report changes that are either statistically insignificant (despite being adequately powered) or all-together nonexistent. Nguyen's study of a TB from the University of Arizona discussing head and neck cancers showed an improvement in 3-year survival by only 8% for surgery/radiation combination therapy and 7% for chemotherapy, a finding shown to be statistically insignificant.[36] A study by Birchall et al. of the South West Cancer

Intelligence Service Tumor Panel (UK) comparing a pre-Calman-Hine cohort in 1997 (no TB) to a post-Calman-Hine cohort in 2000 (with TB) showed nearly identical survival rates; this finding indicates that the presence of TBs did not impact patient care.[6] A study by Keating et al. of 138 US-based Veterans Affairs Hospitals also showed no significant impact of tumor boards via the use of 27 different performance-based metrics.[30] The ambivalent data from these studies, in conjunction with other data showing a positive impact of tumor boards, portray the image of a highly variable field in which little is definitively known.

The reasons underlying this disparity and variability in data are not well understood. Factors could include heterogeneity in disease stage upon initial patient presentation, resource availability, existing comorbidities, advances in therapies, profile of attendees, hospital-specific treatment protocols, etc.[11] Thus, in order to generate a larger and more consistent body of data on the impact of TBs, better metrics need to be developed and applied appropriately. While tumor boards are speculated to improve patient outcome, overall care protocol development, and physician education, results derived from data pertaining to these topics continues to be inconclusive. These improved metrics will allow for greater external validity, providing a better picture of TB effectiveness.

In addition to the variations affecting the measurement of impact of TBs, there are other factors intrinsic to TBs that mitigate the effectiveness of the tumor boards themselves; studies of these factors have lead to conflicting reports on whether TBs are greaten or worsen the timeliness of cancer treatment. Various studies have listed

concordance rates (percentage of TB-based consensus treatments that are actually carried out) between 85% and 98%.[7, 9] Many of these discrepancies are due to unforeseen patient comorbidities. Due to their deviation from the optimally effective consensus treatment, they will invariably affect the data derived fro tumor boards. Another major factor that may diminish the impact of tumor boards on patient outcomes is the wait time caused by increased imaging and pathological workup/review on each patient.[6] Given that cases presented at TBs are generally more severe, this delay could be quite damaging. According to van Hagen et al., the additional work-up required by TBs can cause a 20-day to 5-week delay in treating a patient.[47] Despite these findings, Gabel et al. have reported a shortening in treatment-start time (time from diagnosis to treatment initiation) from 42 days to 30 days, partially as a result of the increased physician assurance provided through tumor boards.[20] Birchall et al. mention that while this is not likely to alter survival rates, it will have some effect on the morbidity and quality of life for the patient.[6] Thus, current research is unclear on whether the need for more workup in TB cases positively or negatively affects the quality of care delivered.

All in all, these factors add to the variability of TB-based data in addition to obscuring the impact of the conferences. While the root causes of these issues can not be eliminated, steps can be taken to reduce their influence as well as measure their effect via the use of better control groups. This topic will be discussed later when outlining new metrics for tumor boards.

CRITERIA OF DOMESTIC TUMOR BOARDS

As mentioned above, the metrics used to evaluate the effectiveness of tumor boards are highly variable. Moreover, some of these indicators are subject to bias, thereby limiting their validity. The following section will serve as an overview of the criteria being used to analyze internal tumor boards in peer-reviewed literature, as well as to promote the use of new indicators.

Much of the existing literature on tumor boards uses a "before-and-after" model of evaluation, measuring the effect of the TB in changing either the diagnosis, staging, or treatment plan for a given cancer. This is often (but not always) accompanied with some kind of rating scale to measure how drastic this change is. In a survey of high-resource Arab hospitals, El Saghir et al. concluded that tumor boards evaluated through "before-and-after" indicators cause change in diagnosis/management or treatment in of 33-50% of cases; however, this seems to be much higher than the measurements of other studies based in the US.[14] In the head and neck tumor board of University of North Carolina, studied by Wheless et al., resulted in a change rate of 25% (diagnosis) and 18% change in treatment plan.[49] Van Hagen's study of an upper-GI tumor board revealed a 34% change in treatment plan, including a 35% change of modality only.[47] Chang's study of multidisciplinary breast cancer management at the University of Pennsylvania showed a 43% change in diagnosis and a 45% change in treatment.[8] A similar study at the University of Michigan by Newman et al. showed a 29% change in pathological diagnosis and a

32% change in surgical management.[35] Thus, as mentioned by Croke before, before-and-after studies show highly heterogeneous results.[11]

In a study of multidisciplinary lung cancer management, Coory address this variability by saying:

> Before-and-after studies provided relative weak evidence of a causal association because of the potential for confounding. Specifically, multiple concurrent changes in cancer care over time, such as increased specialization, better treatments, or increased adherence to evidence-based guidelines, could be the reason for apparent improvement in survival, rather than the introduction of a MD team. Use of historical controls can introduce a bias known as the 'Will Rogers phenomenon', resulting from more accurate staging of more recent patients. This might account for the drift towards more advanced disease observed…[10]

Abdulrahman Jr. et al. reinforces this idea, stating that "before-and-after designs… are considered as weak evidence for determining causal relationships because of multiple potential confounders.[1] New designs should be looked into in future studies and there should be an adjustment for any confounder in case-control studies."[1] Both authors make note of the high prevalence of confounding variables that are unaccounted for, resulting in the aforementioned variation in before-and-after impact estimation. As a result of this, newer and more accurate measures of tumor board impact need to be developed to replace the current before-and-after metric.

A review paper by Croke et al. further demonstrates the effect of confounding factors in before-and-after studies.[11] In its discussion of many studies covering a broad range of cancer types, this paper mentions both a gynecological cancer paper by Gatcliff, showing case alterations in 35% of cases as a result of a TB, as well as a genitourinary cancer paper by Archer showing case alterations in less than 2% of

cases.[6, 23] Comparison of two studies showing significantly different results within the same indicator further shows the variation between studies as well as the influence of confounding and unknown factors on impact evaluation or TBs. In addition to further demonstrating the aforementioned point, Croke et al. bring up another key flaw of the before-and-after metric by stating, "the authors [of a paper using before-and-after metrics] did not assess whether the changes in management affected patient care and survival".[11] Many studies employing "before-and-after" metrics do not include information about patient morbidity and mortality, demonstrating that these indicators are not targeting the constructs they should be evaluating. This brings up the point that before-and-after studies are only relevant if and when it is shown that these changes create a higher quality of cancer care.

