Pre-Hospital Diagnostic Interval in Cancer Diagnosis: What Do We Know?

Lesleigh A. Kowalski and Matthew J. Thompson

Department of Family Medicine, University of Washington

Author Note

We have no known conflict of interest to disclose.

Correspondence concerning this article should be addressed to Lesleigh A. Kowalski. Email:

lkowalsk@uw.edu

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Introduction

Cancer is the second leading cause of death in the United States of America (USA) with approximately 609,360 deaths from cancer expected in 2022 (Islami et al., 2021). Prognosis often correlates with the stage at diagnosis, with fewer curative treatment options for most later stage cancers (Moyer, 2014). For example, lung cancer leads to the most deaths out of all cancer-related deaths, and most people present at an advanced stage with only 15% diagnosed at stage I when it is highly curable (Andreano et al., 2018; Corner, Hopkinson, & Roffe, 2005; Cifu & Davis, 2014; Moyer, 2014; Siegel et al., 2017). An early diagnosis can be as effective as chemotherapy in those with moderate delays (Guide to cancer early diagnosis, 2017). Identifying individuals with cancer before they are aware of symptoms provides a valuable way of early cancer detection, however most cancers are not detected through recommended screening programs (Sarma et al., 2020), but rather as a result of presentation to health care providers. To promote earlier diagnosis and thus improve chances or better outcomes, it is imperative to identify deficiencies in diagnosis where interventions could be directed, including delays in individuals' cancer journeys.

In the context of this paper, the pre-hospital diagnostic interval refers to the period prior to receipt of a cancer diagnosis. An assumption of the pre-hospital period includes individuals discovering a symptom, making the decision to act on this, and visit a health care provider (HCP) who then pursues diagnostic investigations and specialty referral, leading to a diagnosis followed by the appropriate treatment. However, this linear path to diagnosis is the exception rather than the rule and people may endure a more circuitous journey (Walter et al., 2012). The pre-hospital period therefore often comprises a zigzag of HCPs, inconclusive tests, and vague symptoms that

are challenging for patients and providers alike. Furthermore, while cancer is common at a population level, it is generally a rare event for the individual HCP (Hamilton, 2010), which limits reinforcement of optimal diagnostic and investigative practices or skills, and thus a more complicated pre-hospital period. Before diagnosis many patients experience a period of denial, lack of time or resources to seek health care advice, and to receive diagnostic confirmation. This phase can last years, often leading to an advanced diagnosis with a corresponding grim prognosis.

Consider this case: A 63-year-old male presented to his primary care physician for two years with progressing non-specific symptoms. These symptoms included fatigue, a decrease in participation in daily activities, mood changes, shoulder pain, and shortness of breath. The provider repeatedly prescribed antibiotics for suspected bacterial pneumonia, with little improvement in symptoms. Suddenly the man was rushed to the emergency department with severe abdominal pain. Emergency surgery showed metastasized cancer perforating his small intestines. Pathology indicated the origin of his cancer was lung, specifically stage IV non-small cell lung cancer. He died six weeks later.

Although anecdotal and representative of one individual's experience, this case illustrates several themes which are widely documented in the literature around early detection/delayed diagnosis of cancer: non-specific symptoms, repeat presentations to an HCP, diagnostic uncertainty, and finally an emergency presentation (Zhou et al., 2017). Early detection is not merely about more time prior to a similar prognosis, it leads to increased quality of life, improved survival rates, and less expensive treatment compared to later stage diagnoses (Gildea et al., 2017; Guide to cancer early diagnosis, 2017; Neal et al., 2015; Yabroff et al., 2021). For example, breast cancer medical costs in one year after their diagnosis were $60,637, $82,121,

$129,387, and $134,682 for disease stage 0, I/II, III, and IV, respectively (Blumen et al., 2015). Collectively, the total patient economic burden in the USA due to cancer was $21.09 billion in 2019 (Yabroff et al., 2021). In addition to the economic benefit of earlier detection, a systemic review of time to diagnosis and cancer outcomes found that in most cancer types there is an improved quality of life with earlier diagnosis (Neal et al., 2015). Given both the economic benefit and personal benefit of earlier detection, policy and clinical practice initiatives should focus on the earlier detection of cancer to improve the collective well-being and health of people with cancer.

In countries outside of the USA, quality benchmarks define expected standards in the pre-diagnosis phase of cancer for various intervals along the diagnostic pathway; yet these are lacking in the USA. For example, United Kingdom (UK) guidelines recommend an interval of one week for referrals, in Canada less than 30 days from the onset of symptoms to treatment, and 42 days for referral to treatment in Denmark (Jakobsen et al., 2013; Kim et al., 2016; Singh et al., 2010). England created the 2-week-wait referral pathway to expedite those people needing prompt investigation due to signs/symptoms of cancer, which has been associated with decreased mortality (Koo et al., 2021). Denmark designed multidisciplinary clinics for rapid clinical investigation of people with non-specific symptoms (Vedsted & Oleson, 2015). New Zealand and Spain also introduced fast track programs for suspected cancer (Koo et al., 2021). The World Health Organization set a goal of 90 days from symptom onset to starting treatment (Guide to cancer early diagnosis, 2017). The purpose of this paper is to review the state of the current literature in the USA concerning the challenges and opportunities around improving early diagnosis of cancer.

For clarification purposes, the following operational definitions are used:

- *Detection:* refers to the process of determining a cause of ill-health, marked by imaging or other testing performed to diagnose cancer.
- *Diagnosis:* refers to the point at which a person receives a cancer diagnosis, and may include imaging, biopsy, or other procedures.
- *Early detection/diagnosis*: cancer diagnosed at the earliest possible stage. We use the World Health Organization's cancer control components that explicitly differentiate early detection and screening (Guide to cancer early diagnosis, 2017).
- *Screening*: refers to detection of cancer in an asymptomatic population (Moyer, 2014; Guide to cancer early diagnosis, 2017).
- *Delayed diagnosis*: for the purposes of this paper, this term refers to cancer diagnosed at stage III or IV, however, the word 'delay' is used sparingly due to subjectivity of the meaning (Walter et al., 2012).
- *Diagnostic pathway*: the events leading up to a diagnosis of cancer, encompassing the onset of cancer-related symptoms, cancer screening, or cancer-related investigations (Renzi et al., 2019).

