Health Technology Assessment in India (HTAIn)

Health Technology Assessment on the use of PET+CT for cancer care in India

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Regional Resource Hub - Kalam Institute of Health Technology

In Collaboration with

Department of Health Research (DHR)

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Study Title:

Health Technology Assessment on the use of PET for cancer care in India

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List of Abbreviations

LMICs	low- and middle-income countries
CC	Cervical cancer
BC	Breast cancer
OC	Oral cancer
GC	Gastric cancer
PET	Positron Emission Tomography
PET/CT	Positron Emission Tomography Computerized Tomography
CT	Computerized Tomography
MRI	Magnetic Resonance Imaging
SPECT	Single Photon Emission Computed Tomography
NCRP	National Cancer Registry Programme
AAR	Age adjusted rate
FIGO	International Federation of Gynecology and Obstetrics
DWI	Diffusion-weighted imaging
TNM	Tumor node metastasis
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
QUADAS-2	Quality Assessment of Diagnostic Accuracy Studies-2
TP	True positive
TN	True negative
FP	False positive
FN	False negative
PPV	Positive predictive value
NPV	Negative Predictive value
DTA	Diagnostic test accuracy
SROC	Summary receiver–operating characteristics
LR^+	Positive likelihood
LR^-	Negative likelihood
HNC	Head and neck cancer
QALY	Quality Adjusted Life Years
ICER	Incremental Cost Effectiveness Ratio
ROC	Receiver Operating Characteristic
FDG	Fluorodeoxyglucose
HTA	Health Technology Assessment
HTAIn	Health Technology Assessment in India
DHR	Department of Health Research
CAGR	Compound Annual Growth Rate
RevMan	Review Manager
CI	Confidence Interval
CEA	Cost Effectiveness Analysis
WHO	World Health Organization
LOS	Length of Stay
GDP	Gross Domestic Product
PSA	Probabilistic Sensitivity Analysis
NMB	Net Monetary Benefit
WTP	Willingness to Pay
AERB	Atomic Energy Regulatory Board
UMICs	Upper Middle- Income Countries
LICs	Lower Income Countries
HICs	High Income Countries

RAN	Rashtriya Arogya Nidhi
HMCPF	Health Minister's Cancer Patients Fund
NCCP	National Cancer Control Programme
RCC	Regional Cancer Centers

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Executive Summary

Background:

The estimated number of people living with the disease is around 2.25 million. Every year, new cancer patients registered in India are over 11,57,294 lakhs. The risk of developing cancer before the age of 75 years in males is 9.81% and in females it is 9.42 %. One woman dies of cervical cancer every 8 minutes in India. For every 2 women newly diagnosed with breast cancer, one woman dies of it in India. Mortality due to tobacco use in India is estimated at upwards of 3500 persons every day. Tobacco (smoked and smokeless) use accounted for 3,17,928 deaths (approx.) in men and women in 2018. Mortality due to cancer in 2018 was 7,84,821(Men: 4,13,519, Women: 3,71,302). Risk of dying from cancer before the age of 75 years is 7.34% in males and 6.28% in females. Cancers of oral cavity and lungs account for over 25% of cancer deaths in males and cancer of breast and oral cavity account for 25% cancers in females. The top five cancers in men and women account for 47.2% of all cancers; these cancers can be prevented, screened for and/or detected early and treated at an early stage. This could significantly reduce the death rate from these cancers. Nuclear medicine imaging in India has come a long way from the earlier rectilinear scanning to the present-day hybrid imaging of metabolic positron emission tomography (PET) and structural computerized tomography (CT) or magnetic resonance (MR) imaging, commonly referred to as PET-CT and PET-MR. The concept of PET imaging which originated in the mid-1970s as a research tool in cardiology and neurology has in the past four decades evolved into the most sophisticated medical imaging system with its largest application in oncology. India is one of the largest markets for the fast-growing sector of medical devices which encompass a broad and heterogeneous range of technologies. The medical device industry in India is presently valued at USD 5.2 Billion and is growing at 15.8% CAGR. Due to the rising costs associated with introducing of new medical devices and procedures into the healthcare system, payers have started to pay more attention to the clinical and cost effectiveness of such technologies in advance.

