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Abstract

Serious bacterial infections are common clinical events that may serve as under-recognized markers of future malignancy risk. While the oncogenic role of select pathogens such as human papillomavirus, hepatitis viruses, and *Helicobacter pylori* is well established, emerging data suggest that a broader range of acute bacterial infections are associated with increased cancer incidence across multiple organ systems. This narrative review synthesizes current evidence linking serious bacterial infections to subsequent malignancy risk, highlighting both short- and long-term associations. Notably, several infection-cancer associations confer absolute risks that meet or exceed established screening thresholds. Based on these findings, we propose a pragmatic framework in which certain serious bacterial infections are considered sentinel clinical events that inform cancer risk stratification and targeted screening. Incorporating infectious history into routine clinical decision-making for cancer screening represents a potential paradigm shift, enabling earlier detection in otherwise underrecognized high-risk populations.

Introduction

Cancer remains one of the leading causes of morbidity and mortality worldwide, with over 2.1 million new diagnoses and 600,000 cancer deaths expected to occur in 2026 in the United States.[1] A substantial portion of these diagnoses are attributed to modifiable causes, with infectious pathogens accounting for approximately 20% of all tumors.[2] Several well-established pathogen-cancer associations have transformed clinical practice - Human Papillomavirus (HPV) and cervical cancer, Hepatitis B and C and hepatocellular carcinoma, as well as *H pylori* and gastric cancer.[3] These examples illustrate how infectious exposures can define high-risk populations and guide targeted screening strategies. However, emerging evidence suggests that the relationship between infection and malignancy extends far beyond these classic examples.Recent studies demonstrate associations between acute bacterial infections and subsequent cancer risk across multiple organ systems.[4]

Understanding the influence of serious bacterial infections (SBI) on carcinogenesis has important implications for cancer prevention, early detection, and risk stratification. This narrative review synthesizes the current evidence linking SBIs to long-term malignancy risk and proposes a clinically actionable framework for incorporating infectious history into cancer risk assessment. Just as *H pylori*-associated premalignant conditions now warrant surveillance even after eradication, we propose that certain SBIs may similarly identify patients who would benefit from enhanced cancer screening - a paradigm shift that enables earlier detection in otherwise underrecognized high-risk populations.

System	Primary Infection	Associated Malignancy	Quantitative Risk
Pulmonary	Mycobacterium tuberculosis (TB)	Lung	HR 3.32 (≥80 y: HR 92.8)

	Pneumococcal pneumonia	Lung	aHR 4.24
	Empyema / LRTI	Lung	SIR 2.67; aHR 3.2
Gastrointestinal	Appendicitis (>40 y)	Colorectal	10–24× increased risk
	Complicated diverticulitis	Colorectal	~40× increased risk
	Pyogenic liver abscess	Gastrointestinal	aHR 7.55
Genitourinary	Male UTI	Urinary tract	aHR 5.68
	Trichomonas vaginalis	Cervical	OR 5.23
	Acute cystitis	Genitourinary	SIR 7.67
Systemic	Anaerobic bacteremia	Colorectal	5–10× increased risk
	Endocarditis	Hematologic, liver	15–30× increased risk
	Gram-negative bacteremia	CRC, biliary, pancreatic	2.5–10× increased risk
	S. aureus bacteremia	Multi-organ	~1.5× increased risk
	Septic shock	Multi-organ (GI, lung, heme)	Increased global risk
Postoperative	Post-resection infections	Esophageal, CRC, breast	sHR 6.54; HR 4.94; ↓ survival (CRC 74.4% vs 68.1%)

Table 1. Association Between Infectious Exposures and Subsequent Malignancy Risk
HR = hazard ratio; aHR = adjusted hazard ratio; OR = odds ratio; SIR = standardized incidence ratio; CRC = colorectal cancer; LRTI = lower respiratory tract infection.

Pulmonary Infections

Lung cancer is the leading cause of cancer death globally.[5] While tobacco use remains a leading risk factor, a notable percentage of cases occur in individuals without a history of smoking. Furthermore, chronic infection-induced inflammation has emerged as a recognized driver of malignancy across multiple organ systems.[6] With over 1.5 million hospitalizations annually in the US due to pulmonary infections,[7] these SBIs may serve as sentinel clinical events, enabling identification of individuals at increased risk for subsequent malignancy and potentially offering a window for earlier malignancy detection (Table 1).