Early detection and screening efforts are part of overarching cancer control goals (prevention, early diagnosis and screening, treatment, palliative care, and survivorship care) to reduce premature mortality and effectively utilize resources (Guide to cancer early diagnosis, 2017). Although all five aspects of comprehensive cancer control are vital, this paper's focus remains solely on early detection in the USA to examine current research, interconnected socioeconomic variables, and influence of the USA's unique healthcare system on cancer detection and prolonged diagnostic intervals.

Epidemiology of Pre-Hospital Diagnosis of Cancers

The most common types of cancer differ for men and women. These cancers possess varying diagnostic pathways and prognostic outcomes. One commonality between all these cancer types is that when each cancer is found at an early stage, the patient has improved chances of survival. For women, the five most common types of cancer are breast, lung and bronchus, colorectal, uterus, and thyroid (Islami et al., 2021). For men, the five most common types of cancer are prostate, lung and bronchus, colorectal, urinary bladder, and skin melanoma (Islami et al., 2021). The most common cancers are not necessarily the deadliest. Cancer types causing the most cancer-related deaths include, in order of most deadly: lung, breast, colorectal, and pancreas for females, and lung, prostate, colorectal, and pancreas for males (Islami et al., 2021). Lung cancer is the first leading cause of cancer-related death in men and women in most racial and ethnic groups (Islami et al., 2021), with 5-year survival rate survival rates of 64% for localized stage and 8% for distant stage non-small cell lung cancer (NSCLC), and 29% localized and 3% distant stage small cell lung cancer (SCLC) (Islami et al., 2021). Breast cancer is the second leading cause of cancer-related death in women with 5-year survival rates of 99% for localized cancer and 29% for distant cancer (Islami et al., 2021). Prostate cancer's 5-year survival rate is 99% for localized cancer and 31% for distant cancer (Islami et al., 2021). Colorectal cancer (CRC) 5-year survival rates are separated into the colon: 91% for localized cancer and 14% for distant cancer; and rectum: 90% for localized cancer and 17% for distant cancer (Islami et al., 2021). Survival rates for pancreatic cancer range from 42% for localized cancer to 3% for distant cancer (Islami et al., 2021). Knowing the most common and deadliest forms of cancer informs how the USA can prioritize its early detection design (Koo et al., 2021).

Cancer Screening

Screening is one component of early detection strategies that impacts the pre-hospital diagnostic interval by attempting to detect early-stage cancers in target populations. Only four cancer types have screenings recommended by the United States Preventive Services Task Force (USPSTF) with an A or B grade, including lung, breast, colorectal, and cervical (Cancer trends progress report, 2022). Other screening modalities exist for ovarian and prostate cancer, yet these are not implemented at a population level due to lack of evidence for mortality reduction (Grossman et al., 2018; Torre et al., 2015). When discussing cancer screening, it is imperative to note screening is intended for asymptomatic individuals and if a patient is eligible for a cancer screening while simultaneously showing symptoms, the imaging or procedure then received would need to be coded for diagnostic purposes. Additionally important to consider is that a screening must extend the life of a person beyond their predicted cancer-related death, not simply increase the length of time that they possess knowledge of their diagnosis (Juth & Munthe, 2012; Mukherjee, 2010). Screening is an entire process, rather than a sole event, which includes informing a target population of their risk, inviting them to participate, and ensuring results are reported timely and accurately, appropriate confirmatory tests for those screening positive, and cost-effective treatment options if needed (Guide to cancer early diagnosis, 2017). Prior to promoting cancer screening services, a health system needs to first ensure an early diagnosis and treatment capacity is in place (Guide to cancer early diagnosis, 2017).

Screening rates vary with cancer type and various individual or population characteristics. Screening rates are relatively low among eligible participants, especially for low dose computed tomography (LDCT) lung cancer screening (LCS) in which only 4.5% of eligible adults receive screening (Cancer trends progress report, 2022). This is partly due to variation in

Medicaid coverage by state (Rai et al., 2019), as well as HCPs uncertainties regarding the risk/benefit ratio of LDCT LCS (Henderson et al., 2017; Zeliadt et al., 2018). Indeed, guideline concordance of LDCT for lung cancer screening is poor given only half of primary care providers indicate awareness of the USPSTF lung cancer screening recommendations, as it is a relatively new recommendation compared to other cancer screening initiatives (Li et al., 2018). The estimated uptake of mammography for breast cancer screening is much higher than LCS. Among Medicare beneficiaries it is approximately 60%, with higher rates of screening found in metropolitan areas compared to rural areas, and a slightly higher average participation rate of 76.4% with women aged 50-74 (Cancer trends progress report, 2022; Heller et al., 2018). In 2019, colonoscopy for colorectal cancer screening demonstrated a participation rate of 67.1% of eligible participants and 73.5% of women aged 21-65 received cervical cancer screening (Cancer trends progress report, 2022). While increasing screening rates (and decreasing disparities in screening) would improve cancer detection, this is not a replacement for early detection – only four cancer types have screening recommendations in the USA, screening uptake is variable, and screening is only applicable to individuals within certain age (or risk) groups, and at prescribed intervals. Even with 100% guideline-concordance of screening rates, 82% of all cancers would require early detection via another method (Sarma et al., 2020). This reinforces the World Health Organization's dual emphasis on both early detection and screening to reduce pre-hospital delays.

Challenges with Clinical Recognition of Cancers

Symptoms

Despite screening efforts, most cancers are diagnosed after individuals experience symptoms and present to a health care provider (Leijssen et al., 2020; Sarma et al., 2020), and

therefore early detection efforts inevitably should focus on symptoms (Koo et al., 2021). Rather than summarize all cancers and their symptoms, this paper will focus on the dyad of non-specific symptoms, of which an estimated 50% of patients present with (Koo et al., 2021), and alarm/red flag symptoms. Cancers that present with vague, non-specific symptoms without typical alarm symptoms are more difficult to diagnose and often correlate with more advanced stages at diagnosis (Dobson et al., 2014; Macleod et al., 2009). This is noteworthy from a public health standpoint and for HCP education. For example, it is largely understood in public health perceptions that a lump found in the breast requires immediate medical attention (Burgess et al., 2001; Quaife et al., 2014). However, cancer alarm symptoms are not necessarily indicative of cancer, as many people report "cancer alarm symptoms" without having cancer (Svendsen et al., 2012; Vedsted & Olesen, 2015). Nonetheless, cancers with "classic" or alarm symptoms demonstrate a shorter diagnostic interval (Koo et al., 2017; Macleod et al., 2009; Quaife et al., 2014) due to increased awareness about the meaning of these symptoms. Alarm symptoms are typically noticeable to the individual, including hematuria (blood in urine), hemoptysis (coughing up blood), dysphagia (difficulty swallowing), rectal bleeding, palpable masses, or suspicious skin lesions; these alarm symptoms correlate with decreased wait time for help-seeking behaviors (Jones et al., 2007; Maconi et al., 2008; Quaife et al., 2014).