Objective:

In this context, health technology assessment of “Positron Emission Tomography (PET)” in Indian healthcare system was given to Kalam Institute of Health Technology a resource hub to Department of Health Research (HTAIn) Govt. of India by Kerala Govt. As they wanted to know the evidence-based indications for PET–CT in support of facilities planning and to describe a project in which this information can be applied for an investment decision in India.

The cost of establishing and operating PET/CT scan facility is quite substantial. Notably, despite ongoing and controversial discussions about the patient-relevant benefits of PET or PET–CT/or PET-MRI, these technologies have rapidly been adopted abroad. The growth for this imaging modality has been slow owing to issues related to high cost of PET scanner, ready availability of useful biomolecules, and trained technical workforce.

Methods:

To evaluate the diagnostic accuracy of positron emission tomography and computed tomography (PET/CT) in oncology (Head and neck, breast, lung, gastric and cervical cancer) compared to positron emission tomography (PET), computed tomography (CT) and magnetic resonance imaging (MRI).

To evaluate the clinical effectiveness a systematic review was conducted by primary electronic database search. Searches were conducted in PubMed, Google scholar and Cochrane data bases. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement was developed for this project.

To evaluate the cost effectiveness of positron emission tomography and computed tomography (PET/CT) in oncology, cost and Quality Adjusted Life Years (QALYs) were chosen as outcomes and individuals with high risk aged between 30 and 80 are considered to be eligible for diagnosis. A deterministic and probabilistic Markov model was developed with a cohort of 1,000 patients. We chose a cycle length of one year and ran the model for 50 cycles (i.e., 50 years). Cost effectiveness of PET/CT was assessed from societal perspective with time horizon of 5 years, 10 years and lifetime. Direct medical cost, Direct Non-Medical cost and Indirect cost were calculated and depicted as mean along with its standard error and distribution type. Costs are presented in IN Rupees. The costs and Quality Adjusted Life Years (QALYs) were discounted by 3% per year.

Findings:

Diagnosis and detection of different cancers by PET, PET/CT, CT and MRI varies based on the region, recurrence and different stages of cancer. The forest plot was plotted for all five different cancers with a total of 345 studies and their sensitivity and specificity was calculated. The pooled data for the cervical cancer with a sensitivity and specificity of CT 0.62 (0.57, 0.67), 0.92 (0.57, 0.67), MRI 0.52 (0.49,0.55), 0.96 (0.95, 0.96) PET 0.90 (0.86,0.93) 0.93(0.91, 0.94) and PET/CT 0.65(0.62, 0.68) 0.97(0.97,0.98) in detecting LN metastases cervical cancer tumor staging like IA, IB II A, II B, III A and IV A in cervical cancer. The pooled data for the Breast cancer with a sensitivity and specificity of CT 0.87 (0.85, 0.89), 0.35 (0.33,0.38) MRI 0.97 (0.94, 0.98), 0.88(0.84, 0.91) PET 0.89 (0.86,0.90) 0.91(0.89, 0.93) and PET/CT 0.86(0.83, 0.88) 0.91(0.89, 0.93) in detecting local recurrences, lesion basis, distant metastases and breast lesions in breast cancer. The pooled data for the head and neck cancer with a sensitivity and specificity of CT 0.81(0.77,0.85), 0.72(0.70, 0.74) MRI 0.77(0.74,0.79), 0.78(0.77,0.79) PET 0.20 (0.16, 0.25) 0.94(0.92, 0.96) and PET/CT 0.84(0.82,0.86) 0.88(0.86,0.89) in detecting lymph node metastasis, detection of recurrence in patients and detecting neck levels I, II, and III with head and neck cancer. The pooled data for the gastric cancer with a sensitivity and specificity of CT 0.77(0.71,0.82), 0.95(0.93,0.97) MRI 0.84(0.73,0.93), 0.850.78,0.91() PET 0.41(0.25,0.58) 0.96(0.92,0.99) and PET/CT 0.85(0.77,0.91) 0.95 (0.90, 0.98) in detecting recurrent gastric cancer and peritoneal metastases in gastric cancer. The pooled data for the lung cancer with a sensitivity and specificity of CT 0.71 (0.66, 0.75), 0.82 (0.80,0.85) MRI 0.65(0.59,0.71), 0.91(0.89,0.94) PET 0.83 (0.79, 0.86) 0.93 (0.91 0.95) and PET/CT 0.78(0.77, 0.80) 0.90(0.89, 0.90) in detecting mediastinal lymph node Metastases, detecting stage III b, local T and N stage, M-stage lung cancer, solitary pulmonary nodule in lung cancer.