These "before-and-after" metrics, which are used in conjunction with measures of attendance at TBs, are currently being used in evaluation despite high levels of variation and confounding (Table 3). As research on TBs continues, better indicators are needed to develop a realistic idea of the effect of TBs and their effectiveness in qualitatively enhancing cancer care.

Table 3: Commonly Employed Indicators for Non-Collaborative Tumor Boards:

1. "Before-and-after" change in treatment plan and management
2. "Before-and-after" change in prognosis (as guided by pathology services)
3. Attendance

In regards to alternate metrics for tumor boards, a review by Croke et al. outlines a series of studies spanning many types of cancer that use metrics other than before-and-after measurements (Table 4).[11] The authors also cover studies employing alternative and uncommon metrics, including physician concordance with TB consensus treatment suggestions, long-term survival rates (2, 3, and 5 years), operative mortality, and time from diagnosis to treatment initiation, with all of these studies comparing patients receiving TB recommendations to those who did not.[11] Moreover, Ribeiro and Ching-Hon's discussion of twinning partnerships brings up tumor relapse rate and toxicity death rate as important metrics for evaluating cancer-related interventions.[39] Fader et al. also introduce the idea of looking at TB-associated cases from a financial standpoint, mentioning both cost-benefit analysis as well as spending patterns.[16] While economic analysis would beneficial on a policy-making level, it is outside the scope of an individual physician's work and is thus excluded here. Employment of the aforementioned alternative metrics (physician concordance, tumor relapse rate, toxicity-based death rate, operational mortality, long-term survival, diagnosis-treatment time) allows for expansion of knowledge surrounding TBs via the ability to better target at what levels they do or do not improve care.

Regarding case selection, many authors note that only the most severe cases should be presented in order to maximize time-efficiency. Case selection criteria should only allow cases that are either highly complex in presentation, irregular in

presentation, or recurring.[22, 33] Thus, less than 10% of the total case-load should be presented at a tumor board.[31] Thus, as a result of the complexity and severity of cases presented at tumor boards, survival metrics are expected to be lower than that over the overall cancer patient population at a given care center.[22]

The remainder of this section will serve to individually outline each of these metrics, discussing their main analytic objective, current state, and potential confounding factors.

Table 4: Proposed Alternative Metrics for Tumor Boards (Collaborative and Non-collaborative):

1. "Physician concordance"-- concordance between the TB suggestions and the used treatment protocol
2. 3-year tumor relapse rate
3. Toxicity-based death rate/operative mortality
4. Long-term survival
5. Diagnosis-treatment time (time from diagnosis to treatment initiation)
6. Before-and-after" change in diagnosis
7. "Before-and-after" change in treatment and management plan
8. Qualitative Indicators

Physician Concordance with TB Consensus Treatment

Through documentation of TB consensus and follow up on individual patients, concordance between the TB-based consensus and final treatment plans can be studied. Analysis of concordance data allows for study of the effect of TB recommendations on physician decision-making; assuming that TBs always give literature-based suggestions that provide the highest quality of care, concordance percentages measure whether this high standard is carried through to the patient's care in its entirety. Studies of domestic tumor boards, almost entirely from high-resource countries, show that concordance varies from 85% of 98% (Table 5).[6, 7] As explained by Wood et al., the main confounders in physician concordance (causing deviation from TB consensus treatment plans) include comorbidities not mentioned at the TB, newly-discovered metastases, and patient choice.[50] As previously mentioned, cases presented at tumor boards should be the most complex cases seen, whether as a result of advanced stage, comorbidity, or other factors. As a result, these cases often need the most work-up and monitoring of overall health. Given that the most common cause of discord between consensus and final treatments are newly-discovered metastases (an issue more prevalent in advanced-stage cancers) and decompensation due to comorbidities (more common in complex cases), in addition to the case selection process used to select only complex cases, tumor boards as a whole should expect to see lower concordance percentages due to the complexity of cases presented.[50]

The physician concordance indicator, as mentioned by Croke et al., is beginning to gain credence, as it is being used increasingly to measure TB impact.[11] While this measure is inherently biased, its use in conjunction with other indicators gives a clearer picture of how the discussions of tumor boards relate to the quality of cancer care.

Table 5: Studies of Tumor Board Efficacy Utilizing Physician Concordance

Authors	Type of Cancer	Study Size	Findings
Blazeby et al.	Upper GI	273	85% Concordance with consensus, patient choice and undiscovered comorbidity leading causes for discordance
Strong et al.	Upper GI	333	86% concordance with consensus, discordance usually due to decompensation
Schroeder et al.	Breast and Gynecological	479	78% full concordance, 98% partial concordance, discordance most commonly due to patient deterioration

Tumor relapse rate (3-year)

The utility of measuring the rate at which patients relapse from any given treatment is that is provides information on what treatments are useful for any given cancer type and stage. This has additional implications for the developing world, which will be discussed later. Having this information allows the guidance of further tumor boards based on past evidence. For example, if tumor board physicians note that a chemotherapy regimen has a high relapse rate, additional drugs or other treatment modalities could be added to lower the rate of relapse and improve long-term health. While this indicator has not been previously used in the evaluation of tumor board effectiveness, it has been mentioned as a method to measure efficacy in

inter-hospital twinning partnerships, and showed positive outcomes in a partnership between Saint Jude Children's Research Hospital and Recife Hospital in Brazil.[39] These twinning partnerships will be further explored later.

Toxicity-based Death Rate and Operative Mortality (3-year)

Given that chemotherapy and radiation therapy can be highly destructive to the body of the patient, an indicator to measure the toxicity of these treatments should be employed in a tumor board. Similar to the tumor relapse rate, collecting and documenting the toxic effects of a given treatment/management regimen can help guide recommendations of a tumor board. This metric was also used by Ribeiro, and provides tumor board physicians with a method to assess whether a given treatment regimen should be modified due to high toxicity.[39] Measurement of operative mortality provides a similar measurement for surgical interventions, assessing the invasiveness of a treatment operation as it relates to mortality rate.