Tuberculosis

Pulmonary tuberculosis (TB) represents one of the most well-established infectious risk factors for lung cancer. In a population-based cohort study of more than 700,000 insured adults, lung cancer incidence among patients with TB was approximately 11 times greater than in those without TB (26.3 vs 2.41 per 10,000 person-years). After adjustments for sociodemographic variables, TB was associated with a hazard ratio (HR) of 4.37, which remained elevated (HR 3.32) after adjusting for COPD and smoking-related cancers (absolute risk 2.23% over six years vs 0.22%). COPD further increased the risk of both non-smoking-associated lung cancer (HR 6.22) and smoking-related malignancies (HR 15.5).[8]

These findings were reinforced by a systematic review and meta-analysis, which found a pooled standardized incidence ratio (SIR) of 3.20 for lung cancer among TB patients. Cancer risk was greatest within the first year following TB diagnosis (SIR 4.70), but remained elevated for at least five years, supporting both short and long-term oncogenic effects of TB-related pulmonary inflammation.[9] Given that the absolute risk exceeds the 1.3% threshold for screening,[10] we advise annual low-dose CT (LDCT) screening for patients with a history of TB.

Pneumococcal Pneumonia

In a population-based study of more than 22,000 patients with pneumococcal pneumonia and 88,000 matched controls, the incidence rate for lung cancer was 28.2 per 1,000 person-years compared to 8.7 per 1000 person-years in controls. Despite higher incidence risk ratios in younger patients, absolute risk rose with age and exceeded screening thresholds in older cohorts, with absolute risk exceeding screening thresholds in patients >46 years of age.[10] The majority of lung cancer diagnoses occurred within 1 year of pneumococcal pneumonia.[11] We therefore advise a one-time LDCT at 6-12 months post-diagnosis for those over 45 years of age.

Lower Respiratory Tract Infections and Empyemas

A study of over 500,000 adults aged 40 to 70 years found lower respiratory tract infections (LRTI) increased the risk of lung cancer (adjusted HR 3.22).[4] These infections were also associated with increased lung cancer mortality. Likewise, a longitudinal Scandinavian study demonstrated lung cancer in 3.0% of patients with prior pleural infection, compared to 0.6% of controls ($p < 0.001$).[12] 73% of lung cancers in this study were diagnosed within three months of infection, compared to only 6.9% among controls.[12] In a nationwide cohort of over 30,000 patients diagnosed with empyema, cancer risk remained elevated even after excluding diagnoses within one year.[13] We again advise a one-time LDCT at 6-12 months after hospitalization for a pulmonary infection for patients 46-80 years of age.

GI Infections

Gastrointestinal infections represent a substantial and growing burden. Acute appendicitis is the most common abdominal surgical emergency worldwide, with approximately 375,000 estimated cases annually in North America.[14] There are approximately 200,000 hospital admissions annually in the US for acute diverticulitis,[15] with an incidence of ~180 per 100,000 persons per year. The incidence of acute diverticulitis is increasing and is now 2-3 times higher than that of appendicitis in emergency departments.[16] Gallbladder disease affects approximately 20 million Americans annually, with 200,000 diagnosed with acute cholecystitis each year,

resulting in 120,000 cholecystectomies performed in the US annually.[17] Additionally, while the incidence of pyogenic liver abscess (PLA) is relatively low at 3.6 per 100,000 US residents, this corresponds to approximately 12,000 cases per year,[18] with incidence rising internationally.[19] Several of these infections are associated with an increased risk of malignancy and may warrant targeted post-infection screening (Table 1).