Cancers with vague, more ambiguous presentations have historically been referred to as "silent killers" due to the perception that symptoms are unnoticeable until an advanced stage (Corner et al., 2005; Goff, 2022; Goff et al., 2004). This belief may limit patients' awareness of symptoms and HCP's consideration of cancer at an earlier stage if a patient presents with such complaints. Lung, ovarian, prostate, and pancreatic cancer all show evidence of (at least initially) nonspecific/ambiguous symptom presentation. The most common symptoms of lung cancer in

the two years prior to diagnosis are cough, shortness of breath, and fatigue, which are not uncommon symptoms in many benign conditions making lung cancer especially difficult to detect (Hamilton et al., 2005; Lyratzopoulos et al., 2014; Zigman Suchsland et al., 2022). However, research shows positive symptoms can be seen throughout the stages of lung cancer: people diagnosed with stage I or II exhibit similar symptoms as those diagnosed with stage III or IV (Guldbrandt et al., 2017; Zigman Suchsland et al., 2022) although the symptom burden may be higher in a more advanced stage (Iyer et al., 2014). In ovarian cancer, the most common symptoms are abdominal bloating, abdominal pain, and early satiation (Goff, 2012). The most common symptoms of pancreatic cancer are jaundice, abdominal or back pain, and weight loss or poor appetite (American Cancer Society, 2022). Symptoms associated with prostate cancer include problems urinating, blood in the urine or semen, and erectile dysfunction (American Cancer Society, 2022). Brain cancer may present with a combination of worsening headaches, nausea, vomiting, blurred vision, balance problems, personality or behavior changes, seizures, or drowsiness (Grant et al., 2020). Separately, the symptoms are vague and indicative of a myriad of other conditions yet collectively they may indicate concerning underlying disease, thus symptom awareness campaigns should begin with the symptoms of the deadliest cancers (Koo et al., 2021).

Comorbidities

Three out of four patients with cancer also possess a diagnosis of another chronic disease at the time they are diagnosed with cancer, many of which share the same non-specific symptoms as that of several cancers (Koo et al., 2020b; Ritchie et al., 2017; Swann et al., 2018). Conflicting research exists determining whether comorbidities lead to a shorter or longer diagnostic interval, with reasons ranging from a greater contact with the healthcare system

(shorter interval) and intersecting symptoms (longer interval) (Renzi et al., 2019). The difference tends to be the type of cancer. For example, the symptoms of chronic obstructive pulmonary disease (COPD) overlap with the symptoms of lung cancer leading to diagnostic intervals up to twice as long in those with COPD (Smith et al, 2009). Similarly inflammatory bowel disease (IBD) may shadow the symptoms of CRC (Mounce et al., 2017). Aside from the presence of symptoms, certain comorbidities increase the risk of cancer diagnosis, such as obesity, diabetes, and some chronic infections due to underlying biological mechanisms (Extermann, 2007). Simultaneously increased comorbidity may lead to a later stage at diagnosis (Renzi et al., 2019), likely due to the difficulty in differentiating between a benign and malignant cause in people with multiple ongoing symptomatic diagnoses. People with severe disability and psychiatric conditions may also endure a prolonged diagnostic interval and are also less likely to participate in cancer screening programs (Renzi et al., 2019).

Categorizing Types of Delay

The word ‘delay’ is often misused within cancer detection literature and lacks a uniform definition, leading to subjective judgements (Dobson et al., 2014; Walter et al., 2012). In most articles, delay is broadly defined as being diagnosed with a late-stage cancer (either stage III or IV), or of a prolonged interval from clinical presentation to diagnosis lasting more than a certain period of time (Walter et al., 2012). To maintain clarity, this paper will utilize the terminology put forth by the World Health Organization (WHO) in their *Guide to Cancer Early Diagnosis* (2017) in which delay is categorized into three intervals: awareness and accessing care (patient interval), clinical evaluation, diagnosis, and staging (diagnostic interval), and access to treatment (treatment interval).

The patient interval component includes two components: the appraisal interval, the period in which a patient grows aware of an issue or change in their body and appraises the severity, and the health-seeking interval, in which one attempts to access care due to exhibiting symptoms (Guide to cancer early diagnosis, 2017). The patient interval has been called patient delay in the past, yet the suggestion is to move away from this wording as it does not incorporate the numerous contributing factors, such as geographical access, economic access, or societal and/or gender expectations within a culture that influence access to care (Guide to cancer early diagnosis, 2017). Therefore, the term patient interval provides a more holistic representation of the numerous factors that may prevent a patient from seeking timely care.

The diagnostic interval component, sometimes referred to as a system or provider delay, includes the HCP interval, which involves clinical evaluation, diagnosis, and staging, and referral for treatment (Guide to cancer early diagnosis, 2017). This phase includes detection as defined above. For the purposes of this paper, the emphasis will be placed on system factors and the doctor interval up to the point of cancer staging and referral for treatment.

Pre-hospital Factors Impacting Diagnosis

As mentioned above, the patient interval broadly refers to patient awareness and accessing care (Guide to cancer early diagnosis, 2017). The following section delves into more detail regarding specifics of the patient interval, such as symptom appraisal, health literacy, and help-seeking.

Patient Interval

The Modified Andersen Model of Total Patient Delay further defined the symptom appraisal period. Based on the Psychophysiological Comparison Theory, which assumes people

are motivated to maintain a psychophysiological equilibrium and will seek explanation for unexplained signs and symptoms (Andersen et al., 1995), the Modified Andersen Model of Total Patient Delay offers a descriptive model of observing delays in the patient/provider continuum (Walter et al., 2012). This model further breaks down the stages into appraisal, help-seeking, diagnostic, and pre-treatment with continuous processes occurring throughout the delay (Walter et al., 2012). Two vital aspects to consider when applying the Modified Andersen Model of Total Patient Delay are that it is used to inform the context of patient/provider delays rather than predict outcomes, and it demonstrates the path to diagnosis is not a linear process. The evolution of symptoms often over prolonged periods of time, with intervening health care contacts and diagnostic tests, is particularly marked for many cancers, unlike more acute conditions such as acute coronary syndrome.