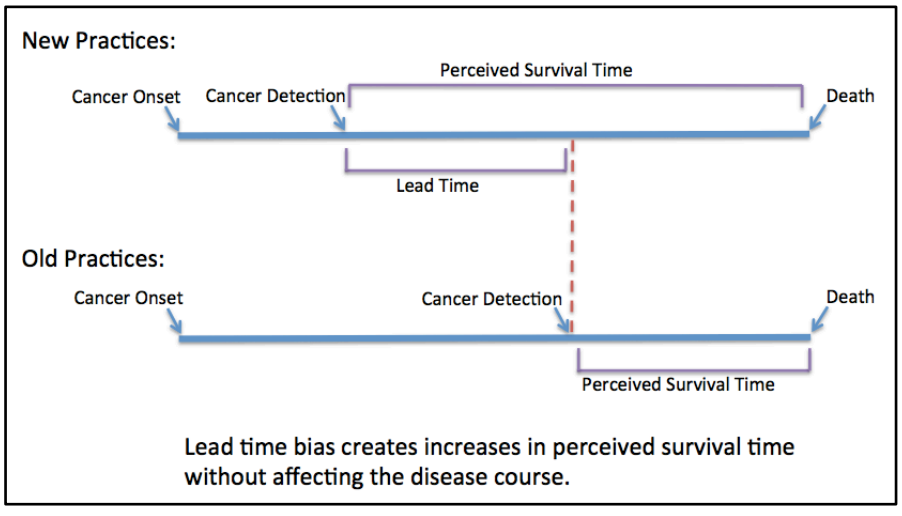
Long-term survival

Unlike concordance data, long-term survival data have a great deal of variation, both in regards to raw data as well as statistical significance. However, their documentation and analysis is crucial, given that the ultimate goal of cancer treatment (and treatment of any disease) is to avoid mortality and improve patient outcomes.

Many studies have pointed to long-term survival as a construct that is highly important in the evaluation of TBs. Lamb points out the utility of survival data, stating that, "Traditional measures of outcome, such as survival data, give a robust

account of whether an intervention is effective or not."[33] Inherent in this issue is lead time bias, the idea that and increase in survival time after diagnosis may not necessarily be indicative of better disease management since the longer survival time may simply be accounted for by better screening procedures (Figure 1).[33] However, Lamb also notes the importance of combining survival data with other short-term metrics.[33] While Welch et al. have also pointed to the tracking and analysis of long-term survival as illogical (due to the lead time bias) and call for use of other indicators to more effectively assess cancer interventions, survival of patients should still be tracked.[48] The rationale behind the continued monitoring of patient survival is two-fold: a) patient survival is a primary goal of any disease treatment, b) Welch specifically mentions that it does have some connection to the quality of cancer care (albeit a tenuous one). The second point demonstrates that patient survival could be useful if combined with other indicators.

Figure 1: Lead Time Bias



Moreover, many studies have used long-term survival as an indicator to show that multidisciplinary teams can improve patient outcomes. A study by Junor et al. does show that use of multidisciplinary TBs enhanced 5-year survival of gynecological oncology patients at a statistically significant level.[29] However, Birchall's study of and English head-and-neck TB points to a slight decrease in survival, highlighting the great variability when using survival as an analytic tool.[6] Croke touches on this topic, stating that, "available [long-term survival] data are weakened by the heterogeneity and vagueness of the studies and their ill-defined endpoints and large number of confounding variables… As a result, firm conclusions cannot be drawn."[11] One method to increase the accuracy and validity derived from long-term survival measurements would be to increase sample size. Even within cancer patient populations, death is a relatively rare and uncommon event. By increasing the number of enrolled participants, the effects of participant variability would be mitigated, leading to increased validity.

Diagnosis-Treatment Time (Time from Diagnosis to Treatment Initiation)

As designated in the title, this metric serves to measure how long a physician takes to implement the treatment recommended by the TB. The construct that this indicator serves to measure is the assuredness of physicians in the chosen treatment; ideally, this assuredness would be improved through reinforcement of the literature-based guidelines presented at TBs. The idea of using diagnosis-treatment time as an effectiveness measurement tool was emphasized in Jazieh's discussion of the role TBs play in cancer care.[28] Jazieh states that development of this indicator, which

serves as a process evaluation tool to measure the expediency of carrying out TB consensus recommendations, could be used to measure the expediency of treatment and improve overall level of cancer care.[28] Moreover, Gabel et al. showed that the use of a breast tumor board reduced diagnosis-treatment time from 42 days to 30 days, corresponding with a greater percentage of curative therapies and greater patient satisfaction with the level of their care.[20] Coory et al. also saw similar decreases with a lung TB.[10] Despite this, it should be noted that not all studies have shown decreases in diagnosis-treatment times. However, this indicator still provides a valuable measurement tool to measure the effect of TBs on physician assuredness. As TBs are implemented, diagnosis-treatment times should continue to drop until reaching a threshold level. Through measurement of diagnosis-treatment times, assuredness of physicians (in their management plans) and treatment expediency can be measured.

"Before-and-After" Changes in Diagnosis and Treatment/Management

Before-and-after metrics are the most frequently used indicators to measure the effectiveness of TBs. This involves comparing the pre-TB diagnosis, prognosis, and treatment administered by the covering physician with recommendations that were provided by consensus at the TB. The previous section outlined multiple studies using "before-and-after" indicators, with each tumor board experiencing varying levels of success in regards to changes in diagnosis and/or treatment plan. Thus, with an effective tumor board, we would initially expect to see a high rate of change for diagnosis and treatment.

One of the main issues surrounding the use of before-and-after metrics to evaluate TB effectiveness (especially when they are used alone) is the confounding variables and biases that are inherent in the use of such indicators. As mentioned by Lamb, studies using before-and-after measures alone do not assess whether the changes in diagnosis and treatment plan actually improve the quality of cancer care. Inherent in this issue is the fact that the before-and-after metric does not place any weight on the use of peer-reviewed treatment protocols.[33] For example, changing from a frontline peer-reviewed treatment protocol to a less effective, non-reviewed protocol is still viewed as a "before-and-after" change, despite the fact that the efficacy may actually be lower. Abdulrahman Jr. mentions this flaw, stating that the overall weakness of the before-and-after metrics does not control for confounding variables.[1] This weakness does detract from the validity of before-and-after metrics; however, these indicators are still useful (when used in conjunction with other indicators) in measuring how ITBs change the clinical reasoning and treatment planning of physicians. This can be seen by comparing before-and-after rates from immediately after ITB implementation to those long after implementation; over this time, before-and-after rates should steadily decrease, showing that physicians of the resource-constrained hospital have a better grasp of the most efficacious therapies (given in a resource-sensitive manner) and are utilizing these therapies before they are suggested in the ITB setting.