Appendicitis

While cancer of the appendix itself may be discovered following appendectomy, malignancy in more distal parts of the colon may be missed after an episode of acute appendicitis (AA). Multiple studies have demonstrated a higher risk of right-sided colon cancer after AA in patients > 40 years of age,[20-22] as high as ten times the risk of the general population,[20] with the elevated risk extending to 6-12 months post-appendectomy.[20-22] Although relative risk is increased in younger patients, absolute risk remains low and does not support routine screening in this population. Nonsurgical treatment of AA has also been associated with increased long-term incidence of colorectal cancer (CRC), with risk rising with age.[22]

The rate of serious adverse events from colonoscopy is approximately 0.23%.[23] Given that post-appendicitis CRC risk exceeds the threshold in patients > 40 years, clinicians should refer these patients for colonoscopy within 6-12 months of diagnosis For individuals ages 76 to 85 the decision to screen should be individualized, based on life expectancy, CRC risk, and personal preference, with screening not recommended after age 85.[24] For patients unable or unwilling to undergo colonoscopy, clinicians may consider alternative strategies such as fecal immunochemical testing or CT-based imaging.

Diverticulitis

Complicated diverticulitis is defined as diverticulitis associated with perforation, systemic inflammatory response, fistula, abscess, stricture, or obstruction.[25] The incidence of CRC with complicated diverticulitis is as high as 7.9%, compared to 0.2% in routine screening populations.[28] Accordingly, guidelines recommend colonoscopic evaluation within six weeks after diagnosis.[27] Risk appears clinically insignificant in patients less than 40 years old.[28] For uncomplicated diverticulitis, CRC risk remains elevated in patients aged 60-75, with rates increasing with age.[28] Recent negative colonoscopy does not eliminate risk in the immediate post-diverticulitis period.[29] We therefore advise colonoscopic evaluation within 6 weeks of diagnosis in patients > 60 years, with individualized decision making for patients over age 75.[24]

Acute Cholecystitis

A SEER-Medicare analysis[30] demonstrated that patients with cholangitis have increased relative risk of cholangiocarcinoma, though absolute risk remains <0.5%. Because the absolute risk remains below established screening thresholds,[31] routine cancer screening is not advised based solely on the history of cholecystitis, cholangitis, or cholelithiasis. One study found that cholecystectomy does not increase the risk of liver or pancreatic cancer.[32]

Pyogenic Liver Abscess

Though rare, the incidence of PLAs is rising[19] and it is among the SBIs most strongly associated with malignancy risk. Although PLA is associated with increased risk of several

gastrointestinal malignancies, the absolute incidence of most non-colorectal cancers remains below established screening thresholds.[34] For CRC, the aHR within 2 years of PLA diagnosis was 7.03. It remained elevated for at least 4 years with an aHR of 7.55,[33] supporting a persistent association between PLA and subsequent CRC diagnosis. Based on this, colonoscopy within 3-6 months of any PLA diagnosis is advised, with optional follow-up 2-3 years later, particularly if other underlying CRC risk factors coexist. Repeat testing can be deferred if PLA was secondary to cholangitis or cholecystitis.

Clostridium difficile

A retrospective study analyzing 78,863 *C difficile* patients found that the organism was associated with a decreased incidence of CRC (odds ratio [OR] 0.59). This finding suggests that not all bacterial infections are cancerous.[35] We do not advise enhanced screening based on this data.

Postoperative Infections After Malignancy Resection and Risk of Recurrence

A single-center retrospective observational study that examined transhiatal esophagectomy for adenocarcinoma of the esophageal gastric junction found that postoperative sepsis of any sort, including bacterial pneumonia and cervical or intra-abdominal abscesses, was a risk factor for increased one-year mortality (OR 7.22). Postoperative sepsis was also found to be a risk factor for one-year recurrence (standardized hazard ratio: 6.54), suggesting that any form of infection, not just surgical site infections, may increase risk of mortality.[37] Additionally, a multicenter retrospective study of 1,668 patients undergoing potentially curative radical resection for stage II/III colorectal cancer found similar results.[37] Postoperative infection affected recurrence-free survival, with a five-year recurrence-free survival of 68.1% vs 74.4% ($p = 0.037$).[37] Current NCCN guidelines recommend routine endoscopic and imaging surveillance following resection. Given that current data suggests postoperative infections place patients at a higher risk of recurrence,[36,37] we advise that patients with postoperative infectious complications be considered for surveillance CT of the chest, abdomen, and pelvis every 6-12 months, as well as endoscopy at one year post resection and every 3-5 years thereafter.[34]