The base-case results of model analyses, which revealed that PET/CT as diagnostic modality gains 4.19, 6.42 and 6.99 QALYs, in the time horizon of 5 years, 10 years and lifetime respectively. The ICER for PET/CT compared to CT were 617; 1,783 and 2,337 respectively for different time horizons. The ICER values obtained from PSA are all somewhere close to the base-case lifetime horizon ICER value. Up to the willingness to pay of ₹ 9,000, CT is cost-effective. When the willingness to pay is high, patients opt for better interventions that give better outcomes. Here, in our study, when the WTP is greater than 9,000, PET/CT is almost 80% cost effective. One-way sensitivity analysis reveals that the uncertainty in the utility of diseased patient, total hospitalization cost with length of stay for PET/CT and CT, total diagnostic cost for PET/CT and CT and utility of health population has the greatest impact on the ICER.

Conclusion:

Total cost of establishing PET/ CT scan facility without cyclotron was calculated to be INR 17.08 Cr (USD 2,339,048.75). Proposing more units would cost the government a huge sum of money where there is no data regarding the utilization levels of the existing units. The cost of performing PET/ CT scans can decrease if the number of examinations increase over the time. Various strategies can be adopted in order to cut down the capital and operational cost of setting up the facilities, which in turn can decrease the unit cost of PET/ CT scan. The total cost of setting up of cyclotron facility was calculated to be INR 58.63 Cr (USD 8,026,734.1). Besides, there are currently 88 units of PET/ CT in the South zone, of which 13 alone belongs to Kerala. Wherein East, North East and Central zones have less than that of Kerala each. It is concluded from the study that setting up of additional PET/ CT units in Kerala is not suggested as nuclear medicine facilities are better than national average in Kerala, rather focusing on other areas where there is dire need of development in PET/ CT infrastructure, would strengthen the nuclear medicine infrastructure in the country.

Time for a National Strategy - India does not have a national approach or national policy for the use of PET/CT as a clinical tool for cancer care and an expansion of PET CT facilities in India. Coordinated action, based on evidence-based guidelines is required as a national approach for optimal utilization of the nuclear medicine resources in India.

Chapter - I

Background

Nuclear medicine imaging in India has come a long way from the earlier rectilinear scanning to the present-day hybrid imaging of metabolic positron emission tomography (PET) and structural computerized tomography (CT) or magnetic resonance (MR) imaging, commonly referred to as PET-CT and PET-MR. The concept of PET imaging which originated in the mid-1970s as a research tool in cardiology and neurology has in the past four decades evolved into the most sophisticated medical imaging system with its largest application in oncology. (2)

India is one of the largest markets for the fast-growing sector of medical devices which encompass a broad and heterogeneous range of technologies. The medical device industry in India is presently valued at USD 5.2 Billion and is growing at 15.8% CAGR. (3) Due to the rising costs associated with introducing of new medical devices and procedures into the healthcare system, payers have started to pay more attention to the clinical and cost effectiveness of such technologies in advance.

In this context, health technology assessment of "Positron Emission Tomography (PET)" in Indian healthcare system was given to Kalam Institute of Health Technology a resource hub to Department of Health Research (HTAIn) Govt. of India. As we know the cost of establishing and operating PET scan facility is quite substantial.

