

Clinicians' and patients' perspectives on incidentally  
discovered silent brain infarction

A thesis submitted by

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in partial fulfillment of the requirements for the degree of

Master of Science

in

Clinical and Translational Science

Tufts University  
Sackler School of Graduate Biomedical Sciences

May 2017

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## **ABSTRACT**

Silent brain infarction (SBI) is a common condition found incidentally on neuroimaging studies obtained for other indications. SBI increases risk for symptomatic stroke and dementia. However, despite decades of research on risk factors and outcomes, there is no clear direction regarding optimal treatment or screening practices for SBI. Currently, in the absence of evidence-based screening, the only clinically relevant scenario is when SBI is discovered incidentally in the setting of routine clinical care. To better define this condition and inform future treatment studies, we sought to explore the perspectives of clinicians and patients with incidentally discovered SBI.

We performed semi-structured qualitative interviews of patients identified with SBI and clinicians who encounter patients with SBI in routine clinical practice. We used purposeful sampling to attain diversity in the clinician and patient characteristics.

Interviews were audio-recorded, transcribed, and analyzed using a constant comparative method to sort emergent themes into a logical coding schema (codebook) and modify the interview guide to explore new themes.

Fifteen clinicians and twelve patients were interviewed. The primary themes in the clinician study were uncertainty about SBI and clinical decision making in response to uncertainty. Clinicians from different specialties endorsed variable consistency in disclosing the neuroimaging findings to patients and different levels of aggressiveness in their approach to managing SBI. Although not universal, clinicians from all specialties endorsed a belief in equivalent prognostic significance between SBI and symptomatic

stroke: “A stroke is a stroke.” Most clinician participants described a willingness to modify clinical practices in response to comparative effectiveness studies, and many had concerns about the feasibility of randomized controlled trials. The primary themes in the patient study were patients’ beliefs in the equivalence of SBI and symptomatic stroke and discrepancies between patients’ and clinicians’ certainty about the significance of SBI. Most patient participants did not distinguish between SBI and symptomatic stroke, viewed SBI as grave, and expressed high levels of distress despite ambiguous messages from clinicians. Many viewed SBI as a “wakeup call,” motivating behavioral changes to improve health. In response to clinicians’ uncertainty, many interpreted ambiguous messages in a catastrophic way.

Incidentally discovered SBI is an unstudied form of an understudied condition, likely with important health consequences. Among clinicians, there remain several areas of uncertainty—diagnostic, prognostic, and therapeutic—that may influence the development of treatment studies for incidentally discovered SBI and the adoption of clinical practice guidelines. Patients with incidentally discovered SBI express fear and concern about the condition, equating its significance with symptomatic stroke. Both clinicians and patients expressed beliefs, attitudes, and preferences that can inform the development of future studies of this condition.

## **ACKNOWLEDGMENTS**

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David M. Kent, MD, MSc

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David E. Thaler, MD, PhD

Robin Ruthazer, MS

CTS program instructors whose guidance contributed to this work:

Jessica Paulus, ScD

Karen Freund, MD, MPH

Amy LeClair, PhD

Robert Goldberg, PhD

Many thanks to my research team including Chrissy Lundquist, MPH, and Gene Weinstein, MD.

Many thanks to the patients and clinicians who participated and shared their perspectives in the studies.

And special thanks to Miya Bernson-Leung, MD, for supporting me in pursuing this path.

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## **LIST OF ABBREVIATIONS**

AHA/ASA = American Heart Association/American Stroke Association

CER = comparative effectiveness research

CT = computed tomography

MI = myocardial infarction

MRI = magnetic resonance imaging

RCT = randomized controlled trial

SBI = silent brain infarction



## INTRODUCTION

Stroke is one of the leading causes of long term disability and death worldwide.<sup>1</sup> This vascular disease of the brain and central nervous system causes neurologic symptoms, often leading to permanent loss of neurologic function that disable normal functions of the human body such as talking, seeing, eating, walking, or thinking. Stroke also leads to other complications including recurrent stroke and dementia (progressive cognitive decline). Clinicians, patients, and the general public usually think of the term “stroke” in reference to this overtly symptomatic version of the disease. However, there is slowly growing recognition of subclinical or “silent” variants of cerebrovascular diseases, including silent brain infarction (SBI), with less certainty regarding appropriate management strategies.<sup>2-4</sup> While there is an extensive literature describing the risk factors, outcomes, and treatments for symptomatic stroke as well as large randomized clinical trials and established clinical practice guidelines to inform the management of patients with symptomatic stroke, there is a relative paucity of evidence guiding the management of patients with SBI.

The most common form of stroke is ischemic stroke, also known as brain infarction: this occurs when a blood vessel supplying a region of the brain with oxygen and nutrients is obstructed, preventing the flow of blood to that region. This can occur through a variety of pathological mechanisms including thrombosis (the development of a blood clot at the site of obstruction), embolism (the development of a blood clot elsewhere in the body that travels with the natural currents of blood flow to the site of obstruction), constriction

or spasm (narrowing of a blood vessel lumen as a result of contraction of the muscles within the walls of a blood vessel or a similar mechanism), dissection (a tear in the wall of a blood vessel that separates the layers, creating a flap that disrupts blood flow in the lumen), or hypoperfusion (loss of blood flow to part of the brain resulting from an impairment of antegrade flow of blood). Like myocardial infarction (MI), ischemic stroke is associated with a variety of risk factors that affect blood vessels including hypertension (high blood pressure), hypercholesterolemia (high blood cholesterol), diabetes mellitus (elevated blood sugar), tobacco use, atrial fibrillation (an abnormal heart rhythm), and more. These mechanisms and risk factors for ischemic stroke have also been associated with SBI in several prior epidemiological studies over two decades, although some associations with risk factors vary in strength between ischemic stroke and SBI.<sup>5-37</sup> Like ischemic stroke, SBI has also been shown to increase the risk of subsequent symptomatic stroke and dementia: specifically, SBI increases the risk for both conditions by two-to-three fold in prospective cohort studies of older adults with screening neuroimaging studies.<sup>38-45</sup>

However, unlike symptomatic stroke, SBI is detected on neuroimaging studies (head computed tomography scans, CT, or brain magnetic resonance imaging studies, MRI) without overt symptoms or neurologic deficits referable to the identified brain lesion.<sup>46</sup> By contrast, most patients with neurologic diseases that present to medical attention are identified when they develop neurologic symptoms. SBI is usually detected in one of two scenarios: on screening neuroimaging scans in observational studies or clinical trials, or as incidental findings discovered in routine clinical care. Currently, screening for SBI is

neither recommended nor evidence-based, so incidental discovery of SBI is the only scenario that presently has relevance to clinical practice. The exact incidence and prevalence of incidentally discovered SBI is not certain, but it may be quite common given the frequency of SBI detected in large, prospective cohort studies of older adults.<sup>2-4</sup> Comparing across cohort studies of screened populations with varying degrees of medical comorbidities, the overall prevalence of SBI is 20% in adults over age 50.<sup>2-4</sup> In one study, the annual incidence of SBI was estimated to be 11-fold greater than for symptomatic brain infarction.<sup>47</sup>

If incidentally discovered SBI is similarly or even more common than SBI in screened populations and also is associated with an increased risk of subsequent stroke and dementia, the detection of this form of SBI offers a unique opportunity for improving population health. The benefit in preventing future symptomatic stroke is apparent: detection of an asymptomatic variant of infarction followed by initiation of prevention measures is preferable to initiation of secondary prevention measures after a symptomatic stroke has already led to permanent disability. However, prevention strategies after detection of incidentally discovered SBI have not been studied: to date, there are no clinical trials or observational studies describing the benefit of medications, testing, lifestyle modification, or other measures for patients with incidentally discovered SBI. There may be several barriers to the development of prevention studies including limited recognition of the clinical significance of SBI by practicing clinicians, uncertainty regarding the prognostic significance of incidentally discovered SBI compared to SBI detected in screened populations, inconsistent reporting of SBI by radiologists for

neuroimaging studies, and uncertainty regarding optimal methods of studying treatment benefit (i.e. comparative effectiveness studies or randomized clinical trials).

Currently, there are no widely recommended or evidence-based screening strategies or prevention therapies for dementia, especially in the early stages of disease when interventions might have the greatest impact on reducing long term disability. Dementia, a group of conditions leading to progressive loss of cognitive functions through gradual destruction of brain infrastructure, has several etiologies and variable presenting symptoms, but the majority progress to a final stage that is refractory to any treatments aimed at alleviating symptoms. Thus far, there are no treatments that truly reverse the course of any form of dementia. Accordingly, developing strategies for early detection and prevention are very high priorities for population health. There is a growing body of evidence establishing the role of cerebrovascular diseases and vascular risk factors in the development of both vascular and Alzheimer's dementia, two of the most common forms of this disease.<sup>48-51</sup> Accordingly, given the increased risk for dementia following SBI, it is possible that the incidental discovery of SBI may provide an opportunity to intervene during the early stages of development of dementias with contributions from cerebrovascular disease.

In the absence of studies guiding the management of patients with SBI, the American Heart Association/American Stroke Association (AHA/ASA) established consensus definitions for silent cerebrovascular diseases (including SBI) and released a scientific statement that highlighted current knowledge gaps.<sup>52-53</sup> The scientific statement also

offered the opinions of an expert panel on the significance of SBI as well as a cautious recommendation to implement strategies proven for primary prevention of ischemic stroke when clinicians encounter patients with SBI. Guideline recommendations for primary prevention of stroke, the prevention of ischemic stroke before one occurs, are markedly different from guideline recommendations for secondary prevention of stroke after an index stroke has already occurred.<sup>54-55</sup> Specifically, secondary prevention measures are more aggressive with regards to blood pressure and cholesterol goals, initiating antithrombotic medications (anti-clotting), initiating statins (anticholesterol medications), and ordering diagnostic studies. Besides potentially having an impact on individual patients and the practices of individual clinicians, the potential differences in strategies following incidental discovery of SBI could significantly influence costs of care, access to specialists and testing, and the approaches of the medical field toward asymptomatic or subclinical conditions.