Bacterial STIs and Genitourinary Infections

Cervical cancer is the third most diagnosed cancer and the fourth leading cause of cancer mortality among women worldwide.[38] HPV is considered the principal etiological agent in cervical cancer, yet only a small percentage of women diagnosed with persistent HPV infections eventually go on to develop cervical cancer, suggesting that additional cofactors may influence progression to malignancy. Common urogenital and sexually transmitted infections (STIs), including *Chlamydia trachomatis* and *Trichomonas vaginalis,* are highly prevalent and capable of inducing chronic cervical inflammation, epithelial disruption, and impaired immune clearance. While viral STIs have been extensively studied as carcinogenic pathogens, less attention has been given to the potential oncogenic relevance of bacterial infections.

Chlamydia Trachomatis

A large, population-based cohort study from Canada evaluated over 110,000 individuals diagnosed with chlamydia, gonorrhea, or syphilis and assessed subsequent cancer risk,

beginning five years after the individual was diagnosed with their first STI.[39] Compared to the general population, women with a history of bacterial STIs demonstrated a significantly increased risk of cervical cancer (SIR 1.9), while women with a history of chlamydia plus a second STI diagnosis were at increased risk of colon cancer (SIR 3.2) as well as cervical cancer (SIR 3.4). Males diagnosed with chlamydia only were at an increased risk of testicular cancer (SIR 2.02) and Hodgkin lymphoma (SIR 1.78).[39] Additionally, a systematic review and meta-analysis of 22 studies covering over 4,200 cervical cancer cases found *C trachomatis* to be an independent predictor of cervical cancer (Odds Ratio 1.76), even after adjusting for HPV infection and age.[40] Despite these associations, absolute cancer risk remains below thresholds to warrant enhanced surveillance; therefore, adherence to standard age-appropriate screening guidelines is encouraged.[23,41]

Trichomonas vaginalis & Bacterial vaginosis

A systematic review and meta-analysis of 29 studies and over 470,000 patients found that women diagnosed with a *T vaginalis* had a significantly increased risk of also being diagnosed with cervical cancer (OR 5.23).[42] A nationwide population-based prospective cohort study analyzing over four million females age 15 or older in Sweden found bacterial vaginosis to increase cervical cancer diagnosis (HR 1.31) as well as carcinoma in situ (HR 1.77).[43] Although absolute risk is below screening thresholds, these infections may serve as an opportunity to reinforce adherence to routine cervical cancer screening.[41]

Urinary Tract Infections

In one study, patients over age 65 diagnosed with a urinary tract infection were later diagnosed with 11.04 episodes of urinary tract cancer (UTC) per 10,000 patient years, compared to 1.96 for those without a urinary tract infection (aHR 11.8).[44] This results in a cumulative 10-year risk of 1.1%, meeting the intermediate risk threshold for cystoscopy.[45] Risk appears higher in men than in women.[44] Taken together, males over age 40 and women over age 50 should have a repeat urinalysis (UA) at 6-12 months post-infection. If >10 RBC/HPF on repeat UA, a history of gross hematuria, or >10 pack years of smoking, patients should be evaluated by urology for consideration of cystoscopy, as their risk of bladder cancer exceeds 1%, as well as renal ultrasound at 6-12 months post-infection.[45]

Post-operative Breast Cancer Infections

There is increasing evidence that major systemic infections within 90 days following breast cancer surgery increase mortality and distant recurrence.[46] Major systemic infection within 90 days was associated with increased risk of distant recurrence (HR 1.23, HR 1.72 for infections within 30 days), overall death (HR 1.47, HR 1.80 for infections within 30 days), breast cancer-specific death (HR 1.27, HR 1.86 for infections within 30 days), but not with locoregional recurrence.[46] Localized post-op wound infections during breast reconstruction for breast cancer have also been found to increase the risk of systemic recurrence (HR 4.94) and decrease the 5-year recurrence-free survival rate (64% vs 89.2%).[47] Current NCCN guidelines recommend PET/CT imaging for surveillance.[50] Given the association between postoperative infection and recurrence, clinicians may consider annual PET/CT surveillance for 3-5 years.