Qualitative Indicators

A number of recent studies have used qualitative indicators to measure constructs including physician education, improved care, and improved communication between members of care team. Indicators such as rational for treatment discordance (discussed later), training/specialization of attendees, patient satisfaction, clinician's perception of educational benefit, attendee's perception of TB case load (too many or too few), case selection process, and attendee satisfaction, have been used to provide a qualitative aspect to TB assessment.[9, 14, 20, 40] While these indicators should not be used alone, their use in conjunction with qualitative measures can provide the reasoning as to why certain results occur.

Implications in Low-Resource Settings

The above section has outlined the current TB impact evaluation indicators and proposed a plan for moving forward with TB analysis. The remainder of this discussion will serve as a discussion ground for the use of TBs in a low-resource setting, as well as how the analysis of such TBs would differ from other TBs.

TUMOR BOARDS ON AN INTERNATIONAL FRONT

As stated before, the principle reason for the creation of tumor boards is to enhance the quality of cancer care and post-graduate education, both through case reviews and literature-based teaching. If effective in these objectives, tumor boards would lower the mortality and morbidity of cancer as well as create ad-hoc guidelines for care (or improve physician knowledge of care guidelines if they already exist). To this end, the use of tumor boards could be extended to an international context, allowing for international case consultation as well as a learning experience enhanced by the variety of case presentations from clinicians working in multiple contexts; through international tumor boards, the scope of cancer care improvements moves from a domestic realm to a global one.[24] This approach would be especially effective in low- and middle-income countries due to their relative lack of specialists, insufficiency of post-graduate training, and dearth of spending on non-communicable diseases.[5, 14. 15] International tumor boards (ITBs) would allow participants to collaborate with and advise each other, resources they would not have access to otherwise. Additionally, international TBs could provide physicians and care-providers with exposure to regionally rare diseases and thus, enhance their knowledge about cancers common in other countries but rarely seen domestically. For example, tumor boards could be used to educate European physicians and nurses on care of Kaposi's sarcoma (seen predominantly in Central and Southern Africa), or to educate Japanese doctors on prostate cancer (seen infrequently in East Asia).[42] Additionally, the use of tumor boards could contribute to the standardization and improvement of

resource-sensitive treatment plans for low- and middle-income countries.[15] In this sense, TBs provide a great avenue for collaboration and improvement of care on an international scale; this point is even more relevant when partnering teams from developed nations to those of the undeveloped world (low- and middle-income countries).

Benefits of ITBs

The major benefits of ITBs are listed in Table 6. As outlined by Eniu, international tumor boards help to outline alternative therapies to a given cancer based on the resources available to low- and middle-income countries (LMCs).[15] Frontline therapies are often not available in these settings as a result of high drug costs, lack of trained specialists, and inaccessibility of advanced facilities and/or therapeutic machines (Ex. Radiation therapy, Immunohistochemistry).[15] Through the use of international tumor boards to discuss resource-sensitive alternative cancer therapies in addition to mentioning frontline therapies, these conferences allow for a sustainable and cost-effective avenue of improving care in LMCs. These alternative therapies can then be compiled into a set of treatment protocols based on the resources of the hospital. This can serve as a stop-gap solution for the short or long term until the government of the LMC is able to allocate more money to cancer therapeutics, training clinicians, and other resource-related issues.[15] This teaching capacity can be further extended via recording of the ITBs, both in terms of the audio/video feeds as well as the slides presented.[24]

Anderson mentions that through the training experience gained via ITBs, LMCs can avoid the "brain drain" that occurs through trainees leaving the country in order to get advanced training. To this end, he mentions a program between Ghana and Norway aimed at improving surgical cancer treatment while limiting the travel costs for Ghanaian surgeons. Through such programs involving further training of trainees and junior physicians, younger physicians may find domestic opportunities more attractive than before, thus reducing the effect of the "brain drain".[5]

One of the potential pitfalls in developing international tumor boards with hospitals of LMCs is that a large number of these hospitals will lack the treatment technology and/or communication technology to make these tumor boards effective. In addition to having difficult obtaining use of radiation therapy or immunohistochemistry or appropriate specialists, hospitals may have issues gaining access to stable internet sources, cameras, or microphones needed for a TB. In order to limit and possibly prevent these issues from arising, hospitals can develop partnerships with local hospitals in order to work together to gather the needed resources. These partnerships, when formalized and structured, can lead to more productive inter-hospital collaboration, greater capacity on both sides, and further expand the scope of a TB with a hospital from a developed nation. *However, it should be noted that such inter-hospital partnerships could cause dependency and become unsustainable.* However, it should be noted that such partnerships should not serve to provide resource-limited hospitals with clinical tools (diagnostics, therapeutics, etc.), seeing as this practice is highly unsustainable in the long-term.

Partnerships should only serve to enhance the communication technology for resource-constrained hospitals, allowing them to engage in twinning partnerships that are more sustainable in the long-term.

Table 6: Benefits of ITBs Between Resource-limited and Resource-rich Clinicians:

1. Production of resource-sensitive guidelines for resource-limited settings
2. Development of protocols/algorithms for optimizing care efficacy
3. Mitigating the effects of clinician shortages ("brain-drain")
4. Informal method to improve training of care-providers
5. Gain communication technology to allow for partnerships

Barriers to international use

Multiple issues must be dealt with before an international tumor board can get off the ground, despite initial interest in collaboration from both sides.