With this background, our primary aim with these studies was to explore the perspectives of clinicians and patients regarding incidentally discovered SBI. Despite two decades of research on risk factors and outcomes of SBI, there appears to be a lack of forwards progress in pursuing treatment studies, likely in part due to a lack of stakeholder engagement and understanding of the perspectives of practicing clinicians and patients with SBI. Many questions have not been answered by prior research: Do clinicians acknowledge SBI as a distinct entity? How do patients respond when informed of the presence of SBI on their brain scans? Do clinicians perceive SBI to be important? Do patients make distinctions between ischemic stroke and SBI? Do clinicians discuss

incidentally discovered SBI with their patients? Do clinicians and patients believe SBI is actionable? Are patients motivated to change their behaviors in response to SBI? What are the major areas of uncertainty that need to be addressed in future studies? What types of studies are likely to influence the practices of clinicians who encounter patients with incidentally discovered SBI? These questions are not well addressed by quantitative methods, so we pursued two qualitative studies using semi-structured interviews to explore the beliefs, attitudes, and clinical practices of clinicians who provide care for patients with SBI and the responses, beliefs, and needs of patients diagnosed with SBI.

## Chapter 2

### **Clinicians' perspectives on incidentally discovered silent brain infarction – a qualitative study<sup>1</sup>**

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<sup>1</sup>Leung LY, Han PK, Lundquist C, Weinstein G, Thaler DE, and Kent DM. Submitted to *Circ Cardiovasc Qual Outcomes*, 3/1/2017.

## **ABSTRACT**

**Background:** Silent brain infarction (SBI) is an insidious condition that increases risk for symptomatic stroke and dementia, but optimal management strategies have not been established. This study explored perspectives of clinicians regarding their approaches to SBI discovered incidentally in routine care.

**Methods and Results:** This study used semi-structured qualitative interviews of practicing clinicians. Purposeful sampling was employed to achieve participant diversity. Interviews were audio recorded, transcribed, and analyzed. A constant comparative method was used to organize emergent themes within a logical coding schema, and to modify the interview guide to examine new themes. A total of 15 clinicians (seven internists, four general neurologists, and four vascular neurologists) were interviewed. Emergent themes fell into two categories: 1) uncertainty about SBI, and 2) clinical decision making in response to uncertainty. All clinicians reported uncertainty about SBI in at least one clinical domain—diagnostic, prognostic, or therapeutic. However, responses to these uncertainties varied. While most vascular neurologists endorsed treating SBI like symptomatic stroke, internists and general neurologists were more variable in their recommendations and in their disclosure of neuroimaging findings to patients. Regarding treatment studies, all internists indicated that they would consider changing their practices in response to observational comparative effectiveness research (CER), whereas half of the neurologists expressed reluctance to modify their practices based on non-randomized studies. Several clinicians expressed concerns about the feasibility of conducting clinical trials, including concerns about whether clinical equipoise is present



(i.e. whether one can ethically withhold treatments shown to be effective in secondary stroke prevention from patients with SBI).

Conclusions: Incidentally discovered SBI is an understudied clinical entity and a focus of substantial uncertainty for clinicians, leading to a wide variety of clinical practices. Most clinicians expressed willingness to incorporate data from observational CER into their future practices and also raised concerns about feasibility of RCTs.

## INTRODUCTION

Silent brain infarction (SBI) is a common, insidious condition with clinically important consequences, but optimal strategies for detection, evaluation, and treatment have not been established. SBIs occur without overt symptoms or the awareness of patients and their clinicians. In neuroimaging-screened cohorts, SBIs are associated with a two-to-three fold increased risk of symptomatic brain infarction and dementia, independent of vascular risk factors.<sup>1-4</sup> SBIs are also more common than ischemic stroke: for U.S. adults over age 50, the estimated prevalence of SBI is 20%, and the estimated annual incidence of SBI may be 11 fold greater than for symptomatic infarcts.<sup>5</sup> However, since screening is not a standard or evidence-based practice, SBI often go undetected, except when discovered incidentally on neuroimaging scans performed for other indications.

To guide future research on SBI, the American Heart Association/American Stroke Association (AHA/ASA) refined definitions for silent cerebrovascular disease in 2013 and released a scientific statement in 2016 highlighting potential harms following SBI, the lack of randomized clinical trial (RCT) data to guide treatment, the probable appropriateness of stroke primary prevention strategies following SBI, and the probable inappropriateness of population screening.<sup>6-7</sup> However, in the absence of screening, it is not clear how clinicians should approach incidentally discovered SBI, the only form of SBI that currently is relevant to patients and clinicians in routine clinical care. There are no studies describing current practices of clinicians encountering patients with incidentally discovered SBI or identifying factors that influence their decision making.

Furthermore, it is not known how clinicians in different specialties will incorporate future evidence from different types of treatment studies (i.e. observational comparative effectiveness research (CER) versus RCTs) into their clinical practices.

We sought to explore clinical practices and attitudes of internists and neurologists providing care for patients with incidentally discovered SBI to 1) better define the entity of incidentally discovered SBI from the clinicians' perspective, 2) identify areas of uncertainty that need to be addressed by future studies and guidelines, and 3) inform the design of future studies on the management of SBI to optimize dissemination and acceptance of study findings.

## **METHODS**

### **Study design, participants, and data collection**

This study used individual, semi-structured qualitative interviews of actively practicing internists, general neurologists, and vascular neurologists, the clinicians thought most likely to encounter patients with SBI and to initiate clinical practices (counseling, testing, treatment, referral) in response to SBI. Participants were recruited through direct contact following review of physician directories from academic and private practices in the greater Boston area. Purposeful selection was conducted to achieve diversity in sex, specialty, practice setting, and experience. A screening tool was used to assess participant characteristics and verify active clinical practice, exposure to patients with SBI, and non-

involvement in SBI research. Participants were also asked to provide an estimate of the average number of patients with SBI they encounter per year. Interviews were conducted by LYL and lasted 30-60 minutes. These were audio-recorded with participant consent and transcribed verbatim by a professional transcription service. Participants were provided \$50 Amazon gift cards as incentives.

### **Interview content**

The interview guide included open-ended questions and clarifying probes to explore several issues including clinicians' perceptions of the nature of SBI and risk of harm, current clinical practices, and approaches to new study findings regarding SBI.

Interviews were conducted in three phases, and the guide was modified between phases to further explore unanticipated, emergent themes.

### **Data analysis**

Line-by-line, software-assisted coding of anonymised interview transcripts was performed by two investigators (LYL, CL) using NVivo (V.11; QSR International, Melbourne, Australia). An initial codebook was developed by three investigators (LYL, PH, CL) through independent review and team-based reconciliation of the first two coded transcripts, using a "grounded theory" approach to categorize thematic content in a hierarchical, logically coherent conceptual schema with the overall goal of generating new theoretical insights.<sup>8-9</sup> The reconciled codebook was then used by two investigators

(LYL, CL) to code the remaining transcripts using a “constant comparative” method.<sup>10</sup>

The three investigators met at the end of each phase of interviews to discuss coding and recruitment decisions, resolve disagreements, and revise the interview guide and codebook.

## RESULTS

Interviews were conducted with 15 participants: seven internists, four general neurologists, and four vascular neurologists. No clinicians declined to be interviewed. A few participants were former or new clinical colleagues, but most had no prior contact with the interviewer and no prior knowledge of the perspectives of the research team. Participant characteristics are described as a group in Table 1.1. All specialties were represented in academic and community practices. Emergent themes fell into two main categories: 1) uncertainty about SBI, and 2) clinical decision making in response to uncertainty. *Uncertainty about SBI* focused on diagnostic, prognostic, and therapeutic uncertainties and the sources leading to these uncertainties (Table 1.2). *Clinical decision making in response to uncertainty* focused on clinical practice variation, evaluation of evidence from new studies, and anticipated translation of research into practice (Table 1.3). Scenarios in which clinicians incidentally discovered SBI are shown in Figure 1.1: clinicians most frequently described discovering SBI on neuroimaging obtained for symptoms not specific to stroke. Derived from these findings, a theoretical model illustrating clinical decision making in response to SBI is shown in Figure 1.2.

## **Uncertainty about SBI: Diagnostic**

### *The “silent” nature of SBI*

Most participants expressed uncertainty about the diagnosis of SBI. In the absence of overt symptoms, participants attempted to define SBI based on interpretation of the neuroimaging findings and patient characteristics that might increase the likelihood of the finding representing infarction (i.e. comorbid vascular risk factors). Some participants questioned whether SBIs were always truly “silent” or if they sometimes had clinical manifestations that were subtle or unrecognized—minimizing any purported distinction between SBI and symptomatic stroke. Several participants suggested that elderly or cognitively impaired individuals might have difficulty recognizing their neurologic deficits, or that low health literacy and low severity of symptoms might limit recognition of stroke as the cause of the symptoms. Neurologists had greater certainty in defining SBI, citing small size and location in subcortical or “non-eloquent” parts of the brain as the primary causes of clinical silence. Terminology used to describe SBI was variable: “silent stroke” and “asymptomatic stroke” were the most commonly used and were considered the most useful in communication with patients and other clinicians.

### *Relationship to white matter disease*

Many participants identified knowledge gaps in differentiating between SBI and white matter disease (WMD). Several suggested that both are on a spectrum where SBI is more

clinically significant and WMD is less clinically significant. Participants were generally less compelled to respond to WMD as aggressively as SBI or symptomatic stroke, but they cited a lack of published studies guiding this practice.

### *Causal uncertainty about SBI*

Most participants suggested that SBIs have similar mechanisms of infarction to symptomatic strokes, but they often described these assertions as hypotheses. Most suggested that SBIs probably occur through thrombotic mechanisms, whereas a few participants (primarily vascular neurologists) acknowledged that embolic mechanisms could cause SBI. Some participants suggested that the “case mix” of mechanisms might differ between SBI and symptomatic stroke. Eight participants across all specialties suggested that subtyping SBI by presumed mechanism was useful. One internist expressed skepticism regarding whether subtyping would change management of SBI.

### **Uncertainty about SBI: Prognostic**

#### *Risk of future stroke*

Despite several areas of uncertainty related to SBI, many participants expressed very strong beliefs regarding the pathophysiologic and prognostic equivalence of SBI and symptomatic stroke. For example, eight participants (two internists, three general neurologists, and three vascular neurologists) emphasized that “A stroke is a stroke.”

Most participants believed that the presence of SBI indicated an increased risk for symptomatic stroke.

However, some participants expressed uncertainty regarding the likelihood or severity of symptomatic stroke following SBI:

"I've not had anybody go on to have a massive stroke later that I can definitely say, 'Oh, they have had this chronic silent stroke before.'" (Internist 7)

#### *Risk of direct harm from a "silent" condition*

In contrast to beliefs about risk of stroke, internists and neurologists had different perspectives regarding the potential for direct harm caused by SBI. Internists generally expressed more uncertainty about specific potential health consequences beyond risk of subsequent stroke, whereas neurologists more readily identified cognitive decline as an important direct sequelae of SBI.