Sepsis and Septic Shock

From 2012 to 2019, the number of sepsis admissions among Medicare beneficiaries nearly doubled and is expected to continue to rise.[49] Likewise, there are approximately 650,000 cases of bacteremia in the US annually, with a 5-fold increase in incidence over the last 30 years.[50] Rather than a localized inflammatory response as seen in previously described abdominal diseases, sepsis by definition is a systemic pro-inflammatory state.[52] As a result, a hospitalization for sepsis often represents a sentinel clinical event - one that not only signals significant physiologic stress but also introduces new complexities in the timing, appropriateness, and interpretation of subsequent cancer screening.

Anaerobic Bacteremia

Although much attention has been afforded to *Streptococcus bovis*,[52] multiple studies have demonstrated other anaerobic bacteremias to be associated with increased CRC risk.[53-55] One study,[53] which analyzed 45,774 anaerobic bacteremia episodes, found the hazard ratio (HR) for CRC detection within one year was significantly elevated for Bacteroides (HR 5.95, 2.1% of Bacteroides bacteremia patients were diagnosed with CRC within the year), as well as for Clostridium (16.9, 4.4%), Fusobacterium (8.51, 3%), gram-positive anaerobic cocci (10.9, 3.6%), and bovis group streptococci (8.46, 4.3%). These are significant elevations compared to 0.4% of matched controls with negative blood cultures that were diagnosed with CRC within a year. When *Enterococcus faecalis* bacteremia was examined, the six-month incidence of CRC was 0.45% (vs 0.12% for matched comparators) and 2.34% (vs 0.48%) for colorectal neoplasia.[54]

These results seem bacterium-dependent rather than infection-site-specific, as one study demonstrated similar findings despite only a third of cases having a documented intra-abdominal infection.[55] While different anaerobes may portray different risk profiles, these studies demonstrate at least triple the risk of CRC diagnosis within 6-12 months of gut-native anaerobic bacteremia, warranting screening colonoscopy at the time of diagnosis.[56] Screening colonoscopy at the time of diagnosis may also alter patients' goals of care, particularly before undergoing more invasive surgical procedures. Providers can consider repeat colonoscopy 6-12 months after diagnosis, regardless of whether patients had undergone colonoscopy within the 6 months before the anaerobic bacteremia episode. Previous data demonstrated that colonoscopy performed after anaerobic bacteremia diagnosis was independently associated with a higher likelihood of neoplasm detection compared to colonoscopies performed within six months before diagnosis (adjusted odds ratio 4.88).[57] However, in accordance with American College of Gastroenterology guidelines for individuals ages 76 to 85, the decision to screen should be individualized, based on life expectancy, CRC risk, and personal preference, and screening is not recommended after age 85.[24]

Gram-Negative Bacteremia

In a nationwide population-based cohort study analyzing over 11,000 cases of gram-negative bacteremia, an increased risk of several cancers was found.[58] Elevated risk has been observed across multiple gastrointestinal and hepatobiliary malignancies, particularly within the first year after infection (Table 1). Looking specifically at new cancer diagnoses within

one year of community-acquired *Escherichia coli* bacteremia in patients aged 50 and above,[59] SIR was 6.12 for esophageal and stomach cancer, 4.45 for CRC, 7.19 for pancreatic cancer, 11.21 for hepatobiliary cancer, 10.47 for kidney cancer, 3.04 for bladder cancer, and 2.54 for prostate cancer. Given the breadth of associated malignancies, clinicians may consider upper and lower endoscopy within six months of diagnosis, and ultrasound + AFP every six months for 3-5 years if other hepatocellular cancer risk factors are present (i.e., cirrhosis, MASH, Hepatitis B or C, alcohol abuse), in line with AASLD recommendations.[31] Additionally, clinicians should consider trending prostate-specific antigen (PSA) levels every six months for two years post-diagnosis, as in one study, despite elevated PSA levels for males with febrile UTIs, 94% of patients had a >25% decrease in PSA levels three months later.[62] Thus, if PSA levels continue to increase, patients should be referred for further urologic workup. Despite the increased risk of pancreatic cancer, the absolute lifetime risk falls below the American Gastroenterology Association's 5% lifetime risk threshold for screening for high-risk individuals.[61]