The first issue is that a method of communication must be usable on both sides. This involves both language barriers between teams as well as technological issues. As for language barriers, use of an interpreter/translator is discouraged as it could cause further separation and alienation of teams, preventing group cohesion and participation. Additionally, use of interpreters limits time efficiency, making tumor boards more time consuming than needed. Thus, it is recommended that tumor boards be held in a language that is common to both teams where possible. When no common language exists, an accredited interpreter with knowledge of medical

terminology should be used as an intermediary. Regarding the technological barriers that may come up, protocols should be created beforehand to determine trouble-shooting procedures. When possible, one member of each team should attempt to set up a stable connection (audio, visual, etc.) 30-60 minutes before the start of the TB. This step will allow time to fix any glitches or issues that come up with minimal delay to the TB. Ideal conditions would entail a stable internet connection allowing for a consistent audio and video connection (for sharing of slide presentations, radiology images, and pathology slides). However, in order to troubleshoot faulty internet connections, alternative solutions with lower bandwidth requirements should be pursued. This may entail using alternate web-conferencing clients, using an audio-only connection, or even using telephone service to hold tumor boards. Another viable alternative may include utilizing the technological equipment at a nearby facility to get a better connection for the ITB.

The second large issue is the presentation of material, specifically involving technology and its use to broadcast images. While domestic tumor boards can be conducted in person, the long-distance nature of international tumor boards necessitates the use of internet-based presentation techniques. Thus, tumor board organizers need to find a presentation medium or application that best supports the needs of the tumor boards; specifically, the medium selected should allow clear oral communications without any time lag, as well as a method for either presenting slide presentations or uploading images (this becomes crucial with pathology and cytology slides as well as x-rays and other imaging). Thus, the minimum requirements for a

presentation client are that both sides can view the slide presentation and engage in oral communication. Communication platforms on which images for an ITB can be hosted are listed in Table 7. While video transmission is ideal so that the members of each team can see each other (has potential to enhance collaboration), this is not necessary for the function of the tumor board. In order to fulfill the requirement of basic image projection, both sides will need a video projector connected to a computer (if the ITB is to be viewed by large groups), and a microphone. This solution is ideal when poor internet connectivity forces the ITB to occur via telephone. If slide presentations are not viewable on one side, this issue can be circumvented by finding a web-based client that supports screen-sharing, allowing one side to look at the presentation via the screen of the other team (although this would require a stable internet connection). If a video feed is also possible, each side will need a camera to establish this.

Table 7: Presentation of Images During ITBs

Method	Description	Advantages	Disadvantages
Video Transmission	Teams switch between viewing each other and the slides	Allows teams to see each other	Requires large bandwidth, lags and crashes, requires multiple cameras
Separate Transmission	Teams have no visual connection, and advance through a slide presentation separately	Works in low bandwidth, no hardware required (telephone), simple to transfer slide presentations	Teams not able to form visual connections, teams may be on different slides without knowing
Screen-sharing	One team projects their computer screen to the other while going through a presentation	Free, easy to install software, ensures teams view same slide, less bandwidth than video	No visual relationship between teams, can be high bandwidth, may lag

In addition to these problems (listed in Table 8), the problems of deploying a domestic TB in a developed nation also apply here, including variability between physicians/hospitals and delayed treatment start times. Additional problems also exist in cancer care as it pertains to TBs, including issues with drug availability, palliation, improper technique, lack of treatment technology, and lack of follow-up. These issues will be discussed later sections.

Table 8: Barriers to ITBs Between Resource-poor and Resource-rich Physicians:

1. Language of communication must be consistent (ideally without interpreters)
2. Technological resources on both sides should be able to support auditory communication
3. Technological resources on both sides should allow for sharing of pathology, radiology, and other types of images
4. A stable internet connection is not necessary, but is supremely helpful in facilitating collaboration

Current State of ITBs

Given the relative dearth of published journal articles and data-based analysis on TBs, there is an even smaller amount of knowledge on ITBs. The need for ITBs is apparent in LMCs, especially given the aforementioned shortcomings of healthcare systems in these countries. These shortcomings include a dearth of specialists,

increasing cancer incidence rates, late-stage patient presentation, low levels of post-graduate training, poorly executed diagnostic testing, poor drug availability, and little collaboration between hospitals[3, 5, 14, 17] The presence of a partnership with a high resource hospital via a TB could help to partially or fully mitigate the effects of each of these issues. However, many barriers exist to the development and effectiveness of TBs, including lack of accessibility, irregular meeting times, lack of pathologists (described by El Saghir as 25% of hospitals in Arab countries), poor attendance due to lack of attending physicians, lack of availability of pathology diagnostics, "brain-drain" of physicians, late-stage presentation of patients, weak healthcare infrastructure, and poor availability and/or accessibility of drugs and other treatment modalities.[5, 13, 14, 15, 52] El Saghir et al. note that, "Most low-resource countries lack the necessary health care system infrastructure to support multidisciplinary breast cancer care", a statement that rings true across all types of neoplastic disease.[14] These issues will be further discussed in a later section.

Some groups have attempted to set up international tumor boards, including the University of Minnesota-Poria Govt. Hospital partnership and the D-43 (Kenya-West Virginia University/ Ohio State University/ SUNY Upstate) partnership. While these groups have not yet disclosed any data or information on patient outcomes, the existence of these partnerships is promising for the development of ITBs. Other examples of international tumor boards do exist, such as the one mentioned by Adam et al.[2] This international tumor board consists of a panel of experts creating a generalized protocol for treatment of this cancer. As such, it does not apply to the

definition of ITB set out by this paper given that it does not focus on case-based discussions to improve care quality and post-graduate training at an LMC-based hospital. Thus, international tumor boards of the type discussed here (ITBs) are scarce and the data produced from them is virtually non-existent in peer-reviewed journals at this stage.