Notably, despite ongoing and controversial discussions about the patient-relevant benefits of PET or PET–CT/or PET-MRI, these technologies have rapidly been adopted abroad. (5) The growth for this imaging modality has been slow owing to issues related to high cost of PET scanner, ready availability of useful biomolecules, and trained technical workforce.

Introduction

The emerging trends in positron imaging based on published data have created a noticeable paradigm shift in cancer management as a result of the early diagnosis, accurate staging, and treatment response evaluation resulting in substantial cost cutting by avoidance of unjustified surgeries and toxic-chemotherapies. The availability of wide range of newer biomolecules produced in compact self-shielded medical cyclotrons and easy to use. PET generators have enabled targeted imaging resulting in the diagnosis of cancer at the time of metabolic dysregulations in the cells that usually predate the anatomical changes, a hallmark of advanced cancer. These developments though exciting are equally challenging for the health-care providers. Creating PET-CT/PET-MRI facilities that are accessible and affordable to resource poor and remote populations requires the highest level of national commitment and a dedicated team of professionals who can oversee the project from conception to commissioning. Any negligence today may create unbridgeable health care gaps tomorrow in executing a comprehensive cancer care and cancer control program.

Cancer Statistics in India

The estimated number of people living with the disease is around 2.25 million. Every year, new cancer patients registered in India are over 11,57,294 lakhs. The risk of developing cancer before the age of 75 years in males is 9.81% and in females it is 9.42 %. One woman dies of cervical cancer every 8 minutes in India (6). For every 2 women newly diagnosed with breast cancer, one woman dies of it in India (7-9). Mortality due to tobacco use in India is estimated at upwards of 3500 persons every day (10). Tobacco (smoked and smokeless) use accounted for 3,17,928 deaths (approx.) in men and women in 2018. Mortality due to cancer in 2018 was 7,84,821(Men: 4,13,519, Women: 3,71,302). Risk of dying from cancer before the age of 75 years is 7.34% in males and 6.28% in females. Cancers of oral cavity and lungs account for over 25% of cancer deaths in males and cancer of breast and oral cavity account for 25% cancers in females (11). The top five cancers in men and women account for 47.2% of all cancers; these cancers can be prevented, screened for and/or detected early and treated at an early stage (12). This could significantly reduce the death rate from these cancers. (13)

Available diagnostic imaging technologies and their applications in healthcare

As we know the use of radiation has revolutionized the field of medical imaging technology. The inner workings of the human body can now be visualized with greatly increased accuracy – making radioactivity scans among the most important tools in the diagnostician's arsenal. The six most common pieces of apparatus used in this field are Positron Emission Tomography (PET), Gamma Cameras, Magnetic Resonance Imaging (MRI), Computed Tomography (CT) scan, Single-photon emission computed tomography (SPECT), or the fusion of these technologies- PET/CT, PET/MR, SPECT-CT.

Table 1: Application in Healthcare

Technology	Problems Addressed	Applications
SPECT	Bone disorders Heart Problems Clogged coronary arteries Reduced pumping efficiency Brain disorders	Diagnose or monitor Bone disorders, as areas of bone healing or cancer progression usually light up on SPECT scans. Diagnose or monitor heart problems Shows how completely the heart chambers empty during contractions. Is helpful in determining which parts of the brain are being affected by • Dementia • Clogged blood vessels • Seizures • Epilepsy and head injuries **Remarks** SPECT scans are not safe for women who are pregnant or breast-feeding because the radioactive tracer may be passed to the developing foetus or the nursing baby
CT	Muscle, bone and joint problems, like complex bone fractures and Tumor's Oncology,	Guide treatment plans and procedures, such as biopsies, surgeries, and radiation therapy Compare CT scans to find out if certain treatments are working To spot tumors or masses and to detect changes To detect blood clots, excess fluids or infections.