The symptom appraisal period is of the utmost importance as most cancers are diagnosed following clinical presentation with symptoms rather than following screening (Sarma et al., 2020), therefore symptom awareness and health literary are salient in facilitating cancer detection. A meta-ethnography identified themes within the symptom appraisal period of patients later diagnosed with cancer, including symptom detection, initial symptom interpretation, symptom monitoring, social interactions, emotional reactions, priority of seeking medical help, appraisal of health services and personal-environmental factors (Khakbazan et al., 2014). This process provides additional understanding and simultaneous complexity to understanding how people experience the onset of a potential symptom. Emotional reactions, such as denial, fear, and embarrassment, are frequently cited as reasons for patients delaying access to care; for example, smokers who were later diagnosed with lung cancer felt fear about being negatively perceived by HCP due to their smoking history (Corner et al., 2005; Fish et al., 2015; Kotecha et

al., 2021; Kowalski, 2021). Social interactions such as discouragement from friends/family to go to an HCP, perhaps due to poor prior experiences, may also contribute to possible delays; however, research demonstrates men are more likely to attend an HCP appointment for cancer symptoms because of family encouragement than on their own accord, which indicates the importance of considering cultural nuance (Fish et al., 2015; Khakbazan et al., 2014; Unger-Saldaña & Infante-Castañeda, 2011). Some individuals experience a late-stage diagnosis due to the perception that their symptoms are not indicative of a serious underlying disease yet rather for lifestyle reasons, for example individuals without a history of smoking later diagnosed with lung cancer (Al Achkar et al., 2021; Corner, Hopkinson, Fitzsimmons, Barclay, & Muers, 2005; Corner, Hopkinson, & Roffe, 2005).

Help-Seeking

Whether or not an individual seeks help is multifactorial. An individual first needs to recognize the symptom as being problematic, demonstrate the ability to navigate the healthcare system well enough to identify a provider and make an appointment at a convenient time, possess both the time and financial resources to visit an HCP, and ultimately make the decision to attend an appointment. Certain factors may act as a barrier or facilitator along the way, ranging from an individual's social support system and whether they are being encouraged or discouraged from seeking help, their psychological state, or to logistical reasons such as possessing a mode of transportation (Fish et al., 2015; Khakbazan et al., 2014; Koo et al., 2021; Unger-Saldaña & Infante-Castañeda, 2011). A plethora of cultural circumstances may facilitate or block each individual attempt at seeking help, such as religious commitment, help-seeking attitudes, and stigma (Brenner et al., 2018; Li et al., 2014). Others may avoid help-seeking due to distrust in HCPs because of the historical context of racism, medical experimentation, and

unequitable treatment in minority populations, especially Black and Native American communities (Mullins et al., 2019; Nuriddin et al., 2020; Washington, 2006). Research of people with cancer shows that certain events prompt help-seeking behavior, such as symptoms that are new or changing (Al Achkar et al., 2021; Renzi at el., 2019). Factors that consistently prolong help-seeking behavior include certain comorbidities as people with mental health disorders, such as depression, and diabetes are more likely to be diagnosed with late-stage cancer (Renzi et al., 2019).

Societal and/or gender expectations within a culture influence a person's access to care and help-seeking behavior. In gender-normative terms, women tend to suppress their own symptoms to care for their family, thereby prolonging their inevitable cancer diagnosis (Burgess et al., 2001). However, men are encouraged to portray stoicism and self-reliance in which help-seeking behaviors are frowned upon (Brenner et al., 2018). Men are more likely to seek help from a religious advisor rather than an HCP (Crosby et al., 2012). Once within the healthcare system, similar cancer symptoms between women and men may be perceived differently by providers, also leading to a longer diagnostic pathway (Lyratzopoulos et al., 2013). Women often feel they are not listened to by HCPs, report more barriers to receiving a colorectal cancer diagnosis than men (Brewer et al., 2020), and female complaints of pain are not taken as seriously (Chen et al., 2008); although men demonstrate less accurate symptom interpretation and embarrassment in help-seeking (Fish et al., 2015). To address these often-unconscious biases, early cancer detection research should reach beyond the patient/provider dyad and focus on cultural and social dimensions to health seeking behavior (Unger-Saldaña et al., 2011).

Health Literacy

Help-seeking and health literacy behavior are intertwined, as one must understand bodily changes and know how to navigate the healthcare system to seek help. The impact of health literacy in pre-hospital diagnostic interval is common among many conditions, including cardiovascular events, sepsis, and cancer. Health literacy affects how patients perceive their own health-related information and participate in the greater healthcare system (Cornett, 2009; Humphrys et al., 2017; Sørensen et al., 2012). Low health literacy is associated with low cancer screening uptake (Humphrys et al., 2017), which may also lead to later, symptomatic cancer diagnoses when the asymptomatic cancer screening window has passed due to disease progression. Furthermore, the complexity of cancer screening decreases patients' engagement in the discussion due to low health literacy (Amalraj et al., 2009). The failure to recognize symptoms due to low health literacy is also an issue (Kotecha et al., 2021). A systemic review of cancer literature indicated accurate identification of one's own symptoms related to decreased patient interval time (Petrova et al., 2020); for example, an inability to differentiate between symptoms such as heartburn, reflux, indigestion was associated with a later diagnosis of esophageal or gastric cancer (Humphrys et al., 2020). In contrast, attributing symptoms to cancer as a potential cause decreases the patient interval (Petrova et al., 2020). If a person is unaware a symptom is problematic, they may not engage in help-seeking behaviors. People are less likely to seek help with symptoms attributed to "lifestyle" (Corner et al., 2005), such as experiencing shortness of breath and smoking. However, others present symptoms to providers without realizing the symptoms represent illness (Walter et al., 2012). Low health literacy may also manifest as an assumption that simultaneous symptoms are unrelated, as seen in patients later diagnosed with cancer (Corner et al., 2005; Koo et al., 2020a). Therefore, public awareness is a

key parameter of early diagnosis in that patients need to attend to symptoms of cancer and receive the appropriate education on what constitutes a worrisome symptom as well as the curability of many early-stage cancers (Guide to early cancer diagnosis, 2017; Petrova et al., 2020).