BARRIERS TO CANCER TREATMENT IN DEVELOPING COUNTRIES AND THIER EFFECT ON ITB INDICATORS

Intro

The following section will outline the barriers to cancer care that exist in developing countries as well as outline a methodology for either circumventing these issues or accounting for them in the impact evaluation of an ITB. The development of more advanced and effective cancer therapeutics has come along in leaps and bounds over the last 40 years, with the development of care infrastructure, the use of multidisciplinary treatment teams, improved protocols, and support systems for families undergoing treatment.[17, 39] Correct implementation and use of these advances is a reasonable and easily-achievable goal in resource-rich areas; however, as pointed out by Ribeiro and Ching-Hon, this proposition becomes infinitely more difficult in resource-poor areas.[39] Many of the issues encountered in cancer care are based in the low access to technology and therapeutics, the underdevelopment of health care systems in developing countries, and the governmental priority (regarding funding) placed on infectious disease instead of non-communicable and chronic disease (including cancer). [5]

These root causes then manifest themselves in many ways in tertiary-level care centers, including few oncology training programs, lack of availability of current diagnostic and therapeutic methods, few tertiary-level healthcare centers at which patients can receive treatment, late-stage presentation of neoplasias (and thus, poor prognosis), lack of evidence-based understanding of how treatment protocols should

differ in developing nations, few medical graduates to assist the few properly-trained oncologists, overburdened systems that subsequently are unable to appropriately address issues of psychosocial and emotional care, etc. (Table 9).[5, 33] Moreover there are a number of factors that are wholly unrelated to the services provided by tertiary-level cancer care institutions, yet still affect the effectiveness of care. These include higher rates of smoking in the developing world, stigmatization surrounding cancer, lack of transport infrastructure to allow easy access to treatment centers, limited governmental funding for screening and prevention programs, poor financing schemes to support patients during their treatment, low quantity and quality of services provided by primary care physicians and community health workers, and the prevalence of HIV and HPV.[17] In combination, these external issues alter the perceived efficacy of any cancer intervention in the developing world, and should

Table 9: Problems Intrinsic to Tertiary-level Cancer Care Institutions in Developing Nations

1. Few oncology training programs
2. Unavailability of current diagnostic and therapeutic methods
3. Few tertiary-level healthcare centers
4. Lack of research on treatment protocols specific to developing nations
5. Late-stage presentation of cases
6. Few medical graduates to assist oncology-trained medical graduates
7. Lack of emphasis on psychosocial care during treatment

be accounted for in impact evaluations.

All of the above factors effectively function as confounding variables in the analysis of ITB effectiveness, underestimating the effects of the tumor boards due to factors that are extrinsic and external to the tumor board itself. Thus, the following section will discuss how the proposed indicators used in impact evaluations of ITBs are altered by the aforementioned factors.

Physician Concordance

As mentioned before, concordance measures whether the physician delivers the treatment/management regimen that was suggested in the ITB. Ideally, this number would be at or near 100%, showing that physician always implemented the consensus suggestions from the tumor board. In studies based in developed nations, physician concordance from TBs is usually near 80%. A study by Blazeby recorded 85% for an Upper Gastrointestinal TB, El Saghir also noted 85% concordance across and Arabian Breast TB, while Schroeder saw a 78% concordance for an internet-based gynecological TB, and Strong reported 86% for and Upper Gastrointestinal TB.[7, 13, 40, 44]

However, physician concordance could drop significantly (and remain low after implementation) with ITBs if resource-sensitive recommendations are not provided. The relative lack of technology and appropriate therapeutics could create a low overall physician concordance. This becomes an even bigger issue with hospitals based in low-income countries, simply because they often do not have the national

healthcare infrastructure to attain many of the current treatment modalities. This could entail not having a trained specialist to perform a treatment (ex. No oncologic surgeons in the entire nation), not having the appropriate materials to deliver a treatment (ex. No equipment to deliver radiation therapy), or both.

These types of issues should be avoided based on the aforementioned use of resource-sensitive guidelines in ITBs. By providing the resource-rich physicians with a list of treatments available to the resource-poor physicians as well as prompting them to adopt a collaborative attitude, physicians at ITBs could discuss both the frontline-therapy as well as a resource-sensitive treatment plan tailored to the materials of the resource-poor physicians.

When outside issues cause physicians into a state of non-concordance with the TB consensus, the rationale for such action should be recorded. For example, if a drug supply chain issue caused a stock-out of the consensus therapy drug, the physician would be forced into discordance with the tumor board consensus; the lack of concordance, as well its causation by the drug stock-out, should be reported. Schroeder et al. took this additional step in their analysis, leading them to the conclusion that while they had only 78% concordance, much of the discordance was due to patient deterioration and subsequent modification of treatment, as shown by 98% partial concordance of their physicians (showing that discordance was not due to lack of available resources).[40] Moreover, Strong et al. qualified their observed 86% physician concordance by noting that 10% of the overall patient load (71% of the discordant cases) occurred due to patient decompensation.[44] While the two

aforementioned studies stated decompensation as the main reason for physician discordance, it is possible that issues external to the clinician will have a similar or greater effect in causing physician discordance in the developing world. Thus, recording the rationale behind physician discord allows for a qualitative assessment of the barriers to care within that specific setting.

Tumor Relapse Rate

The utility of measuring tumor relapse rate, as mentioned before, is to produce a greater amount of evidence regarding what treatments and therapies are the most effective. When applied to the context of developing nations, this indicator becomes even more important given the variation in demographic characteristics and risk factors of developing country constituents. Ribeiro and Ching-Hon touch on this concept in mentioning that more information on resource-poor contexts is needed due to variation in genetic and environmental factors that may play a role in the pathogenesis of cancer (and thus, affect treatment and prognosis).[39] Farmer et al. make a more specific notation of such factors, including the higher rates of smoking in developing countries, the stigma associated with cancer, poor screening and prevention programs (causing late-stage presentation), higher incidence of HIV and HPV, etc.[17] Additionally, Ribeiro et al. demonstrate that treatment abandonment rates are much higher in the developing world, resulting in higher relapse rates.[39] As a result of the aforementioned factors, whose influence is not altered by ITBs, tumor relapse rates will likely remain higher in developing countries than in developed countries. The implementation of ITBs, as well as any other cancer-targeting

intervention, is expected to lower the tumor relapse rate through suggesting treatment protocols whose efficacy has been demonstrated in peer-reviewed literature; however, it is unknown whether any given intervention would lower tumor relapse rates to the levels seen in the developing world, where frontline therapeutics are readily available and external conditions are ideal for minimizing the recurrence of tumors.

On the theme of monitoring relapse rates, Ribeiro states, "With the introduction of intensive, protocol-based chemotherapy…the relapse rate has decreased markedly, and the rate of treatment abandonment has decreased from 16% to less than 1%. The use of more aggressive therapy has resulted in more deaths from infection and hemorrhage, but refinements in patient care have begun to ameliorate these complications. The most recent analysis of event-free survival shows rates similar to those in some highly developed countries." Based on this commentary, we can expect relapse rates to initially start at a high level, but drop down to levels nearing those of the developed world once the ITB has been completely and effectively implemented. However, it should be noted that this cannot occur without an improvement in clinical management of patients as they receive these therapies.