	Cardiology Emphysema or liver masses Internal injuries and bleeding. Blood clots, excess fluids or infections	**Remarks** CT scans use X-rays, which produce ionizing radiation and research show that these sorts of radiations may damage the DNA and lead to cancer. These effects add up to the lifetime. The ionizing radiation is harmful to pregnant women and children as well.
SPECT/CT	Thyroid and Parathyroid and Neuroendocrine tumors, Oncology Sentinel Lymphoscintigraphy Tumors, bone, lung and heart.	SPECT/CT has the most utility in patients with ectopic parathyroid adenoma, those with distorted neck anatomy due to prior surgery, and those with prior failed parathyroid surgery as the cross-sectional multiplanar imaging will precisely specify the depth of the focus and its position with respect to the surrounding and adjacent structures Fusion of SPECT and CT images has been reported to increase the diagnostic accuracy by decreasing the number of patients with false-positive results by 46% SPECT/CT offers enhanced preoperative sentinel lymph node (SLN) localization Can provide enhanced localization and staging of neuroendocrine neoplasms, especially for lesions within the peritoneal cavity, mesentery, and pancreas. Can often clarify the true nature, benign versus malignant, in case of detection of bone metastases and assessment of treatment response in neoplastic disease, especially for those with a tendency toward osteoblastic metastases.
MRI	Brain and spinal cord Heart and blood vessels Other internal organs Bones and Joints Breasts	Examine organs, tissues and skeletal systems Used as imaging test for brain and spinal cord to help diagnose aneurysms of cerebral vessels, Disorders of the eye and inner ear Multiple sclerosis, spinal cord disorders Stroke tumors and brain injury from trauma To assess: • Size and function of the heart's chambers, thickness and movement of the walls of the heart • Extent of damage caused by heart attacks or heart disease • Structural problems in the aorta, such as aneurysms or dissections • Inflammation or blockages in the blood vessels To check for tumors or other abnormalities of many organs in the body including liver and bile ducts, kidneys, spleen, pancreas, uterus, ovaries, prostate To evaluate: • Joint abnormalities caused by traumatic or repetitive injuries, such as torn cartilage • Disk abnormalities in the spine • Bone infections • Tumors of the bones and soft tissues Can be used with mammography to detect breast cancer **Remarks** MRI uses powerful magnets, the presence of metal in your body can be a safety hazard if attracted to the magnet or even the metal objects can distort the MRI images. MRI scans are not invasive, but they are noisy, take more time, and may cause claustrophobia (anxiety due to being in the enclosed space of the machine).

		Patients with tattoos or permanent make up have to get additional consultation with the doctor as some of these dark inks may contain metal. May be harmful to pregnant and breast- feeding women Kidney and liver diseases in patients might limit the use of injected agents during the scan.
PET	Neuroimaging Clinical oncology Musculo-skeletal Cardiology Pharmacology Neuropsychology Inflammatory disorders	Detects cancer cells as it shows up as bright spots in PET scans as they have higher metabolic rate than normal cells. It also can reveal cancer spread, check whether a cancer treatment is working or find cancer recurrence. Although some cancers do not appear on PET scans, many types of solid tumors appear on scans including, brain, cervical, colorectal, oesophageal, head and neck, lung, lymphoma, melanoma, pancreatic prostate and thyroid tumors. It can also reveal areas of decreased flow of heart Also used to evaluate brain disorders such as brain tumors, Alzheimer's disease and seizures **Remarks** Though a radioactive drug will be put into the body for the scan, the amount of radiation the patient is exposed is small. May be harmful to pregnant and breast- feeding women
PET/CT	Neurology Clinical oncology Musculo-skeletal Cardiology Pharmacology Neuropsychology Inflammatory disorders	Staging, assessing treatment response, restaging and follow-up of Lymphoma Restaging and follow-up in colorectal carcinoma Staging, assessing treatment response, and follow-up of lung cancer. Restaging, follow up, and assessing treatment response of breast carcinoma. Bone and soft tissue sarcomas- staging and assessing treatment response. Restaging, assessing treatment response, and follow-up of melanoma. Restaging and assessing treatment response of head and neck tumors, including thyroid tumors. Restaging and assessing treatment response of head and neck tumors, including thyroid tumors. Epilepsy – pre-surgery Dementia, Alzheimer's Cardiac viability. **Remarks** PET/CT can detect abnormal metabolic activity and may provide more accurate diagnoses than these two scans performed separately.
PET/ MRI	Neurology Clinical oncology Musculo-skeletal Cardiology Pharmacology Neuropsychology Inflammatory disorders	Helpful for assessment of liver metastases (hepatobiliary cancer) Used to correctly identify Neuroendocrine tumor lesions. Used for primary staging of cervical and endometrial malignancies, planning of radiotherapy in cervical cancer. Evaluation of response to therapy in ovarian cancer, and detection of recurrence in these malignancies Neuro oncologic PET/MRI uses targeted radiotracers to evaluate different aspects of tumor function and behaviour. Used for staging, detection of occult primary malignancies, assessment of chemo radio- therapeutic response, and differentiation of local recurrence from treatment effect in case of head and neck cancer. PET/MRI has lower levels of radiation **Remarks-** PET/MRI scans of the brain can detect abnormal findings that PET/CT misses in more than 50% of patients scanned