#### **Uncertainty about SBI: Therapeutic**

##### *Uncertainty in the approach to further evaluation*

While neurologists expressed greater certainty in defining and characterizing SBI, both internists and neurologists were uncertain about the optimal strategy for approaching SBI



with regards to further evaluation after initial detection. Most described “probable” steps they would take.

“Would I put someone on a Holter and look for afib for a silent stroke and then commit someone to a lifetime of warfarin because of a silent stroke? Those are things that I would do as part of a stroke workup. Would I do that for a silent stroke? I don’t know that I would. So, I think I might stop the workup.” (Internist 2)

“If you see somebody, do you need to admit them, how urgently? What kind of scans do you need? What kind of investigations do you need to pursue? A lot of these things are unknown.” (Vascular Neurologist 2)

Notably, four participants expressed strong opinions that there are different types of SBI that might warrant different approaches to testing and treatment.

“Treating everyone as if its thrombotic is probably inappropriate. If the proportion (thrombotic versus embolic) is different for silent versus non-silent, that might affect the clinical decision.” (Internist 3)

### **Sources of uncertainty**

Clinicians’ various uncertainties resulted from several sources.

*Limited awareness and dissemination of available evidence*

Despite the availability of dozens of studies on SBI published in peer-reviewed journals, many participants expressed a lack of awareness of any published studies providing insight on the frequency, risk factors, or outcomes of SBI.

“There are not very good prospective studies that I’m aware of that have looked at these patients. A lot of what I’m saying is based on my clinical experience... You don’t know what kind of neurological problems that they’ll have: what is the incidence of recurrence strokes, seizures, dementia-because it also would guide treatment priorities and how you counsel patients and caregivers.” (Vascular Neurologist 2)

In particular, internists and neurologists described different impressions regarding the frequency of SBI: internists generally assumed they were uncommon, and neurologists generally assumed they occur frequently.

Attesting to their lack of awareness of empirical evidence, all participants were surprised when informed of the estimated prevalence of SBI in screened cohorts of older adults in the U.S.

"Oh wow!"

"That's high."

"Wow!"

"I think that's a big number."

"So I think it tells you that this is a major area that still needs more work."

### *Lack of treatment studies and guidelines*

Participants described that a lack of available evidence or guidelines fostered uncertainty in managing patients with SBI. Several participants cited concerns about undertreatment.

“I’ve been doing the work-ups for symptomatic stroke. I’m not sure if I’m doing this the right way or am overdoing it, given that these are silent strokes. I’ve noticed that a lot of patients with these findings are not aware of them and they are not being informed by previous doctors, so I’m not sure whether we are undertreating these silent stroke patients.” (Internist 6)

### **Responses to diagnostic uncertainty**

#### *Influence of the “incidental” nature of SBI*

Despite often viewing SBI as equivalent in significance to symptomatic stroke, some participants described that their approach to SBI was shaped by the “incidental” nature of

their discovery. Two internists expressed beliefs that incidental findings in general should be ignored (unless there is a strong guideline recommendation to take action).

“In the case of silent stroke, more often than not I do nothing... In terms of other incidental findings, unless it’s a cancer risk, I tend to ignore them... I try to minimize the incidental findings as much as possible.” (Internist 1)

One general neurologist suggested that the incidental discovery of SBI could be harmful by leading to unnecessary screening.

“You asked about silent strokes causing harm, and I think about two things: one is similar to incidentally discovered pulmonary nodules. It can sometimes subject people to increased screening down the line...” (General Neurologist 1)

Others acknowledged that incidental findings could be clinically important (e.g. occult malignancy) or could sometimes represent opportunities to prevent related diseases.

“I equate them to silent MI (myocardial infarction), which is a similar concept: still an MI.” (Internist 3)

In some cases, the incidental nature did not generate the same sense of urgency as symptomatic stroke.

“For incidental findings, I will manage it in a non-urgent way. Instead of getting a full workup within a week, I feel like I can take time. The patient can come by and have a test done, one-by-one.” (Internist 6)

Some clinicians described no longer perceiving the SBI as “incidental” once the SBI was interpreted as warranting a response, emphasizing that the term connotes a lack of need for action.

“I might initially say they had an incidental stroke, but then eventually that will become something that is actually put in a different assessment. It becomes an assessment of its own that we have to work up... it goes from ‘incidental’ to all of sudden me, ‘clinically’ doing something about it.” (General Neurologist 2)

#### *Influence of neuroimaging interpretation by a radiologist*

Neurologists reviewed neuroimaging studies directly and generally were not substantially influenced by radiologist language, whereas internists only reviewed imaging reports and were dependent on the radiologist's certainty in determination of infarction. Internists cited that uncertainty or lack of specificity in the radiologists' terminology would influence their actions, making them less likely to respond to incidentally discovered SBI.

#### **Responses to prognostic uncertainty**

### *Obligation to take action upon discovering “incidental” SBI*

Participants had different views regarding their obligation to respond to SBI discovered in routine clinical care. Possibly due to their high levels of prognostic certainty and specialty focus, vascular neurologists uniformly felt obligated to respond aggressively to SBI despite substantial diagnostic and therapeutic uncertainty. Internists and general neurologists often described being more conservative in their approach, including some who felt no obligation to take action.

### *Disclosure to patients*

Two participants (internists with high prognostic uncertainty and less aggressive approaches to SBI) described difficulty in explaining SBI to their patients, fearing negative responses from the patients.

"It's just going to be hard for them to hear news from me and not view it as significant and it's hard for me to communicate, 'Oh, I found this thing but it doesn't matter.'" (Internist 1)

"I don't usually talk about small vessel ischemic disease because I feel like it's something that is not surprising. And to me, it's a little tough to talk to them about what that means." (Internist 5)

Several participants described their strategies for delivering the diagnosis to patients, emphasizing the opportunity for prevention of adverse health consequences.

"I would say to you, 'It looks like you had a stroke at some point in the past. And we need to make sure that another one doesn't happen. And we need to manage all of the issues, we need to treat you to prevent another one.'" (Internist 4)

Some participants also emphasized the perceived chronicity and size of the infarcts as a means of reassuring patients.

"There's nothing acutely going on in your brain right now, but there is a suggestion that maybe you've had disease before, but nothing that we need to acutely do right now." (Internist 7)

In this sample, most participants described usually or always reporting the finding of SBI.

"I always tell patients about any imaging findings, because if they don't hear from me... I'd rather have them have an intelligent guide through a report than have them sort of left in the lurch." (Vascular Neurologist 4)

### **Responses to therapeutic uncertainty**

*Specific strategies for responding to "incidental" SBI*

In the absence of treatment studies or guidelines, participants described several specific—and sometimes overlapping—strategies guiding their clinical practices. Four participants across all specialties described an approach tailored to the suspected mechanism of infarction. Twelve participants across all specialties described an emphasis on tailoring care to the individual patient, particularly with regards to age, infarct chronicity, and vascular risk profile. In particular, most internists and general neurologists emphasized vascular risk factor modification as their most consistent response to SBI. Nine participants across all specialties described similarities between their approach to SBI and the evaluation and management of symptomatic stroke.

"If it is a silent infarction that I see on a CT scan, I will probably do a full work up, just like how I treat a symptomatic stroke." (Internist 6)

"I don't think that silent versus symptomatic changes what type of tests I'm ordering." (Vascular Neurologist 4)

### *Etiologic testing*

Participants across all specialties described pursuing tests for stroke etiology investigations similar to those used for symptomatic stroke but with variable degrees of comprehensiveness.



### *Specialty referrals*

Participants expressed inconsistency in their referral practices, with internists sometimes referring to neurologists and general neurologists sometimes referring to vascular specialists. Referrals to other specialties included Cardiology, Endocrinology, Hematology, Nutrition, Rheumatology, Vascular Surgery, and the Emergency Department.

### *Lifestyle modification*

Almost all participants described using the discovery of SBI as an opportunity to counsel on lifestyle changes. Most focused on tobacco cessation, followed by exercise, diet, weight loss, and treatment compliance.

### *Medication management*

A majority of participants across all specialties described initiating or modifying treatments including antiplatelet medications, anticoagulants, anticholesterol medications, antihypertensives, and antiglycemic medications. Many of these treatments were extrapolated from guidelines for secondary prevention of ischemic stroke. Of these, antiplatelet medications and statins were the mostly commonly described.

### **Evaluation of evidence and translation into practice**

*Variable acceptance of evidence from new studies*

Participants differed by specialty regarding their willingness to change their clinical practices based on the findings of observational CER and RCTs. All internists expressed willingness to incorporate the findings of well-designed observational studies into their practices without requiring an RCT. Half of the general neurologists and half of the vascular neurologists cited the need for data from randomized studies to guide their practices.

In response to “Do you think a well-done, observational, comparative effectiveness study would be enough to convince you to change your practice?”:

"Yeah, I think it would affect my practice... It (an RCT) is always nice. But is it necessary? I know there are some people out there who feel unless they've been shown a randomized controlled trial, 'I don't believe the results.' I tend to be a little more flexible in my thinking, for better, for worse." (Internist 2)

“Definitely. Yes. Absolutely. I think I would still love to see a randomized trial, but I think with that type of data, if there was a large enough observational study that demonstrated (a treatment effect), it would be enough for me to change my practice.” (General Neurologist 3)

"It's really difficult to convince people to do something, just based on observational data if the data were not randomized." (Vascular Neurologist 3)

#### *Concerns about observational studies*

When asked about concerns regarding observational studies, only a few participants cited specific concerns. One internist and one general neurologist emphasized that observational studies are unable to prove causality. A few participants raised concern about generalizability of observational studies, although this is often cited as a strength of observational CER.

"The main thing I'd want to know about the methods section is how were patients selected for asymptomatic stroke. In the end, I think these people get scans for many reasons. Those reasons are heterogeneous." (Vascular Neurologist 4)

#### *Concerns about lack of equipoise and recruitment into clinical trials*

Despite uncertainty about the management of patients with SBI, lack of equipoise at the individual clinician level was described by some participants across all specialties as a major potential barrier to the conduct of RCTs for SBI.

"I would have a little trouble telling someone not to take aspirin and a statin when I found a stroke on their head CT." (Internist 3)

### *Skepticism about the feasibility of RCTs for SBI*

Some participants, including those describing that they would need RCTs to modify their practices, cited concerns about the feasibility of conducting RCTs for SBI. These concerns included the required duration of followup to assess relevant outcomes (e.g. dementia), the projected effect size of treatments, and difficulty with recruitment.