***Staphylococcus aureus* Bacteremia**

A nationwide population-based cohort study analyzing just under 13,000 cases o*f S aureus* bacteremia (SAB) revealed an increased incidence of cancer diagnoses in the first year of follow-up (1.3% vs 0.8%) with an incident rate (IR) of 3.78.[62] While multiple myeloma, leukemia, sarcoma, cervical, liver, pancreatic, and UTC were all increased one year after SAB, all had <0.1% absolute incidence. Given the low absolute incidence of individual cancers, routine cancer screening based solely on SAB is not supported. However, [18F]-FDG-PET/CT scanning represents an intriguing option, having demonstrated improved outcomes in SAB,[63] and one study incidentally detected cancer in 4.7% of SAB scans.[64] PET/CT performed for evaluation of metastatic infection may provide an opportunity for incidental malignancy detection in this population.

Endocarditis

In two nationwide studies, an increased rate of CRC, esophageal/stomach, hematologic, liver, and gynecologic-related cancers was found after an endocarditis diagnosis.[65,67] Additionally, there was a 50-times or more increased risk for detection of several rare cancers within three months, including cancer of the heart, Kaposi sarcoma, and meningeal cancer.[65] Cancer risk was highly elevated during the first three months of follow-up (standardized incidence rate ratio [SIR] 8.03), partly due to a 15- to 30-fold increased risk of hematological or liver cancers.[65] Risk remains elevated beyond the immediate post-diagnosis period, though absolute incidence varies by cancer type (Table 1). In another study analyzing endocarditis patients,[68] those under age 55 had an adjusted subhazard ratio (aSHR) of 8.12 for hematologic malignancy vs 3.26 for those over age 55, with higher rates in males than in females (aSHR 5.4 vs 2.15). Clinicians should consider patients six months post-diagnosis with persistent lymphocytosis, cytopenia (in the absence of nutritional deficiency, autoimmune disease, or liver disease), or hypercalcemia be referred to hematology for consideration of bone marrow biopsy.[67,69]

In general, for endocarditis patients, clinicians should consider lab testing at six months (CBC, metabolic panel) to screen for hematologic malignancy, as well as gynecologic screening (HPV testing + cytology) annually for three years, then return to standard screening intervals.

Consider PET/CT for the detection of metastatic infection and for surveillance of malignancy while inpatient. If PET/CT is unable to be performed, consider upper and lower endoscopy within the year, as well as RUQ ultrasound + AFP every six months for 3-5 years in patients with other hepatocellular cancer risk factors.

Uncomplicated Septic Shock

Cancer Type	SEER-Medicare (1–2 yr) aOR	SEER-Medicare (3–5 yr) aOR	Danish ICU Study (Overall SIR)
Liver	1.42	1.56	~2 (F), ~3 (M)
Cervical	1.72	1.38	~8
MDS	1.40	1.26	—
CML	1.63	1.58	—
Colorectal	—	—	~1.5–1.6
Lung	—	—	~1.6–1.8
Pancreatic	—	—	~1.6–1.8
Renal	—	—	~1.5–1.6
Esophageal	—	—	~2 (M), ~5 (F)
Stomach	—	—	~2
Hematologic	—	—	~1.6–2.5

Table 2. Risk of malignancy following sepsis by study and cancer type.

Unspecified septic shock

A population-based case-control study using the SEER-Medicare database analyzed sepsis admissions in patients aged 65 and older.[69] This study found an increase in diagnosis of multiple cancers within 1-2 years after sepsis admission, and remained elevated at 3–5 post diagnosis (Table 2). A Danish registry analyzed one-year sepsis survivors ages 18 and older who were admitted to the ICU from 2003-2017 and followed them until 2018.[4] This study found that women were more likely than men to be diagnosed with any cancer, with a standardized incidence rate ratio (SIR) of 1.74 vs 1.31, and found that younger patients had higher SIRs. Cancer-specific risk estimates are summarized in Table 2. Notably, cervical, CRC, liver, lung, and hematologic cancer incidences were increased in both studies, with esophageal, pancreatic, renal, and stomach cancer being increased in patients admitted to the ICU. These associations may reflect both inflammation-driven carcinogenesis and the unmasking of occult malignancy during severe illness.