Toxicity-based Death Rate/ Operative Mortality

As shown by the St. Jude Children's- Recife Hospital twinning partnership (includes an ITB as well as other programs) described by Ribeiro and Ching-Hon, it should be expected that toxicity-related deaths would initially be high (in the initial phases of ITB implementation), but would decrease over time as a result of greater use of literature-proven treatment protocols. Not only does this reflect better use of

therapeutics, but also better management of patients as they receive chemotherapy and radiation therapy. Operative mortality, given that it serves to measure the harm done by surgical intervention, provides the same function as toxicity-based mortality for a different set of therapies. However, the operative morality data of developing nations may never reach the same levels as developed nations, simply because of the late-stage presentation that exists in the developing world, unless stratified by stage at presentation (causes include stigma, poor screening and prevention programs, etc.) and the subsequent need for more radical surgical intervention. Moreover, the lack of available treatment resources further compounds this issue and leaves the resource-poor nations behind the developing world in operative mortality.

Long-term Survival

From a survival point of view, we should expect that all datasets collected from resource-poor settings and/or low-income countries will have lower survival percentages that datasets collected from resource-rich, high-income countries. This is a result of many different factors, including the higher quantity and quality of primary care and preventive care, better disease screening programs, a higher standard of living, better healthcare financing mechanisms, etc., in resource-rich settings.[17] It should also be noted that as a result of the much less extensive healthcare infrastructure existent in most low-income countries, the ability to track former patients for survival is much lower and thus, leads to a greater number of patients lost to follow-up.[5] For these reasons, survival percentages from the developing world

should never be compared to those from the developed world. However, we would expect long-term survival to be improved as a result of ITB implementation.

Long-term survival of patients treated at resource-poor hospitals should not necessarily be drastically different form patients treated at resource-rich hospitals. While the developing world does have an overall lower life expectancy and higher annual mortality rate, this may not necessarily become a large factor in altering the long-term survival of cancer patients. The reason for this, as mentioned by Welch et al., is the overall variability of patients used to calculate long-term survival.[48] This could lead to systematic error and thus, reduces the viability of this indicator as a stand-alone measure of ITB effectiveness. Still, given that it measures one of the constructs most heavily targeted by ITBs (life expectancy), it should still be measured and combined with other indicators to improve its validity.

Diagnosis-Treatment Time (Time from Diagnosis to Treatment Initiation)

As mentioned before, diagnosis-treatment time is used to measure the assuredness of the physician in the consensus treatment from the ITB. Diagnosis-treatment times would likely decrease as a result of ITB implementation, given that it provides clinicians with reassurance and reinforcement for their treatment plan. This is especially true for clinicians in LMCs, who may be less aware of current treatment guidelines.[3, 27, 52] Given that ITBs entail the provision of resource-sensitive guidelines to resource-poor hospitals, diagnosis-treatment times of developing-world hospitals would be expected to decrease until reaching those of developing-world hospitals. As discussed before, Jazieh has discussed the utility of this metric and

Gabel et al. showed that TBs can significantly reduce diagnosis-treatment time.[20, 28] Similar results regarding diagnosis-treatment time should be expected in evaluating ITB outcomes in developing countries.

"Before-and-After" Changes in Treatment/Management and Diagnosis

As mentioned before, while these currently-used indicators are not necessarily the most valid measures of effectiveness, their utility can be enhanced when combined with the other aforementioned indicators. Ideally, measuring the changes in diagnosis and treatment before and after an ITB would show the level to which improper and/or ineffective diagnoses and therapies have been corrected to those based in peer-reviewed literature. Thus, using these indicators in tandem with indicators tracking patient outcomes would allow investigation of whether higher percentages of "before-and-after" changes do in fact correlate to a better quality of care. Given that one of the main objectives of ITBs is to promote more effective and more common use of research-based resource-sensitive treatment protocols, it would be expected that the implementation of ITBs would causes the "before-and-after" metrics would reflect a high number of changes, especially in the initial phases of ITB implementation. As time progresses, these before-and-after numbers would be expected to drop as a result of the resource-poor physicians developing a better understanding of the most effective therapies available at their disposal.

As mentioned before, these metrics are confounded by the fact that a change in either diagnosis or treatment protocol, as measured by the before-and-after indicators, does not necessarily reflect an improvement in care. For this reason, it is

crucial that a) recommendations only be made based on peer-reviewed literature regarding cancer in low-resource settings (when possible), and b) data obtained on the outcomes of patients presented at ITBs be reviewed regularly to ensure that recommendations given by ITB physicians do in fact lead to better clinical outcomes.

INTERNATIONAL TUMOR BOARDS AS A SPRINGBOARD FOR FURTHER COLLABORATION

Rather than being a stand-alone intervention, ITBs should serve as the basis for the development of further projects allowing resource-rich and resource-poor hospitals to collaborate further. Such collaboration, mentioned by Ribeiro et al. as "twinning partnerships", can include trainee exchanges, teleconsultation services, and other interventions aimed at improving the quality of cancer care in resource-poor settings. Twinning partnerships have been shown to decrease the rate of negative events surrounding cancer care, including treatment abandonment, toxicity, and relapses in tumor development.[39] Such partnerships, which have been taking place at increasing rates over the last 10 years, allow hospitals to build momentum in improving the quality of care, jointly develop protocols with physicians of resource-rich hospitals, gain the aid of other physicians in managing their patients via consultation, develop cancer registries to understand the burden of cancer, and provide a rallying point for charity groups.[39] As such, the development of an ITB, especially after it has become fully and effectively implemented, can allow for additional interventions that work alongside the ITB to further increase patient outcomes.