"I don't think of silent stroke as something that I identify particularly often on an anecdotal basis. I definitely worry about recruitment. Also, like an effect size, we're talking about a treatment effect. I would imagine you'd have to have a pretty big n. We know it's hard to get these people enrolled in these big stroke trials. Absolutely, I have concerns about feasibility for it." (Vascular Neurologist 4)

## **DISCUSSION**

Despite two decades of published research on the prevalence, risk factors, and outcomes of SBI in screened cohorts, clinicians in our diverse sample expressed uncertain and conflicting views regarding SBI—its pathogenesis, its prognostic significance, and the appropriate diagnostic and therapeutic approach—when it is discovered incidentally in the course of routine care.<sup>1-4</sup> This uncertainty and practice variation points to the need for future studies of SBI to address clinically relevant questions in this unstudied group of patients with SBI (i.e. incidentally discovered, rather than detected by protocol driven

screening of research cohorts). Our study also uncovered substantial commitment to treating incidentally discovered SBI similar to symptomatic stroke among a subgroup of clinicians—a finding that needs to be confirmed and accounted for in efforts to disseminate clinical practice guidelines and to design future treatment studies.

Based on the findings of this study, it appears that incidentally discovered SBI is an important clinical entity that calls for a paradigm shift in how clinicians approach clinically “silent” and “incidental” findings in relation to cerebrovascular diseases. These are important psychological barriers that influence the practices of clinicians as well as efforts by researchers to study different types of SBI: currently, there are no studies guiding clinical decision making for incidentally discovered SBI. The “silent” nature of SBI makes it difficult for clinicians to define it as a clinical entity, forcing them to rely on interpretations of radiologic imaging and the individual patient’s risk factors for stroke. Of note, since internists far outnumber neurologists, most patients with incidentally discovered SBI are probably encountered first by internists. However, internists rely on radiologists to unequivocally identify brain infarction on neuroimaging studies. Radiologists may not consistently identify or emphasize these findings—reinforcing lack of awareness of SBI or its clinical significance among internists. Consensus radiologic criteria have been proposed, but it is not known if radiologists routinely follow them.<sup>11</sup> Accordingly, it may be difficult for internists to address incidentally discovered SBI without standardization in the radiologists’ approach to these findings. If this can be achieved, internists may be willing to approach SBI in a similar manner as silent MI. Another important psychological barrier is the difficulty in reconciling the incidental

nature of the discovery of SBI and the potential need for action: the label “incidental” sometimes implies insignificance or lack of urgency. However, several clinicians acknowledged that some incidental findings are clinically important, such as an incidentally discovered occult malignancy. To this end, we propose the term “incidentally discovered SBI” to highlight the potential utility in the “discovery” of these SBI for prevention of stroke and dementia.

In our study, many clinicians viewed incidentally discovered SBI as having equivalent prognostic significance to symptomatic stroke. However, this assumption is currently unproven since outcomes after incidentally discovered SBI have not been studied.

Evidence to resolve this issue will be difficult to obtain as there is likely considerable heterogeneity in the reasons for which these patients undergo neuroimaging studies, some of which make them ineligible for interventions aimed at stroke prevention (at least temporarily, as would be the case with intracranial hemorrhage and antithrombotic medications). Nonetheless, with the exception of perioperative SBI (which was only cited by one participant in our study), it is possible that some SBI discovered incidentally in routine care portend similar risks of symptomatic stroke and dementia as SBI detected through neuroimaging screening. Based on the responses of the clinicians in this study and the recruitment of patients with incidentally discovered SBI in another study we are conducting, this eligible subgroup of patients clearly exists and is not rare. Even if screening for SBI were to be implemented in the future, SBI eligible for stroke prevention will continue to be discovered incidentally. For all of these reasons, more research is needed to understand the factors that influence the prognosis of individual

patients with incidentally discovered SBI, and to determine how to identify those patients for whom stroke prevention measures are most effective.

Despite their uncertainties, many clinicians described responding to SBI with practices extrapolated from stroke prevention—i.e., by recommending primary prevention, secondary prevention, or an intermediate approach. Importantly, secondary stroke prevention is more aggressive, involving more medications and diagnostic evaluation, than primary prevention.<sup>12-13</sup> In our study, vascular neurologists endorsed secondary prevention strategies whereas internists and general neurologists often endorsed a wider variety of less aggressive approaches. More aggressive approaches were associated with a belief in the prognostic equivalence of SBI and symptomatic stroke. This strong belief may be incompatible with the relatively conservative recommendation to implement primary prevention strategies for patients with silent cerebrovascular diseases, endorsed in a recently published AHA/ASA scientific statement.<sup>7</sup> Consequently, our data suggest that at least some stroke specialists as well as some internists and general neurologists may be reluctant to adhere to this guideline and instead continue to offer more aggressive care. This practice variation emphasizes the need for evidence to reduce uncertainty about optimal care for patients with incidentally discovered SBI.

Although our study was not intended to be broadly representative, it highlights potential barriers for future treatment studies for SBI. Specifically, several clinicians expressed concerns about the infeasibility of RCTs and a reluctance to enroll their patients in such studies due to their beliefs in the prognostic equivalence of SBI and symptomatic stroke.

Given these concerns, observational CER may be the most acceptable and pragmatic approach for informing treatment of patients with incidentally discovered SBI.

This study had several limitations. Because interviews by their nature are not anonymous, some clinicians may have misrepresented their practices. For example, some participants may have been reluctant to report that incidentally discovered SBI are not routinely discussed with patients. Additionally, the sample of clinicians in our study was relatively small and restricted to a limited geographic area. Finally, this study assessed clinicians' beliefs and attitudes but did not directly measure clinical practices. Nevertheless, this study also had several strengths. Our multidisciplinary research team included internists, vascular neurologists, and a radiologist with a broad range of clinical experience and perspectives. The participants represented a diverse group of clinicians in academic and community practices, seven hospitals, three specialties, and inpatient and outpatient settings. All participants had substantial experience providing care for patients with SBI—further enhancing the validity of this study's findings.

## **CONCLUSIONS**

Incidentally discovered SBI is a completely unstudied and potentially common condition encountered by internists and neurologists in routine clinical care that involves a wide range of uncertainties—diagnostic, prognostic, and therapeutic—and a wide range of responses to these uncertainties. More research is needed to reduce uncertainties about the management of patients with incidentally discovered SBI, and to identify individual



patients who will benefit the most from stroke prevention interventions. Based on the findings of this study, observational comparative effectiveness research may be a viable and acceptable option for guiding the clinicians most likely to encounter patients with SBI.

## **REFERENCES**

(As per Sackler requirements, references have been renumbered and incorporated into the Bibliography section.)

## **ACKNOWLEDGEMENTS**

None.

## **DISCLOSURES**

None.

**Table 1.1. Characteristics of clinician participants.**

<b>Characteristic</b>	<b>Subcategory</b>	<b>n or median (IQR)</b>
Sex	Men	9
	Women	6
Specialty	Internal medicine	7
	General neurology	4
	Vascular neurology	4
Practice Setting	Inpatient only	1
	Outpatient only	0
	Both	14
Institution	Academic	12
	Community	3
Years of experience	< 5 years	2
	5-10 years	6
	> 10 years	7
Estimated encounters with patients with SBI per year	Internal medicine	10 (5-15)
	General neurology	22.5 (15-35)
	Vascular neurology	20 (13.75-27.5)

**Table 1.2. Uncertainty about SBI – types and sources.**

<b>Categories (Level 1)</b>	<b>Subcategories (Level 2)</b>	<b>Subcategories (Level 3)</b>	<b>Representative quotations</b>
Types of Uncertainty	Diagnostic	The “silent” nature of SBI Relationship to white matter disease Causal uncertainty	<p>“I think the biggest question for me would be what exactly you consider a silent stroke.”</p> <p>“Should I assume all white matter disease is a silent stroke outside of people who have multiple sclerosis or something like that?”</p> <p>“Is this a different subset of stroke patients in terms of etiologies? I don’t think I know the answer.”</p> <p>“I think the size and shape and location probably suggests there’s a difference between them (SBI). But again, I wouldn’t profess to have much certainty there.”</p>
	Prognostic	Risk of future stroke Risk of direct harm	<p>“A stroke is a stroke.”</p> <p>“I think it’s really, really hard to implicate silent strokes for any individual patient as the cause of the problem.”</p>
	Therapeutic	Approach to further evaluation	<p>“The truth is I don’t have an algorithm yet. I’m sort of figuring it out case by case.”</p>
Sources of Uncertainty	Limited awareness and dissemination of available evidence	Prevalence of SBI Outcomes following SBI	<p>“I have no idea how common they are.”</p> <p>“I would like to know a couple of things: one would be how frequent they actually are, because I don’t think anybody knows that.”</p> <p>“I think one of the things that is not very well recognized is that these patients are at risk of harm... That there is an urgency to treat... That they need to be treated just like any other stroke patients in terms of secondary prophylaxis.”</p>
	Lack of treatment studies and guidelines	Benefit of referral to specialist Benefit of treatment Consensus Guidelines	<p>“When would a referral be beneficial? What would a neurologist add because it’s not clear to me there’s really much to do?”</p> <p>“I’d like to know whether others are treating them the same way I am.”</p>

		Outcomes Testing	“I know that we don’t have any guidelines on how to address these.”
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**Table 1.3. Clinical decision making in response to uncertainty – practice variation, evaluation of evidence, and translation into practice.**