Cyclotrons

Cyclotrons are the primary tool for producing the shorter-lived, proton-rich radioisotopes currently used in a variety of medical applications. Although the primary use of the cyclotron-produced short-lived radioisotopes used in PET/CT (positron emission tomography/computed tomography) and SPECT (single photon emission computed tomography) diagnostic medical procedures, cyclotrons are also producing longer-lived isotopes for therapeutic procedures [22]. Increase in prevalence of cancer and rise in the demand for nuclear scans for precise diagnosis are key factors driving the cyclotron market. Cost advantage over outsourced radioactive tracers and accessibility of technologically advanced diagnostic devices, such as positron emission tomography scan (PET/CT) and a single-photon emission computerized tomography (SPECT), are playing a crucial role in propelling the cyclotron market from 2020 to 2030(23)

Radionuclides and Radio-Nuclide Generators commonly used in Nuclear Medicine

List by AERB-

Table 1: List of Radio- nuclides

	Radionuclide	**Half-life**
1.	Fluorine-18	110 min
2.	Iodine-131	8days
3.	Lutetium- 177	6.7 days
4.	Phosphorus-32	14 days
5.	Chromium -51	28 days
6.	Iodine -125	60 days
7.	Iron-59	46 days
8.	Rhenium-186	3.8 days
9.	Samarium-153	47 hours
10.	Strontium -89	50 days
11.	Yttrium-90	64 hours
12.	Cobalt-57	272 days
13.	Copper-64	13 hours
14.	Gallium-67	78 hours
15.	Indium-111	2.8 days
16.	Iodine - 123	13 hours
17.	Thallium-201	73 hours
18.	Actinium-225	10 days

Table 2: List of Radio-nuclide Generators

	Generators	**Parent/Daughter**	**Half - Life**
1	Molybdenum-99	Parent	66 hours
	Technicium-99m	Daughter	6 hours
2	Tungsten-188	Parent	69.4 days
	Rhenium-188	Daughter	17 days
3	Germanium-68	Parent	271 days

	Gallium -68	Daughter	68 min
4	Strontium-82	Parent	25 days
	Rubidium -82	Daughter	1.26 min

Nuclear Medicine infrastructure In India and other countries -

Table 4: Installed base of Computerized tomography, magnetic resonance imaging, and Positron emission tomography in India and other countries versus cancer statistics (24)