Informed and shared decision-making (SDM) falls within the broad concept of health literacy. The four stages of informed decision making are awareness, perception, evaluation, and decision making (van der Heide et al., 2015). This framework helps to deconstruct specific areas of intervention for increasing health literacy by considering opportunities to increase awareness, inform perception, improve one's evaluation, and refine decision making through patient education initiatives and the provider/patient interface. SDM between an HCP and patient is vital, and evidence of such conversations is even mandated for certain procedures, such as lung cancer screening (Rai et al., 2019). People who participate in formal SDM visits later experience less regret and more confidence over their decisions (Søndergaard et al., 2019). Health literacy is woven within the provider/patient interface, as it exists in a patient's skills in not only appraising their symptoms intrapersonally but also in describing their symptoms interpersonally. Significant weight needs to be placed upon the provider/patient interface given the power it possesses to shift the trajectory of a patient's cancer journey. These encounters need to be a major focus of early cancer detection research in the clinical setting (Singh et al., 2013).

Diagnostic Interval

System factors are extremely important within an increasingly complex healthcare environment, and system delays can occur from scheduling delays, policies, or procedures (Singh et al., 2010). For example, in people with CRC a median interval of 123 days was found after a referral for a colonoscopy to completion of the procedure (Singh et al., 2012). This was

attributed to system issues, such as inefficient referral and scheduling processes and wait times for gastroenterologists (Singh et al., 2012). Prolonged time from the first diagnostic test to receipt of a definitive diagnosis is also an illustration of the diagnostic interval as well, indicating an overall lack of communication between the healthcare system and the patient and/or inefficiencies in diagnostic work ups (Gildea et al., 2017). Organization and delivery of healthcare may be a greater contributor to delayed diagnoses in cancer than provider performance (Lyratzopoulos et al., 2014). However, the USA lacks clinical quality measures in the diagnostic interval to aid in determining if providers and systems are performing to a benchmark or not. A recent study from Washington state attempted to define a clinical quality measure for lung cancer, yet more research is needed (Zigman Suchsland et al., 2022).

Provider-caused prolonged intervals are attributed to misdiagnoses, failure to recommend follow-up tests, or misinterpreting symptoms (Burgess et al., 1998). The provider diagnostic continuum includes perception, comprehension, forecasting, and choosing appropriate actions (Singh et al., 2011). Examples of these applied to lung cancer included failing to notice weight loss over time (misperception), inaction or inappropriate action such as attributing symptoms to a less severe cause (comprehension), failing to plan the next step both in disease progression and system function (forecasting), and ordering necessary tests in a timely manner (choosing appropriate action) (Singh et al., 2011). A study comparing videos of patient/provider encounters with providers' medical record documentation in patients with possible upper gastrointestinal cancer, indicated more misalignments than alignments in symptom interpretation, demonstrating a gap between what a patient communicated and what the providers documented (Hardy et al., 2022). Similar results were found when examining a disconnect between patient and provider recorded symptoms in individuals with colorectal cancer (Högberg et al., 2020).

HCPs' misinterpretation of non-medical descriptions of symptoms may lead to missed opportunities and thus delayed diagnosis (Hardy et al., 2022; Singh et al., 2010). HCPs are less likely to specifically ask about non-disease specific symptoms and may not feel knowledgeable about how to ask questions regarding certain vague or functional measures (Wagland et al., 2017). This provides an opportunity for improvement in clinical practice. Moreover, some symptoms are experienced more by an individual's change in participation in activities (e.g., feeling less interested in a hobby, getting more tired walking), which can be overlooked by HCPs (Kowalski, 2021; Scott et al., 2019; Walter et al., 2019). However, disease-based symptoms are typically the focus during a healthcare visit (Menon et al., 2019).

Within the diagnostic interval exists the US healthcare system adds yet another layer of complexity, namely different payment models. The essential question is whether different payment models impact cancer detection, yet few studies have been able to answer this definitively. One such study which examined early detection of CRC among patients in the Veterans Health Administration (VHA) system, which is an integrated care model that emphasizes primary care and preventive services, found similar or better cancer outcomes than fee-for-service (FFS) Medicare (Landrum et al., 2012). This study also found an earlier stage of cancer at diagnosis in the VHA cohort compared to the FFS Medicare cohort among people with non-small cell lung cancer (Landrum et al., 2012). Health maintenance organizations (HMO) have been found to detect cancers earlier than FFS when those cancers are part of routine screening (Kirsner et al., 2010; Riley et al., 1994; Roetzheim et al., 2008). Further exacerbating the complexity is that Medicare beneficiaries may enroll in either an HMO or FFS coverage (Medicare enrollment, claims, and assessment data, 2022). Additionally, patients with managed care insurance tend to present to a healthcare provider at an earlier stage in the illness (Grewal et

al., 2021). While more research that specifically examines detection efforts and payment models is needed, it appears that models with a focus on primary and preventive care are better suited to detect cancer at an earlier stage.

Role of Primary Care

Primary care is often viewed as the gateway into healthcare: its clinicians the gatekeepers and referrers, the source of knowledge and leaders of health in the community, and the preventers of disease (Bodenheimer et al., 2010). Many individuals ultimately diagnosed with cancer will pass through primary care on their diagnostic journey, and thus the role of primary care in cancer control is pivotal (Rubin et al., 2015). Primary care faces many obstacles, such as provider shortages and provider burnout, long waitlists for appointments, and short appointment times (Agarwal et al., 2020; Ku et al., 2020). These issues are exacerbated in rural areas and since the start of the COVID pandemic (Ku et al., 2020). The high and growing need for primary care services juxtaposed with current challenges in primary care delivery have fueled multiple efforts at primary care expansion and alternative ways of delivering services, such as wider use of allied health providers, expansion of pharmacy-based clinics, and telemedicine—many of which have unknown impact on cancer detection.

Occupational therapists (OT), physical therapists (PT), and other allied health professionals can practice within their current scope of practice to provide services in primary care (Pyatak et al., 2019; Richardson et al., 2012; Role of occupational therapy in primary care, 2020). Opportunities exist to utilize allied health professionals such as OT's and PT's expertise in assessing impact of symptoms on functional outcomes to potentially support identification of patients with early non-specific symptoms of cancer, and, although not currently billable per policy, conduct shared decision-making counseling sessions to support lung cancer screening

(Kowalski et al., 2021; Pyatak et al., 2019). Furthermore, given the prevalence of comorbid chronic conditions of people later diagnosed with cancer, primary care can utilize OTs and PTs to monitor physical functioning as a health outcome in that population (Richardson et al., 2012). Integration of allied health professionals in primary care may alleviate the workload on primary care physicians and allow for a more holistic, multidisciplinary approach to primary care, which aligns with the three goals of healthcare reform (Berwick et al., 2008).