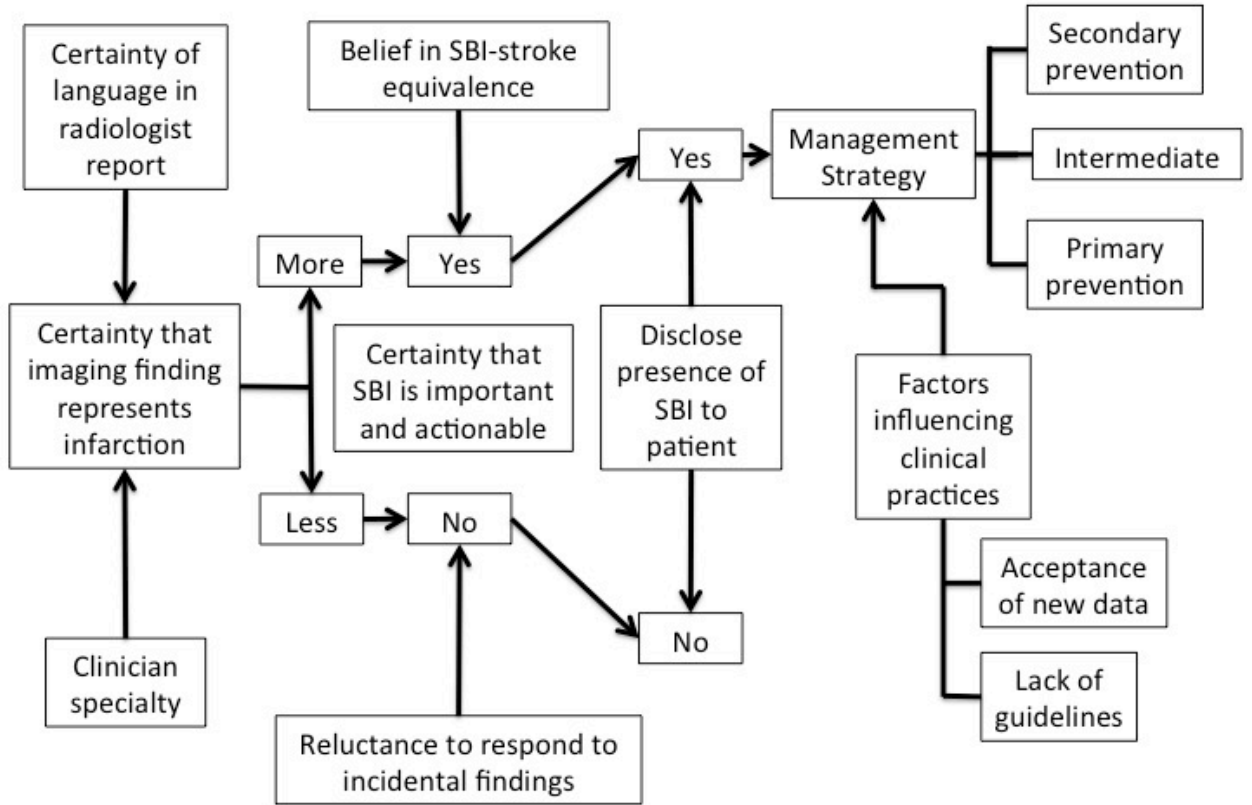
<b>Categories (Level 1)</b>	<b>Subcategories (Level 2)</b>	<b>Subcategories (Level 3)</b>	<b>Representative quotations</b>
Practice variation	Response to diagnostic uncertainty	Influence of the “incidental” nature of SBI Influence of neuroimaging interpretation by a radiologist	<p>“If it’s an incidental finding like a lung mass, that would be a lot different, but I guess if it’s not causing symptoms and if it’s a small incidental finding, I would be less likely to jump on it right away.”</p> <p>"Well, if they say infarction (I would respond). If they just say microvascular or white matter disease or chronic microangiopathy... (I might not)."</p>
	Response to prognostic uncertainty	Obligation to take action upon discovering “incidental” SBI Disclosure to patients	<p>“I think it’s really an individual thing for me, and I’m not sure I have a definite, set way for this.”</p> <p>“I think probably in the situations where they come up in the hospital, we haven’t usually (addressed SBI) because in the inpatient setting, we’re dealing with the presenting problem. If we really don’t think it’s related, I haven’t thought too much about it.”</p> <p>"I tell them that we looked at the imaging, and it looks like in the past they had a small stroke that they were likely unaware of.... we should work this up as if it was something more significant, then we can prevent having larger strokes in the future."</p>
	Response to therapeutic uncertainty	Specific strategies Etiologic testing Lifestyle modification Medication management Specialty referral	<p>"Guidelines are good, but that's what they are: guidelines. You always want to have individualized care."</p> <p>"I think they have to be aggressively managed, as you'd manage any other stroke patient."</p> <p>"I'll use the finding of the silent stroke as additional impetus to, hopefully, motivate them to stop smoking."</p> <p>"If they have signs of a silent stroke and they are not on an antiplatelet and things like that,</p>

			at least I'll give them a baby aspirin."
Evaluation of evidence and translation into practice	Variable acceptance of evidence from new studies	Observational CER RCT	"It (an RCT) would be more ideal, but I think an observational study would be useful."  "I think an all-comers observational study of this probably would not change my management."
	CER design	Generalizability	"I think these people get scans for many reasons."
	RCT design	Equipoise Feasibility Recruitment	"I think if they have known vascular risk factors, to not give an aspirin is probably malpractice. I wouldn't recommend doing that in the study."  "I think it (an RCT) is actually impossible."

**Figure 1.1. Scenarios leading to incidental discovery of SBI.**

Asymptomatic, abnormal neurologic examination finding
Perioperative
Symptomatic stroke or transient ischemic attack (with detection of an unrelated SBI)
Symptoms not specific to stroke
Altered mental status (confusion, lethargy)
Cognitive decline
Dizziness
Gait difficulty
Generalized weakness
Headaches
Lightheadedness
Memory loss
Seizures
Syncope
Trauma

Figure 1.2. Theoretical model for clinical decision making for SBI.





## Chapter 3

### **Patients' perspectives on incidentally discovered silent brain infarction – a qualitative study<sup>1</sup>**

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<sup>1</sup>Leung LY, Han PK, Lundquist C, Weinstein G, Thaler DE, and Kent DM. To be submitted to *JGIM*, 4/1/2017.

## **ABSTRACT**

**Background:** Silent brain infarction (SBI) is common in neuroimaging-screened cohorts of adults and is associated with an increased risk for stroke and dementia. However, it is unknown how patients understand this condition or respond to its incidental discovery in routine care.

**Objective:** To explore patients' perceptions of SBI and associated health risks.

**Design and Participants:** We performed semi-structured interviews of patients with incidentally discovered SBI who were aware of their imaging findings. We recruited patients by pairing radiographic identification with clinician determination of clinical silence, identification by clinicians, and patient self-identification. We used purposeful sampling to achieve diversity in acuity, setting, and recruitment strategy.

**Approach:** We used a constant comparative method to develop a coding schema, find consensus, and modify the interview guide. We interviewed 12 patients to achieve thematic saturation.

**Key Results:** Study recruitment was impeded by infrequent clinician reporting: many patients identified radiographically were not informed. Among informed patients, the primary themes were patients' beliefs in the equivalence of SBI and symptomatic stroke, discordance between patient and clinician certainty about the significance of SBI, and high variability in patients' responses to clinicians' uncertainty. Most did not distinguish

between SBI and symptomatic stroke, viewed SBI as grave, and expressed high levels of distress despite ambiguous messages from clinicians. Many viewed SBI as a “wakeup call,” motivating behavioral changes to improve health. In response to clinicians’ uncertainty, many interpreted ambiguous messages in a catastrophic way.

Conclusions: Patients with SBI express fear and belief in the pathological importance of SBI and are motivated to improve their health.

## INTRODUCTION

Silent brain infarction (SBI) is very common in older adults, but it is not known how an incidental discovery of SBI affects the behaviors and decisions of patients. In cohort studies of screened adults, the estimated prevalence of SBI among U.S. adults over age 50 is 20%, and the estimated annual incidence is about 11 million per year, more than 11 fold greater than symptomatic ischemic strokes.<sup>2-4,47</sup> These longitudinal studies have established that SBI is associated with a two-to-three fold increased risk for symptomatic brain infarction and dementia.

Given its subclinical nature and absence of routine screening, SBI likely remains undetected in most cases. Nonetheless, SBI is commonly discovered incidentally when neuroimaging is obtained for other indications. However, the clinical significance of incidentally discovered SBI is poorly understood. There are currently no treatment studies examining outcomes of patients with incidentally discovered SBI, and there are no evidence based guidelines on how clinicians should approach this condition. The American Heart Association/American Stroke Association has highlighted these knowledge gaps with a scientific statement describing the need for future studies to guide clinical decision making.<sup>53</sup> However, no prior studies have examined patient-centered outcomes or explored patients' perspectives on SBI.

To address these evidence gaps, we interviewed patients with incidentally discovered SBI to better understand their perspectives and to explore their concerns and needs.

## **METHODS**

### **Study design, participants, and data collection**

This study employed individual semi-structured qualitative interviews of patients with incidentally discovered SBI to explore their concerns and needs in addressing this condition. Participants were recruited from inpatient and outpatient practices at a tertiary care medical center (Tufts Medical Center, Boston, MA). Participants were adults ages 18 and over; had no prior clinical history of stroke, transient ischemic attack (TIA), or dementia; had to consent and participate in the interview in English; and had to be aware of the neuroimaging finding of SBI prior to the interview. Participants were prospectively identified and recruited through at least one of three strategies: (1) identification through radiologic reporting of brain infarction with verification of clinical silence, (2) identification by a treating clinician, and (3) participant self-identification. A study vascular neurologist reviewed neuroimaging studies directly to confirm infarction (based on proposed consensus definitions for imaging findings of infarction) and performed verification of clinical silence through review of associated clinical documentation or discussion with treating clinicians.<sup>2,59</sup> Purposeful sampling was conducted to achieve variance by sex, race, acuity of SBI, clinical setting, and recruitment strategy. A screening tool was used to verify eligibility. Participant characteristics were collected from the electronic medical record including demographics, medical history, and SBI

features. Interviews were conducted by LYL and lasted 30-60 minutes. Interviews were audio-recorded and transcribed verbatim by a professional transcription service.

### **Interview content**

The interview guide included open-ended questions and closed-ended probes to explore themes including reactions to the diagnosis, advice from clinicians, perceptions of harm, and projected behavioral changes. Interviews were conducted in three phases with iterative revisions to the interview guide between phases to explore unanticipated themes.

### **Data analysis**

Two investigators (LYL, CL) performed line-by-line, software-assisted coding of anonymised interview transcripts using NVivo (V.11; QSR International, Melbourne, Australia). Three investigators (LYL, PH, CL) developed an initial codebook through independent review and team-based reconciliation of the first two coded transcripts, using a “grounded theory” approach to categorize thematic content in a hierarchical logically coherent conceptual schema.<sup>56-57</sup> Through a “constant comparative” method, emergent themes were incorporated into the codebook following each phase of interviews, independent coding, and coding reconciliation.<sup>58</sup> The three investigators met at the end of each phase of interviews to discuss coding and recruitment decisions, resolve disagreements, and revise the interview guide and codebook.