Country	Australia	France	New Zealand	United States	India	Japan
Total CT units	1782	1222	76	14750	5324	14126
Units per million population	70.25	18.24	15.44	44.94	**3.93**	111.49
Total MRI Units	375	1034	76	13275	1800	6996
Units per million population	14.78	15.43	15.44	40.44	**0.69**	55.21
Total PET Units	102	167	5	1790	279	586
Units per million population	4.02	2.49	1.02	5.45	**0.20**	4.62
Total Population in Millions	25.0	66.9	4.9	327.2	1354.1	126.4
New cancer cases	197876	455618	35897	2129118	1157294	883395
Units per thousand cancer cases	0.51	0.36	0.13	0.84	**0.24**	0.66
5-year prevalent cases	755062	1390878	133716	7279710	2258208	2127559
Units per/thousand 5-year cancer prevalent cases	0.13	0.12	0.037	0.24	**0.12**	0.27

Table 5: Current scenario of nuclear medicine infrastructure in India – 2020(24)

India	CT	PET/CT	PET/MR	SPECT	SPECT-CT
Total Units	5324	279	3	194	79
Units per million population	3.93	0.2	0.00221	0.143	0.058
Units per thousand cancer cases	4.6	0.24	0.0025	0.17	0.068
Units per/thousand 5-year cancer prevalent cases	2.36	0.12	0.0013	0.086	0.035