Given the breadth of associated malignancies, clinicians should consider PET/CT for patients diagnosed between 40 and 70 years of age anticipated to have meaningful functional outcomes. This can be performed either as an inpatient for the detection of metastatic infection and/or surveillance of malignancy, or within 6 months of hospital discharge.

Discussion

This review demonstrates that SBIs represent an underrecognized risk factor for subsequent malignancy across multiple organ systems. The evidence spans both well-established and emerging associations linking SBIs to elevated cancer risk. Importantly, the magnitude of risk for several infection-cancer associations rivals or exceeds that of established indications for existing cancer screening strategies.

Several patterns emerge from this narrative review. First, cancer risk is often highest in the first 6-12 months following infection, suggesting both a window for early detection and a potential role for occult malignancy predisposing patients to SBI. Second, the association appears to be pathogen and site-specific rather than a nonspecific consequence of inflammation, as evidenced by the differential risk profiles for anaerobic versus gram-negative bacteremia and the lack of increased risk following *C difficile* infection. Third, postoperative infections following cancer surgery are associated with increased recurrence and mortality, underscoring the bidirectional relationship between infection and malignancy.

Based on the evidence, we propose that clinicians incorporate infectious history into cancer risk assessment, particularly for patients aged 40-75 with reasonable life expectancy. For infections where absolute risk remains below established screening thresholds - such as cholecystitis, bacterial STIs, and urinary tract infections - these encounters nonetheless represent teachable moments to reinforce adherence to age-appropriate cancer screening.

Several limitations warrant acknowledgment. Much of the available evidence derives from retrospective cohort studies and administrative databases, which are subject to detection bias, residual confounding, and variable follow-up. The distinction between infection unmasking occult malignancy versus infection promoting carcinogenesis remains incompletely resolved. Cost-effectiveness data for infection-triggered screening strategies are limited, and prospective validation is needed. Future research should prioritize prospective studies with standardized screening protocols and mechanistic investigations linking infection to carcinogenesis. Emerging technologies, including multi-cancer early detection assays and expanded use of PET/CT in infectious evaluation, may provide opportunities to integrate cancer surveillance into post-infection care.

The recognition that HPV infection confers cervical cancer risk fundamentally changed how we screen, vaccinate, and counsel patients. We propose that SBIs be considered not as direct carcinogens, but as sentinel clinical events that identify patients at elevated risk for subsequent malignancy. Incorporating infectious history into cancer risk stratification represents a paradigm shift with the potential to improve early detection and outcomes across multiple organ systems.

Primary Infection	Current Standard of Care	Proposed Screening Strategy
Appendicitis (>40 y)	Colonoscopy within 6–12 months	No change
Pneumococcal pneumonia / LRTI	Bronchoscopy if concern for obstruction	Low-dose CT at 6–12 months (age 40–80)
Anaerobic bacteremia	Colonoscopy for *S. bovis*	Colonoscopy within 6–12 months for all
Cystitis / Pyelonephritis	Urology referral if recurrent	Repeat UA at 6–12 months; refer if >10 RBC/HPF, gross hematuria, or >10 pack-years
Pyogenic liver abscess	Imaging to resolution; consider colonoscopy	Colonoscopy at 3–6 months; repeat in 2–3 years
Septic shock	No oncologic workup; ± ICU follow-up	PET/CT within 6 months (age 40–70)
Endocarditis	Workup guided by organism	CBC at 6 months; annual HPV/cytology ×3 years; PET/CT or endoscopy within 1 year; RUQ US + AFP q6 months (if HCC risk)
S. aureus bacteremia	No standard oncologic follow-up	Inpatient PET/CT for metastatic infection/malignancy
Gram-negative bacteremia	Colonoscopy based on organism	Upper/lower endoscopy within 6 months; RUQ US + AFP q6 months (if HCC risk); PSA q6 months ×2 years
Postoperative infections	Standard oncologic surveillance	No change for GI; annual PET/CT ×3–5 years for breast

Table 3. Proposed Clinical Screening Framework Following Certain Serious Bacterial Infections

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