## RESULTS

Recruitment proceeded simultaneously with all three strategies described in the Methods section. For strategy (1), between December 2015 and May 2016, 102 patients meeting inclusion criteria were prospectively identified as having possible SBI by neuroradiologist report. There were no patients with more than one study identifying SBI during this time period. 90 patients with SBI were not informed of the imaging findings. Reasons for not reporting SBI are shown in Figure 2.1. One of the remaining 12 informed patients did not respond to requests for interview. Three were recruited after the investigators contacted the treating clinicians, seven were independently referred by their treating clinicians for the study through strategy (2), and one patient self-referred for the study through strategy (3). One additional patient recruited through strategy (2) had a brain MRI reporting SBI at another facility; direct imaging review was performed by a study neurologist to verify the findings. In total, 12 participants completed interviews. Characteristics of the participants are shown in Table 2.1.

Analysis of the interview transcripts revealed three primary themes: 1) patients' beliefs in the equivalence of SBI and stroke, 2) discordance between patients' and clinicians' certainty about the significance of SBI, and 3) high variability in patients' responses to clinicians' uncertainty. The first focused on the tendency of patients to equate SBI and symptomatic stroke and to perceive the need for urgent behavioral change in response to SBI (Table 2.2). The second focused on sources of discordance between the perspectives of patients and clinicians, perceived inaction and lack of guidance by clinicians, and

patients' expectations about uncertainty expressed by clinicians. The third focused on the behaviors patients endorsed in response to clinicians' uncertainty about SBI (Table 2.3). Drawing from these findings, a theoretical model illustrating how patients understand the diagnosis of SBI is shown in Figure 2.2.

### **Patients' beliefs in the equivalence of SBI and stroke**

#### *Similar diagnostic terminology*

All but one participant were told by clinicians that they had a "stroke," usually with a modifying descriptor such as "silent," "small," or "old." The exceptional participant reported being told by a neurosurgeon and a vascular neurologist that she had a "TIA." However, despite the use of modifying descriptors, participants did not perceive SBI and symptomatic stroke as distinct entities. Those who were told they had a stroke described fear, panic, despair, or anxiety upon receiving the diagnosis.

"Being told I had, should I say, a 'slim stroke,' scared the life out of me. I didn't know what to expect." (Patient 1)

Most of the participants also described surprise or shock upon learning that they had a stroke.



“She said it showed I have had a previous stroke. It was a big surprise, I had no idea at all. No one has ever mentioned that to me.” (Patient 6)

“I was surprised. I was under shock how I had stroke, because I didn’t feel nothing special.” (Patient 8)

In at least one instance, use of the word “stroke” impaired a participant’s memory of the clinical evaluation.

“I honestly don’t remember part of the conversation after that because I was so stuck on the word ‘silent stroke.’” (Patient 3)

In contrast and attesting to the powerful psychological impact of diagnostic terminology, the lone participant for whom the term “stroke” was not used did not endorse any of these responses:

“It wasn’t a big deal. He showed me all of the MRIs of my body and he just said, ‘Oh look at this white spot here, I think that’s a TIA.’ But he didn’t seem overly concerned about it.” (Patient 9)

*Similar gravity of SBI and its consequences*

Consistent with their expressed beliefs in the diagnostic equivalence of SBI and stroke, almost all of the participants perceived the health consequences of SBI to be serious.

"I don't want this to be the 800 pound gorilla on my back for the rest of my life."

(Patient 10)

Most singled out symptomatic stroke and dementia as their greatest concerns. Some expressed concerns about death or loss of independence resulting from disability. These were largely derived from prior assumptions regarding the consequences of symptomatic stroke and their beliefs in the equivalence of SBI and symptomatic stroke.

"I'm not afraid of dying. I'm more afraid of living and having to depend on somebody to take care of me because I've had a stroke." (Patient 2)

For a few participants, fear of SBI appeared to arise from uncertainty about the future and their inability to detect recurrent SBI.

"It is scary not knowing when you're going to have one, if I'm ever going to have another one again, and if I do have another one, is that one going to show physical signs next time?" (Patient 12)

*Similar implications for behavior*

Most participants expressed strong motivation to make changes in their lives in response to the discovery of SBI. Several described the discovery of SBI as a “wakeup call.”

"You have to make it into a positive... 'oh my life is over and I can't... I'm so fragile'. No, I had this happen, and it was a wake up call, and it's never going to happen again, God willing, because I'm going to do everything in my personal power to make sure." (Patient 3)

Several participants described that the discovery of SBI led them to reflect on their age, prior health, lifestyle choices, and quality of life.

"I would like to know if I did something in my past that may have caused this."  
(Patient 2)

Several endorsed that findings from future research studies could further influence their actions. Regarding specific behavioral responses to SBI, participants cited a wide range: lifestyle modifications, taking medications, and sharing their diagnosis with others. Many preferred to focus on lifestyle changes and expressed some resistance to taking more medications.

"I'm sure I'm going to have to change my eating habits... Everywhere I go I walk. I eat a lot more vegetables and fruits because I used to love junk food. I've cut out-ice cream is my biggest thing." (Patient 11)

In response to the discovery of SBI, several participants described sharing the diagnosis and seeking support from family, friends, and in one case, another person with SBI.

"That's better for me because I talk with my friend, and we try to make joke about it, because when they see that I'm depression and I scared, they try nice talk with me." (Patient 8)

"I think my family and my friends and everybody around me knows that it could happen, so they're aware of everything. They know what to look out for and that type of things." (Patient 12)

### **Discordance between patients' and clinicians' certainty**

In contrast to the participants' beliefs in the equivalence of "silent stroke" and "stroke," many perceived confusion and uncertainty on the part of clinicians. They perceived clinicians as failing to provide a clear diagnosis, being equivocal about the prognostic significance of SBI, and being indecisive in its management. This discordance had several sources, was manifest in perceived inaction of the clinicians, and tied to expectations about the acceptability of clinicians' uncertainty.

#### *Sources of discordance*

The involvement of multiple clinicians from different specialties in the care of the participant was one source of discordance, as different clinicians often conveyed conflicting interpretations.

“It actually caused a lot of confusion because one doctor said there was nothing, another doctor looking at the scan was concerned, and then after speaking to the doctor at Tufts... it’s just very confusing.” (Patient 3)

Delayed discovery and a lack of reporting also contributed to discordance. One participant (patient 4) discovered the finding of SBI by reading her radiology report without any other prior communication by a clinician, after which she sought consultation with a neurologist.

“Nobody actually knew what happened, when it occurred, so it kind of puzzled everybody at the same time.... Nobody knew anything, so nobody had any answers at the right time.” (Patient 12)

Lack of knowledge was another contributing factor. Despite recognition of their diagnosis of “silent stroke” and their identification by clinicians as patients who were previously informed about SBI, several participants described lacking a clear understanding and adequate counseling about their condition (either SBI or stroke).

“I know very little about the diagnosis.” (Patient 5)

“I know nothing about my diagnosis. I didn’t even know I had the strokes until they let me know that I had two stroke spots on my brain.” (Patient 11)

Another contributor to this discordance was variability in the terminology clinicians used to describe SBI. While "silent stroke" was the most common term patients recalled, they reported the use of other terms including bleed, blood clot, blood spot, ischemia, mini-stroke, minor stroke, prior stroke, small stroke, stroke, stroke spot, and white matter disease.

*Perceived inaction and lack of guidance from clinicians*

Whereas participants felt certain that SBI was a serious condition demanding urgent behavioral change, they often perceived that their clinicians took insufficient action and provided limited or no guidance on how to respond to SBI. Many expected to receive medical treatment or recommendations for lifestyle modification, and they were disappointed and concerned when they did not.

"Even though they just came out and just told me, they didn't ask me any questions or anything. I mean, I would have liked to have known some things. You get nervous when you hear things like that. And they don't ask questions. They don't give me any medicine. So you're like, 'It sounds serious, I had two

strokes. Are you going to give me any medicine to start me doing something?' So that kind of worried me." (Patient 3)

"I'm having a hard time wrapping my head around what I can do when I really don't know what I can do. I mean, is there a stroke diet? Is there a stroke regimen that you could, you know, if you do this particular thing, if you swam or if you exercise or if you change behavior, will that reduce the chance of having another one?" (Patient 10)

#### *Expectations about the acceptability of uncertainty*

Participants expressed differing views regarding whether it was normal for clinicians to have uncertainty about SBI and how much uncertainty was acceptable. Upon learning there were no published guidelines for the prevention of adverse health consequences after the discovery of SBI (at the time of the interviews), half expressed concern about the perceived lack of scientific evidence:

"I'd be very concerned. How can I be treated if a doctor has no guidelines or any studies in the past?" (Patient 2)

The other half accepted this absence of evidence as a normal situation:

"Probably not any more concerned. I mean, understanding a lot of things are trial and error, basically... I would certainly get that a lot of things are seeing what works best, based on information that you have. So yeah, there's no set hard guidelines: I get that's often the case." (Patient 4)

### **High variability in patients' responses to clinicians' uncertainty**

Confronted with clinicians' uncertainty regarding the nature of SBI or recommended actions, participants exhibited a number of responses.

#### *Information seeking*

Seeking additional information about the symptoms of stroke and recommended behavioral changes after stroke was a common approach endorsed by several participants, sometimes involving asking more questions of their clinicians or searching for information elsewhere (the library, the Internet, etc.). These participants did not seek information to clarify the nature of SBI as a distinct entity from symptomatic stroke, but rather, focused on information that could guide their future behaviors.

#### *Minimizing or discounting risk*

A few participants described partially successful attempts by clinicians to provide reassurance in the face of diagnostic uncertainty; these attempts attenuated but did not



completely alleviate their fears. Participants still expressed beliefs in the equivalent risks of adverse health consequences after SBI and symptomatic stroke, but they took comfort in the belief that it was preferable to have a silent stroke than a symptomatic stroke. They also were partly reassured that their silent strokes were behind them, having occurred in the more distant past.

“I think I was more relieved that they told me everything was okay, but that I had at some point one that occurred. I was more or less concentrated on just being relieved that they had ruled out the possibility of a stroke at the time. They did mention it occurred in the past. So I kind of left it there.” (Patient 5)

#### *Obtaining multiple opinions*

Regarding recommended treatments and lifestyle modifications, some participants sought multiple opinions from clinicians representing different specialties following the discovery of SBI. One participant described an attempt to weigh opinions of multiple clinicians to reduce uncertainty introduced by conflicting expert opinions.