In order to effectively address cancer detection improvement, research should focus on methods to innovate primary healthcare, and expanding the provider team to include allied health professionals and new models of primary care delivery.

Impact of Inequities on Diagnosis

Disparities occur when observable differences exist between populations, such as race, ethnicity, sex, or socioeconomic status, often due to systemic inequities. This creates underserved populations as these groups of people tend to encounter difficulty accessing healthcare, often driven by social, economic, and geographic factors (Thompson, 2021). Inequities impact the pre-hospital timeframe that prevent people from accessing appropriate care, including those who live in rural areas, do not have health insurance, or have state-funded Medicaid, are people of color, and are women.

Geography

Where one lives greatly influences access to healthcare. Typically, those who live in metropolitan areas have improved access to healthcare due to proximity to large hospitals and academic medical centers. Geographical access also impacts cancer care specifically. In a 2015 review of literature, results demonstrated that the further a patient must travel from their home

the more advanced their cancer stage was likely to be (Ambroggi et al., 2015). Due to home-to-hospital travel requirements and fewer providers, access delay for cancer detection as long as six months has been documented in more rural areas within the USA (Nadpara et al., 2016). Additionally, areas in the USA with decreased access to healthcare may not receive the option for screening as frequently as more accessible areas, leading to even greater health disparities and inequities (Cook, 2018). For example, in Alaska, 44%-65% of people aged 55 to 79 lack access to a LDCT lung cancer screening center compared to the national average of 14.9% (Eberth et al., 2018). Older populations who live in rural USA, especially those in the Midwest, demonstrate a higher stage at diagnosis as well as a decrease in diagnostic access prior to receipt of a diagnosis (Nadpara et al., 2016; Primm et al., 2022). Geography does not only refer to the urban/rural dichotomy; individuals often minorities, who live in lower socioeconomic areas encounter higher risk factors for developing cancer, such as decreased access to healthy food choices, environmental hazards, and opportunities for physical activity, as well as less access to an HCP; these social determinants of health lead to greater inequalities in cancer (Alcaraz et al., 2020).

Economic Access

The unique healthcare system in the United States acts as both a facilitator and a barrier to access cancer detection services depending on one's economic means and health insurance type. Lower socioeconomic status increases the likelihood of an advanced cancer stage at diagnosis (Primm et al., 2022). Individuals who participate in state-sponsored health insurance, Medicaid, experience higher mortality related to cancer than those with commercial insurance, yet when individuals (who may have previously lacked any insurance) gain Medicaid coverage as a result of state Medicaid expansions, rates of advanced stage cancer decrease (Le Blanc et al.,

2020; Niu et al., 2013). Fourteen states have not expanded, meaning many people may unnecessarily receive delayed cancer diagnoses. Coverage with any health insurance is a strong determinant of cancer outcomes and people with private insurance are more likely to be diagnosed with early-stage cancer (Han et al., 2018; Robbins et al., 2015), than those who lack insurance. Simply by expanding Medicaid coverage the opportunity exists to promote earlier detection of cancer. Lack of healthcare insurance also impacts help-seeking behaviors, as people may delay going to an HCP due to fear of financial hardship, thus leading to a more advanced diagnosis and less treatment options (Patel et al., 2021). This fear is validated by research indicating approximately 2/3 of bankruptcy in the USA is due to medical costs (Shrime, 2021).

Individuals with Medicaid and Medicare are more likely to use the emergency department for care due to access issues than those with private insurance (Capp et al., 2014). Emergency department usage for eventual cancer diagnoses is associated with worse prognostic outcomes, worse patient experiences, and more advanced cancer stages, even when accounting for cancer stage and type (Elliss-Brookes et al., 2012; McPhail et al., 2013; Salika et al., 2018; Zhou et al., 2017). Expanded insurance coverage would be expected to lead to more ambulatory care detection, thus an earlier diagnostic cancer stage. This is partially due to the organization of screening services in ambulatory care (covered by Medicare), plus the opportunity for continuity of care (to detect changes in symptoms over time) and coordination of diagnostic and specialty care (Preventive & screening services, 2022). Medicaid covers screening services as well, however not every state Medicaid program covers the cost of all cancer screenings according to updated guidelines (Rai et al., 2019; State lung cancer screening coverage toolkit, 2022). As previously mentioned, lung cancer screening rates are very low; over half of those eligible for the

screening are either uninsured or received Medicaid, of which coverage of LDCT lung cancer screening varies by state (Jemal & Fedewa, 2017).

Race and Ethnicity

Research demonstrates several disparities exist between racial and ethnic groups regarding early detection, treatment, and survival. In most cancers, Black people are more likely to be diagnosed at Stage IV and die of cancer (Fabregas et al., 2022; Islami et al., 2021). In breast and ovarian cancers, minority women are more likely to be diagnosed at an advanced stage and endure higher mortality compared to White women (Ko et al., 2020; Primm et al., 2022; Torre et al., 2018). Similarly, Black men are diagnosed with a more advanced stage of prostate cancer and are three times more likely to die than White men (Fabregas et al., 2022; Hoge et al., 2020). People of Color are more likely to present with advanced-stage lung cancer compared with White patients (Islami et al., 2021). Racial disparities exist in screening participation as well; for example, a study of minority women in Chicago attributed nonadherence to breast cancer screening to lack of knowledge of resources, denial or fear, competing obligations, and embarrassment (Nonzee et al., 2015). These demonstrate any early detection initiative must prioritize reducing racial disparities in cancer detection. Equalizing early detection methods among all racial groups requires a multifactorial, systemic approach.

Pediatric Cancer Detection

Pediatric cancer causes more childhood deaths than any other disease, making it the second leading cause of childhood death after accidents (Childhood and adolescent cancer, 2022). Current evidence on detection of cancer in children shows conflicting conclusions regarding impact of diagnostic interval on survival; some research has shown improved survival and psychological outcomes (Brasme et al., 2012; Lethaby et al., 2013) and others found no

difference in outcomes based on length of time to diagnosis (Chen et al., 2017). Cancer in pediatric populations is rare which makes detecting cancer even more challenging than in adults. For example, the incidence rate of all childhood cancers is 19.1 per 100,000 compared to the incidence of just lung cancer in adults, which is 57.3 per 100,000 (Cancer statistic center, 2022). Due to the low incidence and complexity of pediatric cancer detection, few studies have specifically examined the diagnostic interval in pediatric cancers within the United States (Carberry et al., 2018).