Moreover, the development of ITBs can allow for greater research regarding the burden of disease in developing countries. As mentioned by Farmer et al., this continues to be a large barrier to effective care in resource-poor settings given that there is little understanding of which therapies are successful and which are not in

resource-poor settings.[17] Given that many developing countries differ from their developed counterparts in countless environmental factors as well as a number of genetic variables, more investigation needs to be done as to what the most effective treatments are in these settings.[15] This is seen not only through a variation in therapy effectiveness, but a variation in disease burden itself. The prevalence of certain cancers are much higher or lower in the developing world as compared to the developed world. For example, while penile cancers represent only 0.5% of the cancer burden in the US and Europe, it represents nearly 10% of all cancers in developing nations.[44] The drastic difference in frequency of penile cancer only further highlights the variability between the developed world and the developing world, and the subsequent need for more research regarding treatment efficacy in the developing world.

ITBs aid in initiating research on cancer in the context of the developing world by a) providing a discussion ground on which doctors can further discuss the variability between resource-rich and resource-poor contexts, b) developing a running list of patients presented at ITBs alongside the diagnoses and therapies they received, and c) facilitating the development of twinning partnerships in which cancer registries including the (clinical therapy received) are created. Through each of these pathways, more information will come to light regarding the variability of cancer treatment efficacy as it differs by context, further allowing for improved cancer care in resource-poor settings.

CONCLUSION

Tumor boards have gained momentum over the last 20 years, as shown by the increased implementation of TBs on a global scale and the 1995 Calman-Hine ruling. However, their use in a twinning partnership between hospitals of the developed and developing world is a relatively new notion, demonstrated by the relative lack of peer-reviewed literature on the topic. While a handful of initiatives have sprouted up in recent years, data collection has not been initiated. Given that domestic tumor boards have such poor evaluation metrics, new indicators of effectiveness need to be developed. This paper serves to outline several metrics that should be used to measure TB effectiveness (international or otherwise), as well as to discuss how the barriers existent in low-resource settings would affect these indicators. Throughout this discussion, one apparent theme is that no single indicator is sufficient to measure TB impact, and as such, multiple metrics need to be used in unison to gain a much deeper perspective into the true effect of TBs and ITBs. Moreover, ITBs themselves should not exist in unison, but as the initial foundation for further collaboration between hospitals. The development of "twinning" partnerships between hospitals can allow for further development of multiple aspects of care and improve the quality of services the patient receives.

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VITA

JASON A. SREEDHAR

Address: 30 Rutland St., Apt 8
Boston, MA 02118

Email: jason.sreedhar@gmail.com

Year of birth: 1990

Education: University of California Berkeley
B. S. Microbial Biology, May 2012

Boston University School of Medicine, Boston, MA
Candidate for M. A. Medical Science, May, 2014

Boston University School of Public Health, Boston, MA
Candidate for Masters in Public Health, May, 2014

Research Experience:

02/11 to 07/12 Ryan Lab
-University of California Berkeley
-Studied the role of Penicillin-Binding Proteins ("PBP1as", involved in peptidoglycan cell wall construction) in cell division of the model organism *C. crescentus*. This included cell biology techniques such as PCR, electrophoresis, gel extraction, and bacterial cloning.

06/09 to 08/09 Ward Lab
-Virginia Commonwealth University Health System (Richmond, VA)
-Assisted on studies of perfluorocarbon blood alternatives and developing hemostatic devices on both swine and rabbit models. Prepared the animals for trials, measured arterial blood gases, and assisted on laparotomies.

Medically Relevant Experiences

03/13 to present Global Oncology-Queen Elizabeth Central Hospital Initiative

-Boston, MA
-Development of hospital-twinning partnership
-Development and facilitation of international multidisciplinary cancer case conferences between physicians of Malawi and Boston
-Assistance in implementing a web-based physician consultation service between Boston and Malawi

01/10 to 03/11 Global Health Brigades
-Berkeley, CA as well as multiple sites in Honduras
-Brigade work: triaging patients, taking vitals, translating for doctors, explaining medication regimens, giving small lectures on public health measures
-Brigade planning: organizing fundraising events with third-party companies

07/07 to 01/13 Shadowing Physicians at VCU Health System
-Richmond, VA
-Shadowed physicians of many specialties
-Observed surgeries such as shunt revisions, craniotomies, and ventriculostomies

07/04 to 08/08 Summer Volunteer at VCU Health System
-Richmond, VA
-Spent 4 consecutive summers volunteering at a hospital
-Performed a number of different roles, including working in the child life department and facilitating patient-doctor interactions in the Pediatric ER.

Awards and Presentations

-Santander Universities Scholarship: March 2014
-Global Oncology Symposium 2014 Presentation: February 2014
-Sponsored Projects for Undergraduate Research Grant: Spring 2011, Spring 2012
- UC Berkeley Microbiology Student Group Symposium Research Presentation: 2012
-UC Berkeley SPUR Research Presentation: April 2012

Volunteer Work

05/14 to 07/14 Community Health Strategy Evaluator for the Kenyan Ministry of Public Health (Oloitokitok Sub-County)
-Based in Kimana, Kenya

-Created and conducted surveys to gather quantitative and qualitative information on health services in a southern Kenyan area
-Analyzed data to come up with a set of resource-sensitive recommendations for the Ministry of Public Health
-Presented findings to Ministry of Public Health officials as well as community members
-Received funding from the Santander Universities Scholarship

01/14 to 05/14 Implementation Consultant for Health Protection and Environmental Sanitation (HEPENS)
-Boston, MA; working for HEPENS (based in Cape Coast, Ghana)
-Produced a set of recommendations to improve human resources and staffing of HEPENS as they expand their projects
-Developed a data collection tool for an economic development initiative
-Created a phone app to track data obtained during health outreach

09/11 to 07/12 Student Advocate at East Bay Sanctuary Covenant
-Berkeley, CA
-Worked with immigrants to help them obtain asylum status, work permits, green cards, etc.
-Assisted clients in filling out paperwork, translated for lawyers, prepared clients for court dates, performed informal interviews

01/10 to 03/11 Global Public Health Brigades
-Berkeley, CA and multiple sites in Honduras
-Worked through an NGO to implement public health initiatives in rural Honduras
-Built outhouses, ventilated stoves, and concrete floors in homes

<u>Skills and Interests</u>

-Proficient in Microsoft Office, PowerPoint, Word, Excel
-Laboratory experience in a bacterial cell biology lab: PCR, electrophoresis, cell cultivation, plasmid generation, bacterial cloning
-Soccer, rock climbing, running, reading