"I have differing opinions from my primary and neurologist... Which way to lean, you know? Not sure which one, but at this point, I was actually leaning towards not taking the medication because I'd rather not... I guess the cardiologist will hopefully break the tie here, decide what I'm doing from there. It's hard and

obviously everyone's going to have different opinions. Being a patient, you're like, 'Well, who do I listen to?'" (Patient 4)

### *Placing full trust in clinicians*

Despite discordant certainty in the clinical significance of SBI between participants and their clinicians, many described strong relationships with their clinicians. These relationships allowed them to overcome uncertainty introduced by clinicians by placing full trust in the advice of those clinicians, even if those recommendations were given in the context of diagnostic uncertainty.

"I need to respect what doctor tell and try follow what is good that stroke don't come back." (Patient 8)

"I have a great deal of respect for her... She'll make a recommendation, and I trust her implicitly." (Patient 10)

## **DISCUSSION**

This study yields important insights into the perspectives of patients diagnosed with incidentally discovered SBI. The most significant finding is that many patients consider incidentally discovered SBI to be a high priority, serious medical condition demanding urgent action, in contrast to some clinicians who consider SBI to be clinically

unimportant. Participants in our study expressed considerable fear and concern regarding the discovery of SBI, and they generally treated SBI as a form of stroke with similar clinical importance. Although our participants were often uncertain about the best approach to reducing health risk related to SBI in the context of limited guidance from clinicians, most were motivated to seek information about stroke prevention and independently change behaviors to improve health. These findings clearly indicate that patients with incidentally discovered SBI have an important stake (their health) in future studies to determine optimal management strategies for this understudied condition.

The beliefs of our participants contrasted with the uncertainty they perceived of their clinicians. This uncertainty, furthermore, seemed to provoke highly variable responses. In many cases, it may have exacerbated their feelings of the risk associated with SBI, consistent with a response that decision theorists have termed “ambiguity aversion”—the tendency to appraise risks pessimistically.<sup>60</sup> Ambiguity aversion represents an “alarmist response” to risk information, a “tendency to devote excessive attention to the worst case scenarios” whenever risk information is “ambiguous”—of questionable reliability, credibility, or adequacy.<sup>61</sup> When clinicians introduced uncertainty about the significance of SBI to participants (by not fully acknowledging them as “strokes”), most participants endorsed worst case scenario beliefs that SBI and symptomatic stroke were essentially the same entities. This discordance, in turn, led some participants to follow the advice of their clinicians without question and inspired others to seek alternative sources of information.

Despite clinicians' uncertainty about the significance of incidentally discovered SBI and lack of clarity when delivering the diagnosis, our participants were clear about their priorities: they were interested in reducing risk of future symptomatic stroke, dementia, and loss of independence. These should be considered patient-oriented outcomes included in future treatment studies for patients with incidentally discovered SBI. Future treatment studies and guidelines should also address the reluctance of patients to initiate new medications by providing clear statements regarding whether or not medical therapies are needed for the prevention of stroke or dementia following incidentally discovered SBI, particularly if it is determined that incidentally discovered SBI does not confer the same risk as symptomatic stroke.

Finally, the importance of the language of clinicians in describing SBI cannot be overstated: in the eyes of most patients, a "stroke is a stroke." Excluding SBIs that may be expected to have low or no possibility of recurrence (e.g. perioperative), incidentally discovered SBIs likely have similar risk factors and prognostic significance to SBIs in screened populations. If the significance of incidentally discovered SBI is less than that of symptomatic stroke, future guidelines will need to provide clearer messages for clinicians to convey to patients. If the significance of this form of SBI is comparable to symptomatic stroke, then the equivalence of incidentally discovered SBI and symptomatic stroke should be emphasized in guidelines and in designation of outcomes in future treatment studies, including those for patients with SBI. In any case, more evidence is needed to establish the prognostic significance of incidentally discovered SBIs in individual patients.

This study has several strengths. First, no prior studies have assessed the perspectives of patients with incidentally discovered SBI. This study is particularly unique in its timing: incidentally discovered SBI is a condition for which there is no consensus regarding optimal strategies for counseling, detection, and management. While the American Heart Association/American Stroke Association has introduced a scientific statement suggesting an approach to SBI for clinicians, findings from our qualitative interview study of clinicians on incidentally discovered SBI indicate that some internists and neurologists may be unwilling to adopt those recommendations.<sup>53</sup> As a result, patients with incidentally discovered SBI are faced with numerous ambiguous or conflicting messages and recommendations from their treating clinicians. Secondly, our sample of participants was recruited through strategies aimed at increasing diversity: there were differences in the acuity of the imaging findings (which likely influences clinician certainty in the diagnosis and recommendations), clinical setting, type of clinician conveying the diagnosis, and method of identification (including self-identification by one participant). Accordingly, our participants encountered clinicians who provided a wide spectrum of perspectives on the importance of SBI and variable recommendations. We suspected that patients may learn of this diagnosis in a variety of different circumstances, and we were able to capture some of these differences.

This study also has important limitations. First, because only a minority of patients we identified through radiologic reporting were informed, the sample included in our study may represent a select group of patients for whom SBI was interpreted by reporting

clinicians as being important to the patient's health. It is possible that incidentally discovered SBI may often be considered by clinicians to be a low priority for patients with competing risks (i.e. acute illnesses, perioperative, other intracranial pathologies, etc.). As such, this sample of patients is likely representative of patients with SBI who come to medical attention as possible candidates for stroke prevention: this potentially treatment-eligible population needs further definition. Secondly, the sample was small, but prior studies have indicated that this number of interviews is reasonable for achieving thematic saturation.<sup>62-63</sup> Thirdly, our study may have influenced the care of patients referred by treating clinicians to the study, although the findings indicate that clinician recommendations for patients were variable, unclear, or limited.

## **CONCLUSIONS**

Incidentally discovered SBI is an important condition for patients that can motivate behavioral change to improve health. Since SBI has meaningful clinical implications including an increased risk for symptomatic stroke and dementia, standardizing language in the delivery of the diagnosis and assessing the effectiveness of clinical practices will hopefully help patients reduce the clinical and psychological impacts of incidentally discovered SBI.

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(As per Sackler requirements, references have been renumbered and incorporated into the Bibliography section.)

## **ACKNOWLEDGEMENTS**

None.

## **DISCLOSURES**

None.

**Table 2.1. Characteristics of patient participants.**

<b>Characteristic</b>	<b>Subcategory</b>	<b>Median (IQR) or n</b>
Age		61 (54-72)
Sex	Men	3
	Women	9
Race	Black	2
	White	10
Acuity of SBI on neuroimaging	Acute/subacute	4
	Chronic	8
Location of SBI	Only deep/subcortical	8
	Only cortical/juxtacortical	2
	Both	2
Presence of white matter disease	Yes	10
	No	2
Clinical setting	Inpatient	4
	Outpatient	8
Type of clinician delivering the diagnosis	Internist	1
	Neurologist	7
	Other	4*
Patient recruitment strategy	Identified from radiologic study first	3
	Referred by treating clinician	8
	Patient self identified	1
Comorbidities	Hypertension	7
	Hypercholesterolemia	6
	Diabetes	4
	Coronary artery disease	2
	Atrial fibrillation	1
	Obstructive sleep apnea	1
	Obesity	2
	Current tobacco use	1
	Migraine	6

\*Other includes two instances of SBI reported by Neurosurgeons, one by a Cardiologist, and one where the patient read the imaging report directly.



**Table 2.2. Patients' beliefs in the equivalence of SBI and stroke.**

<b>Categories (Level 1)</b>	<b>Subcategories (Level 2)</b>	<b>Subcategories (Level 3)</b>	<b>Representative quotations</b>
Equating SBI and stroke	Similar diagnostic terminology	Fear Surprise	"I was in a panic, in a big panic."  "I couldn't believe that I had a stroke."
	Similar gravity of SBI and its consequences	Dementia Fear from uncertainty Loss of independence Stroke	"Basically, I'm going to have dementia or a major stroke. I mean, these were minor strokes that I didn't even feel... any time I get a headache now I'm concerned."
	Similar implications for behavior	Strongly motivated Lifestyle modification Perception of SBI as a "wakeup call" Resistance to medications Sharing the diagnosis	"There's a lot I'm going to change."  "As long as it's not a drug."  "I'm more concerned, just because it was kind of like a wake-up call. Nobody is promised tomorrow..."  "I would prefer to modify the diet and the exercise without taking another medication."  "I don't hide my sickness from nobody. Not my friends, not my children. I call them up and I tell them."

**Table 2.3. Discordance between patient and clinician certainty about the significance of SBI and the impact on patient behavior.**