In a US-based study examining diagnostic error in pediatric patients later diagnosed with cancer, researchers determined 28% of patients experienced diagnostic error that led to a prolonged diagnostic interval (Carberry et al., 2018). The primary reasons these errors occurred were due to inappropriate treatments (i.e., antibiotic prescription for assumed infection) and misinterpreted laboratory or imaging studies (Carberry et al., 2018). Type of cancer has also been found to impact time to diagnosis, with leukemia exhibiting the shortest diagnostic interval and brain and bone tumors exhibiting the longest diagnostic intervals (Chen et al., 2017). The evidence base in pediatric cancer demonstrates more rapid detection in urgent care and emergency department settings compared to primary care (Carberry et al., 2018); however unlike in adult cancer detection, this did not correlate to worse prognosis (Chen et al., 2017) and is attributed perhaps more to the availability of diagnostic capabilities (i.e., imaging opportunities) in emergency care settings (Carberry et al., 2018).

Disease-specific and health care system factors, as with adult cancer detection, also add to the complexity of pediatric cancer detection (Carberry et al., 2018); many issues overlap that lead to prolonged diagnostic intervals. This includes patient factors such as health literacy, provider factors such as difficulty attributing non-specific symptoms, and system factors such as

lack of insurance coverage or poor geographical access to pediatric specialists. However, factors that add to the complexities of pediatric cancer detection need to be considered, including the addition of the parent/provider relationship and concerns about over-testing children. Prolonged diagnostic interval related to the parent/provider relationship may be exhibited by providers not seeming to take parents seriously if they consider them to be a "worrier" or providers not trusting the expertise of the parents regarding their child (Clarke et al., 2014). Additionally, the combination of a plethora of common childhood illnesses many of which cause repeated symptoms and clinical presentations, with the very low incidence of cancer in this age group, presents a significant diagnostic challenge for pediatricians (Chen et al., 2017).

New Detection Technologies and Opportunities for Improvement in Cancer Detection

The healthcare system cannot rely solely on prevention to reduce cancer, as not all cancers are preventable, or emphasize screening as the only strategy to improved early detection for the reasons noted above (Guide to early cancer diagnosis, 2017). Culture needs to shift to promote earlier cancer diagnoses, including changes in political, administrative, clinical leadership, medical education and HCP support, and symptom awareness initiatives (Chowienczyk et al., 2020; Green et al., 2015; Vedsted & Olesen, 2015).

In this section, we focus on advances in diagnostic technologies that may complement these initiatives, to advance cancer detection in the pre-hospital settings. Diagnostic tests for cancer have in many ways barely advanced in many pre-hospital settings; almost no new biomarkers have been introduced in several decades for ambulatory care. Access to endoscopy procedures and advanced imaging remain the mainstay of diagnostic workup, but each has their challenges of cost, access and invasiveness. Wearable diagnostics and biosensors are gaining in production and utilization for some diseases such as cardiovascular, esophageal, and Parkinson's

disease, yet not as quickly for cancer diagnostics with the needed specificity (Hazra et al., 2021). HCPs want easier point-of-care detection opportunities utilizing technological advancement in order to streamline clinical care and provide more comprehensive services for their patients (Kowalski, 2020). Many options have been researched extensively, such as liquid biopsy, biosensors, artificial intelligence, and radiogenomics, yet none currently have robust evidence for implementation in pre-hospital settings (Haque, 2018; Phallen et al., 2017; Prabhakar et al., 2018). Still, opportunities to investigate cancer detection capabilities in wearable technology exist as technological advances occur rapidly. An important consideration, however, is that while some research focuses on the physical wearable technology, other research must simultaneously consider the imperative issues of equitable access, patient education, provider education, and cost effectiveness. Otherwise, the risk exists of further exacerbating disparities. Additionally, any point-of-care diagnostic test needs to follow the criteria outlined by the World Health Organization according to the acronym ASSURED, meaning tests should be affordable, sensitive, specific, user-friendly, rapid, equipment-free, and delivered (Land et al., 2019; Hazra et al., 2021). Fortunately, with the general acceptance of mobile phones and wearable devices, great potential exists to connect this technology with a targeted population for the purpose of cancer detection.

Wearable Technology

One potential area of cancer detection technology is wearable devices. A growing range of smart watches and wearable fitness trackers are now in common use and largely aim to support an individual's wellness and health goals (Cook et al., 2015). In addition, smartphones are increasingly fulfilling similar roles among a wider segment of the population, given the ubiquity of smartphone ownership. Wearable devices and smartphones monitor a range of

physiological parameters, motion and activity through various interfaces such as LED sensors, acoustics, accelerometers, gyroscopes, as well as from adhesive patches (Hazra et al., 2021). Some of the potential cancer-specific use cases include detecting changes in skin integrity or temperature for breast cancer detection, adhesive patches to monitor UV radiation to detect potentially cancerous cells, or wrist bands that may identify microRNA biomarkers for detection of optical cancers (Hazra et al., 2021; Shi et al., 2018). Monitoring of changes in body weight may be one area where simple technologies could provide evidence of unexpected weight loss as a possible indication of cancer (Nicholson et al., 2020; Nicholson et al., 2021). Other sensors that are in development for wearable devices could include ways of measuring hemoglobin (to detect anemia) or to detect jaundice but determining evidence for cancer diagnosis specifically will be challenging. Additionally, bioadhesive ultrasound technology is being studied as a means of providing continuous organ imaging, which poses possibilities of cancer detection in the future (Wang et al., 2022). Wearable technologies for the purpose of cancer detection are promising yet remain in the development phase and are not ready for public use (Ciui et al., 2018).

Liquid Biopsy

The potential to use samples of blood or other body fluids to detect cancer circulating tumor cells (CTC) has recently emerged as a potentially ‘game changing’ technology (Liu et al., 2021). In addition to CTC, other cellular components in liquid biopsy research include examining cell-free DNA, circulating tumor DNA, RNA editing, exosomes, and tumor educated platelets (Alimirzaie et al., 2019; Ullah, 2020). Circulating biomarkers may detect colorectal, pancreatic, breast, head and neck, prostate, and brain cancers (Tabore, 2019). Potential concepts that continue to be researched include peripheral vein collection via continuous sampling, which isolates circulating tumor cells with higher sensitivity than traditional phlebotomy samples (Kim

et al., 2019) and biosensors that can identify biochemical signatures within blood or other fluids, much like continuous glucose monitoring (Hazra et al., 2021). Several multicancer early detection (MCED) tests are undergoing trials for screening and diagnosis; challenges with initial evidence have been relatively low sensitivity which is challenging for low prevalence conditions (such as cancer). However, potential use of MCEDs as a supplement to other diagnostic tests (which could serve to elevate pretest probability of cancer) could mitigate this (Liu et al., 2021; Sala et al., 2020). The use of MCEDs in ambulatory care settings could also fundamentally transform the role of the primary care provider in early cancer detection, potentially reducing the need for some specialty services or diagnostics to investigate patients for suspected cancer and expediting diagnosis when an MCED indicates a potential tissue of origin. However, introduction of these tests could also serve to exacerbate health equity issues.