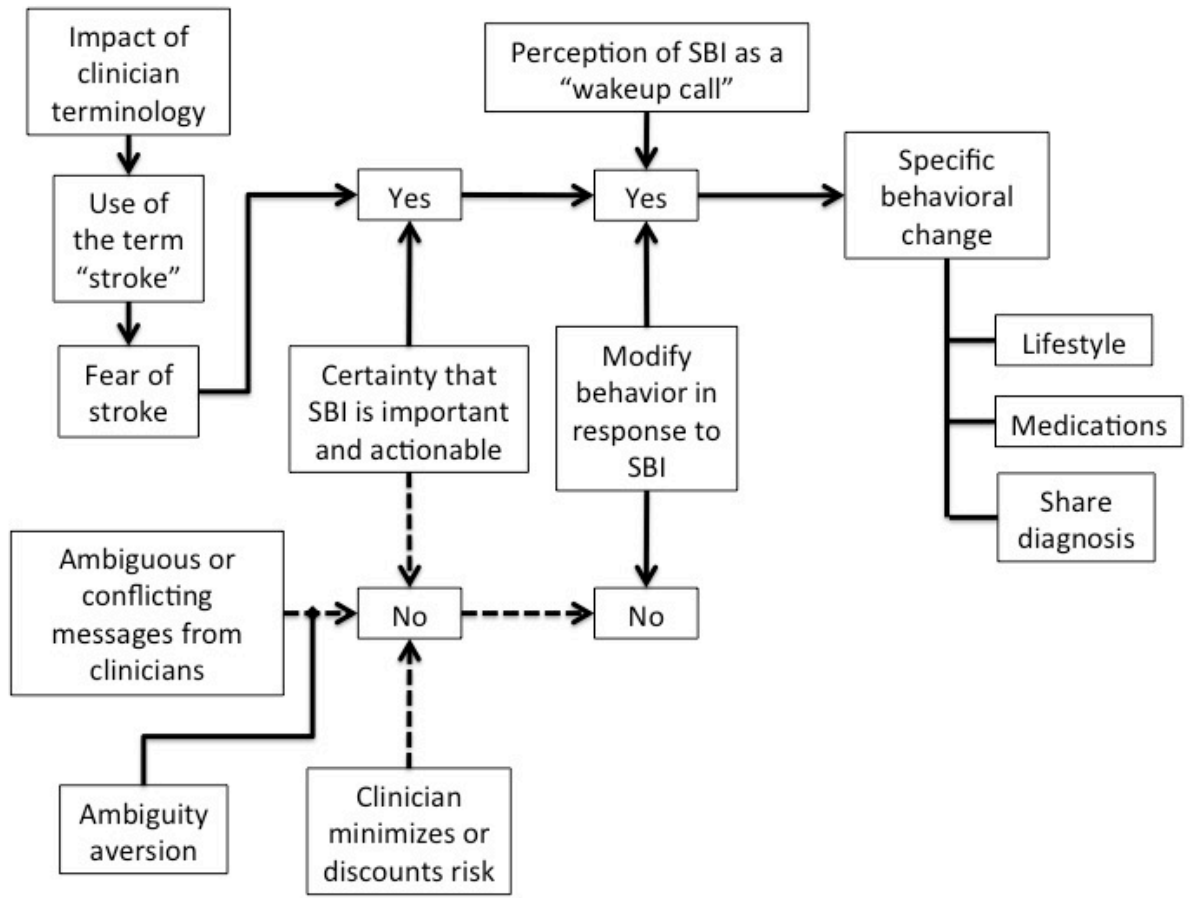
<b>Categories (Level 1)</b>	<b>Subcategories (Level 2)</b>	<b>Subcategories (Level 3)</b>	<b>Representative quotations</b>
Discordance between patients' and clinicians' certainty	Sources of discordance	Conflicting interpretations Delayed discovery Inconsistent terminology Lack of counseling Lack of reporting	"What is the difference between a stroke with symptoms and a stroke without?"  "Stroke is stroke. Doesn't matter big stroke or a little stroke."  "Well, I know very little except I had an MRI of my brain."  "Nothing was mentioned about a stroke to me originally..."
	Perceived inaction and lack of guidance from clinicians	Lack of engagement Limited guidance	"I haven't been told there are five steps that I should take to deal with it... I don't really know what to do.
	Expectations about the acceptability of uncertainty	Lack of guidelines	"Oh, it (the lack of guidelines) affects it (my level of concern) very much. Because if they don't know, how am I supposed to know?"
High variability in patients' responses to clinicians' uncertainty	Information seeking Minimizing or discounting risk Obtaining multiple opinions Placing full trust in clinicians		"I think I'll ask more questions regarding this and gather more information."  "I would take the doctor's advice, whatever they tell me to do. I really would. Then if you're not going to, then why go to the doctor?"

**Figure 2.1. Reasons for lack of reporting of SBI to patients.**

Comorbidities
Acute illness or injury
Intracranial pathology
Death
Health care setting
Discharge from the Emergency Department
Discharge to hospice
Inability to confirm with the treating clinician that the patient was informed
Clinician could not recall informing the patient
Clinician did not document informing the patient
Other
No reason provided
Clinician not aware of diagnostic study results from another health care setting

More than one reason may apply to an individual patient.

**Figure 2.2. Theoretical model for the patient’s understanding of the diagnosis of SBI.**



## **Chapter 4**

### **Discussion**

SBI is an important medical condition with clinically significant consequences including symptomatic stroke and dementia, and yet there is no consensus on how to manage this condition or how to design future studies to determine optimal management strategies. In the absence of relevant evidence to guide clinical practices, these two studies illustrate the discordant uncertainties patients and clinicians have regarding SBI and how they respond to those uncertainties. Over two decades of prior research has focused on the identification of risk factors and outcomes of SBI in neuroimaging-screened cohorts, but the knowledge gained from these studies may not be applicable to patients with SBI in routine clinical practice: there are no current screening practices for SBI, and thus, the population of patients with SBI in these studies do not have a real world correlate. In the absence of evidence-based screening practices, the only potentially meaningful scenario (for patients and clinicians) in which SBI is detected is through incidental discovery on neuroimaging studies obtained for other indications. Understanding that “incidental” findings on diagnostic studies have variable degrees of clinical significance, we sought to gain an understanding for how practicing clinicians and patients with incidentally discovered SBI approach this condition. Together, these qualitative studies provide valuable insights on the perspectives of these two key stakeholder groups on incidentally discovered SBI and how they may respond to evidence from future studies.

First and foremost, the patient study illustrates that this condition is perceived by some patients to be serious, concerning, and deserving of a response. This “alarmist” reaction primarily appeared to arise from the beliefs of patients that incidentally discovered SBI and symptomatic stroke are equivalent in prognostic significance. Interestingly, while

many participants in the clinician study also endorsed this belief, the clinicians providing care for the participants in the patient study did not necessarily provide clear or strong messages regarding the prognostic significance of incidentally discovered SBI. In other words, the patients often independently came to the conclusion that incidentally discovered SBI is clinically important and similar to symptomatic stroke. Both patients and clinicians used the phrase “A stroke is a stroke” to emphasize this concept. Nonetheless, despite this shared belief, there was considerable discordance between clinicians of different specialties regarding management strategies following the incidental discovery of SBI as well as discordance between clinicians and patients regarding whether or not the clinicians should provide specific recommendations to patients. Both the shared belief in prognostic significance of incidentally discovered SBI and the discordance between clinicians and patients emphasize the urgent need for studies guiding the management of this condition.

Secondly, these two studies provide important information on patient-oriented outcomes and clinician attitudes towards different types of evidence that could affect acceptance of findings and study dissemination. Participants in the patient study intuitively identified symptomatic stroke and dementia as consequences of SBI without guidance from their clinicians, and they described that fear of these potentially disabling consequences elevated SBI on their lists of health-related priorities. Both conditions should be considered patient-oriented outcomes in future treatment studies for SBI. Regarding treatment studies, the majority of clinicians acknowledged the potential difficulties of studying interventions for this condition. Most participants in the clinician studies

suggested that they would be willing to incorporate the data from well-designed, observational comparative effectiveness studies into their clinical practices. Many cited preferences for data from RCTs, but there were many concerns regarding feasibility and also lack of equipoise at an individual clinician level. Specifically, some clinicians emphasized that they would avoid enrolling their patients in such trials if required to withhold treatments proven for secondary prevention of stroke such as aspirin. At present, these findings suggest that observational CER may be the most feasible and pragmatic strategy for designing studies guiding the management of patients with incidentally discovered SBI.

Finally, these studies suggest a need for a paradigm shift in how clinicians may be influenced by the “incidental” and “silent” nature of findings on neuroimaging studies. “Incidental” findings (e.g. adrenal adenomas, thyroid nodules, etc.) are often considered to have unclear significance, and yet, concerning diseases are sometimes detected inadvertently (e.g. occult malignancies). By their nature, most incidentally discovered conditions are also “silent” or lacking in overt symptoms described by patients: many participants in our clinician study viewed clinical silence as a necessary condition for incidental discovery (data not shown). The participants in the clinician study cited a few examples of these “silent” conditions that have clear health consequences: occult malignancies will continue to progress into more extensive cancers, and “silent” MIs may lead to additional ischemic injury to the heart. One key feature distinguishing incidentally discovered conditions that require a response and those that do not require a response is the clinicians’ belief in the prognostic significance of the condition. In the clinician study,



most participants endorsed beliefs that SBI can lead to subsequent symptomatic stroke, a potentially disabling illness. This risk of symptomatic stroke needs to be confirmed in future studies of patients with incidentally discovered SBI. However, despite this belief, uncertainties regarding the nature of incidentally discovered SBI and appropriate management strategies appeared to lead to wide variation in clinicians' recommendations for patients. There may be subtypes of incidentally discovered SBI (e.g. perioperative) that are unlikely to portend a high risk of subsequent symptomatic stroke and subtypes where therapies proven for secondary prevention of stroke may be potentially harmful (e.g. SBI detected in the setting of intracranial hemorrhage) or unlikely to provide benefit due to competing risks (e.g. terminal brain malignancy). However, based on the findings of the patient interview study, there are patients with whom clinicians share the diagnosis of SBI and whom clinicians may believe are eligible for stroke prevention. It is probable that some of these patients closely resemble patients with SBI in studies of neuroimaging-screened patients who have increased risk for symptomatic stroke and dementia, but this remains to be confirmed in future studies. Furthermore, the heterogeneity of clinical practices suggested by these two studies needs to be confirmed in a broader, quantitative analysis of clinicians' practices in the setting of incidentally discovered SBI. Nonetheless, this wide practice variation is suboptimal for these patients who are considered potentially eligible for stroke prevention therapies as they may be currently undertreated or overtreated. In order to improve care for these patients with incidentally discovered SBI, future research will need confirm the prognostic significance of this form of SBI. If these are clinically significant, clinicians will need to overcome the

psychological barriers related to “incidental” findings and “silent” conditions in order to optimize the care of these patients.

These studies have several strengths. First, the use of individual qualitative semi-structured interviews allow for a rich exploration of the thought processes, beliefs, and attitudes of clinicians and patients in the setting of the incidental discovery of SBI. Alternatively, quantitative analyses would not provide sufficient explanation for the reasons and decision making leading to actions exhibited by clinicians and patients. Second, our use of purposeful sampling and multiple strategies for recruitment of patients with incidentally discovered SBI allowed for diversity in participant characteristics that might influence their perspectives. Third, the research team represented clinicians and researchers from multiple specialties (internal medicine, vascular neurology, and radiology) in order to minimize potential bias in the conduct of the study, including the development of the interview guides.

The studies have several limitations as well. First, as these are qualitative studies with small sample sizes, the participants were not truly representative of all practicing clinicians encountering patients with SBI or patients with incidentally discovered SBI. In particular, the patient participants likely represent a select group of individuals perceived to be eligible for stroke prevention treatments. The perspectives of this group, however, are highly relevant for the development of treatment studies as this group represents the target population for eligible recruitment into these studies. Second, these studies were not accompanied by a quantitative study to further explore the practices of clinicians or

the behaviors of patients. However, a quantitative assessment of clinicians' practices in response to incidentally discovered SBI will soon follow, and its design is informed by the findings of these two studies.

## **CONCLUSIONS**

Incidentally discovered SBI is an understudied condition that likely carries significant risk of adverse health consequences for patients. The findings from these studies suggest an urgent need for studies further defining the condition, assessing outcomes, and testing treatments for incidentally discovered SBI. Future symptomatic stroke and dementia are the most salient outcomes identified by patients, and clinicians endorsed observational comparative effectiveness studies as a pragmatic approach to studying treatment for patients with incidentally discovered SBI.

## **Chapter 5**

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