Machine Learning

Machine learning (ML), a type of artificial intelligence (AI), poses potential methods for increasing detection efforts utilizing software that employs past experiences to predict the future as provided by algorithms (Adamson et al., 2019; Liu et al., 2021). ML may be especially helpful with interpreting images due to the speed at which ML can accomplish this task from multiple subjects, ranging from patient to tissue to cells (Adamson et al., 2019; Giger, 2021). Researchers also attempt to combine these methods, for example combining ML with liquid biopsy for earlier cancer detection (Liu et al., 2021). This may help to prevent delayed diagnoses and increase access to care, for example, in geographic areas that lack qualified HCPs. AI can be used in three different manners, by acting as an aid to the primary radiologist, as a primary reader, and by replacing human observation altogether (Giger, 2021). Current research needs to focus on how to streamline the process to utilize ML as a primary reader to rule-out negative images thereby

allowing radiologists to focus on those images needing a more discerning interpretation (Giger, 2021). ML does come with cons though, such as a failure to properly consider darker skin types in skin cancer detection, which is seen in its homogenous data set and poses yet another example of racial disparity in cancer detection (Guo et al., 2021). Additionally, ML exhibits difficulty with earlier detection, compared to advanced stage imaging, when the subtle nuances between cancerous and non-cancerous cells even cause pathologists to disagree, thus increasing the potential for overdiagnosis (Adamson et al., 2019; Elmore et al., 2017).

Data Science

Mining written and coded data, rather than images, also demonstrates new frontiers in cancer detection research. One method of extracting data is natural language processing (NLP), in which algorithms capture narrative documentation from medical records rather than relying solely on Current Procedural Terminology (CPT) or International Classification of Diseases (ICD) codes. Recent projects outside of cancer detection demonstrate the ability of NLP to harvest significantly more symptom-based data recorded by HCPs compared to coded data alone (Lybarger et al., 2021). NLP has been applied to detect evidence of symptom signature in individuals later diagnosed with lung cancer, identifying a possible signal earlier than use of coded symptoms alone (Prado et al., 2022; Zigman Suchsland et al., 2022). This is an area ripe for continued exploration within early detection research as the data can illuminate often-overlooked trends in care provision and symptom progression (Prado et al., 2022; Zigman Suchsland et al., 2022).

Developing and testing predictive tools, rather than retrospective analyses, could also potentially be used to aid detection efforts, identifying trends and patterns in clinical signs, symptoms, lab tests and consultation patterns that are invisible to the individual HCP. Many

patients present with symptoms considered to be caused by cancer, yet most people will not have cancer, therefore predictive tools can assist HCPs to differentiate which patients to investigate further (Walter, 2021). The positive predictive value (PPV) is created by an algorithm that considers lifestyle factors (e.g., smoking, alcohol consumption), family history, combination of symptoms, deprivation index, age, race and ethnicity, and comorbidities (Hippisley-Cox & Coupland, 2015). This may appear as a simple risk stratification chart or a more detailed computerized algorithm. PPV has been used in the past to quantify signs and symptoms only (sans the other factors mentioned previously) to aid in clinical decision making in order to create a threshold for investigation (Del Giudice et al., 2021; Hamilton, 2009). Additionally, medical record data analyzed via AI has been shown to predict if someone will develop cancer using digital patient screening (Wang et al., 2019; Yeh et al., 2021).

Conclusions

To promote earlier detection of cancer, a systems approach needs to be considered utilizing multidisciplinary perspectives. Focus should be equally distributed among the main components discussed: patient awareness and accessing care (patient interval), clinical evaluation, diagnosis and staging (diagnostic interval), cancer screening, and technological advancements. Given the prevalence of racial inequities in cancer care, additional emphasis is needed for the populations that lack appropriate care. Mitigating strategies to address racial and ethnic inequities may include Diversity, Equity, and Inclusion (DEI) initiatives, robust public policy to directly combat disparities, and coordinated funding/use of resources in a shift from equity to justice (Tossas, 2021).

Additionally, the COVID-19 pandemic affected cancer detection in known and unknown ways. It is understood at this point that the pandemic reduced access to care, especially in the

initial months of shutdowns and employment loss, and postponed routine care. This led to delayed screenings, preventive care visits, and symptom follow-up care (Riera et al., 2021). What remains unknown is the true extent of this and how many more advanced stage diagnoses will rise (Hamilton, 2020; Riera et al., 2021).

Decreasing the pre-hospital interval in cancer detection requires a collective education effort across the patient, provider, and system continuum. Public education initiatives should focus on the curability of most cancers when detected early, the aggregate toll of multiple symptoms, cancer screening awareness, and how to access the healthcare system effectively. Cancer detection efforts from the UK may serve as a feasible and cost-effective guide for intervention and implementation (Sarma et al., 2022). Education for HCPs should include skills for improved communication with patients, the most up-to-date technological advancements, increasing HCP support, and cancer screening protocols. System-wide initiatives are needed to reduce referral delays, eliminate racial and ethnic disparities in cancer detection, and increase access to care through economic and geographic efforts. Technological advancements, such as wearable technology and liquid biopsy, pose potential to assist in early detection efforts as well, with possibilities in streamlining the care continuum between primary care, emergency medical services, and emergency department care. However, risk stratification will still be necessary to ensure the right technology interfaces with the right patient.

Within these initiatives, significant research opportunities exist to promote earlier detection of cancer. Based on this review of the literature, the most important research questions to reduce delays in cancer diagnosis are: How can racial and ethnic disparities be eliminated in cancer detection? What policies need to be created and/or changed to promote earlier cancer detection? How can cancer screening programs reach the highest risk populations? Can clinical

quality measures or benchmarks be developed that reduce cancer diagnostic intervals while balancing the risks of over-testing and overdiagnosis? How can health literacy be improved to reduce prolonged cancer diagnostic intervals? How can new technologies be applied to advance early detection efforts in ambulatory settings?

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