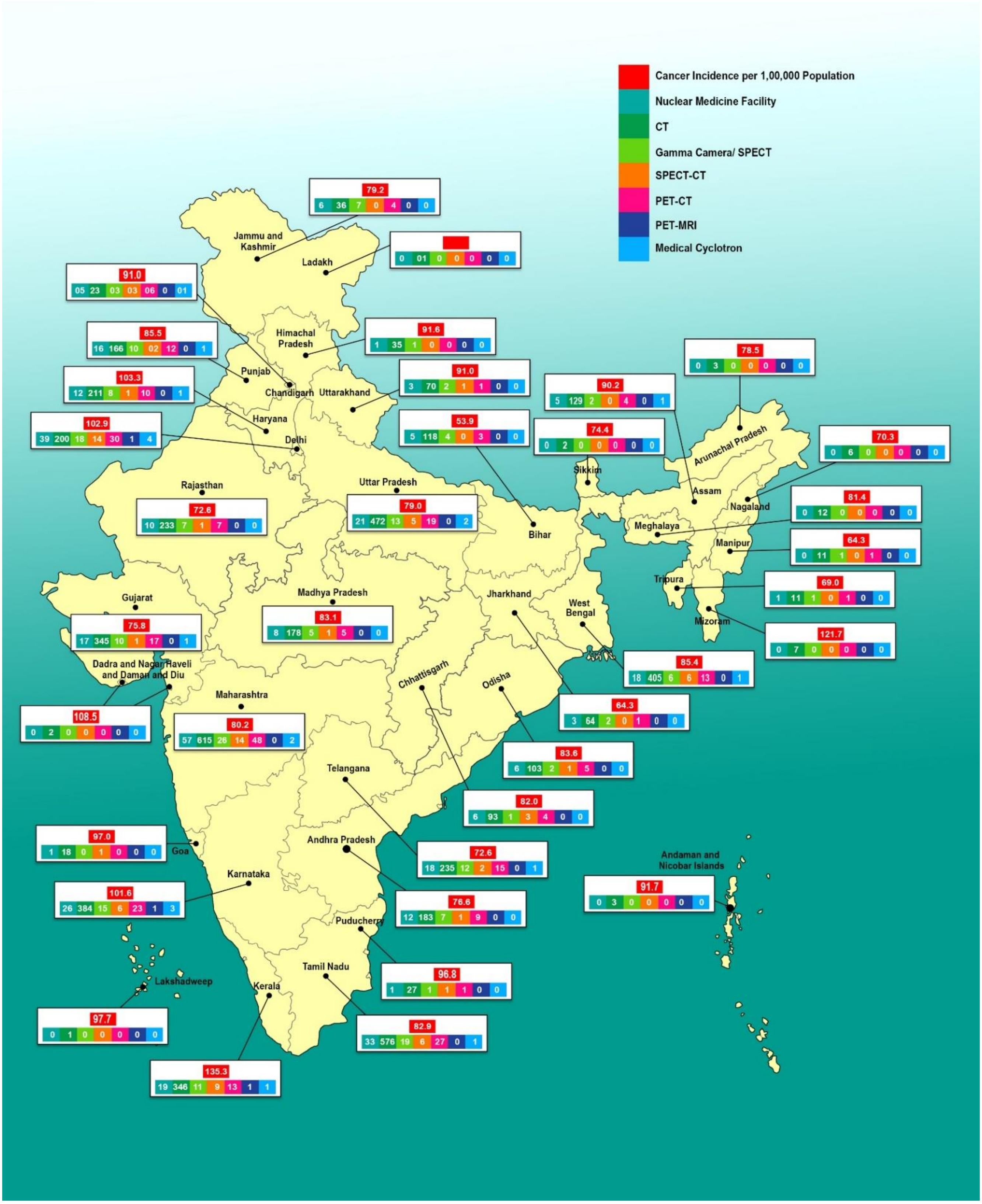

Figure 1: Mapping of Nuclear medicine infrastructure in India vis-à-vis Cancer Incidence (24-25)

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Chapter – II

Clinical Effectiveness

Statement of need

This study was undertaken as assigned by DHR upon the request put forward by the government of Kerala on setting up an additional PET/CT facility in Kerala. Owing to the rising number of cancer cases in the country, there is a critical requirement of National policy based approach for cancer diagnostics.

Aim

To identify oncological conditions for which PET /CT is likely to be shown to be diagnostically accurate.

Objective-

To evaluate the diagnostic accuracy of positron emission tomography and computed tomography (PET/CT) in oncology (Head and neck, breast, lung, gastric and cervical cancer) compared to positron emission tomography (PET) computed tomography (CT) and magnetic resonance imaging (MRI).

Inclusion criteria-

P – Population/ Participants – high risk cancer patients with cervical cancer, breast cancer, Lung cancer, Head and Neck cancer and gastric cancer, 18-65 years in both male and female.

I – Intervention –Positron emission tomography and Computed Tomography (PET/CT)

C - Comparator –Positron emission tomography (PET), Computerized Tomography (CT) and Magnetic Resonance Imaging (MRI)

O- Outcome – Sensitivity, Specificity, likelihood ratios and predictive values.

Exclusion criteria

Excluded studies from the data were pancreas, bladder, or ureter cancer, colon cancer, ovarian cancer and thyroid cancer.

Types of studies

The studies that are included in the review are retrospective and prospective studies.

Methodology

Literature search database

The systematic review was conducted by primary electronic database search. Searches were conducted in PubMed, Google scholar and Cochrane data bases. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement was developed for this project.

Screening process

All articles identified by the search were initially screened for eligibility on title and abstracts. The search results were exported to the reference management software EndNote X7. Duplicate articles were removed, and the remaining titles and abstracts were screened. Full-text articles were retrieved and assessed for eligibility using predefined criteria, for inclusion in the review. The target population was patients suffering with Cervical cancer, Breast cancer, Head and neck cancer, Gastric cancer and Lung cancer.

Assessment Criteria

The methods should contain information on eligibility criteria, information sources, search, study selection, risk of bias in individual studies, data items, and synthesis of the results and risk of bias across studies.

Data extraction

The first stage of the data extraction is calculation of sensitivity and specificity for each study, which is conducted as per the standard 2 × 2 table which is shown below.

	Condition	
Positive	Present	Absent
	TP	FP
	FN	TN
Negative		

Risk of bias in individual studies

Risk of bias in the included studies refers to the addressing of specific aspects that may have introduced systematic errors (i.e., bias) into a study. The most widely accepted tool for methodological appraisal of the studies included in the review is the Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2) tool, which assesses the quality of the included studies in terms of biases affecting their applicability in four domains: patient selection, index test, reference standard and flow and timing. A summary estimate of data combined in meta-analysis is considered to be the highest level of evidence. The data will be combined clinically, methodologically, and statically having similar characteristics with same outcomes.

Prisma

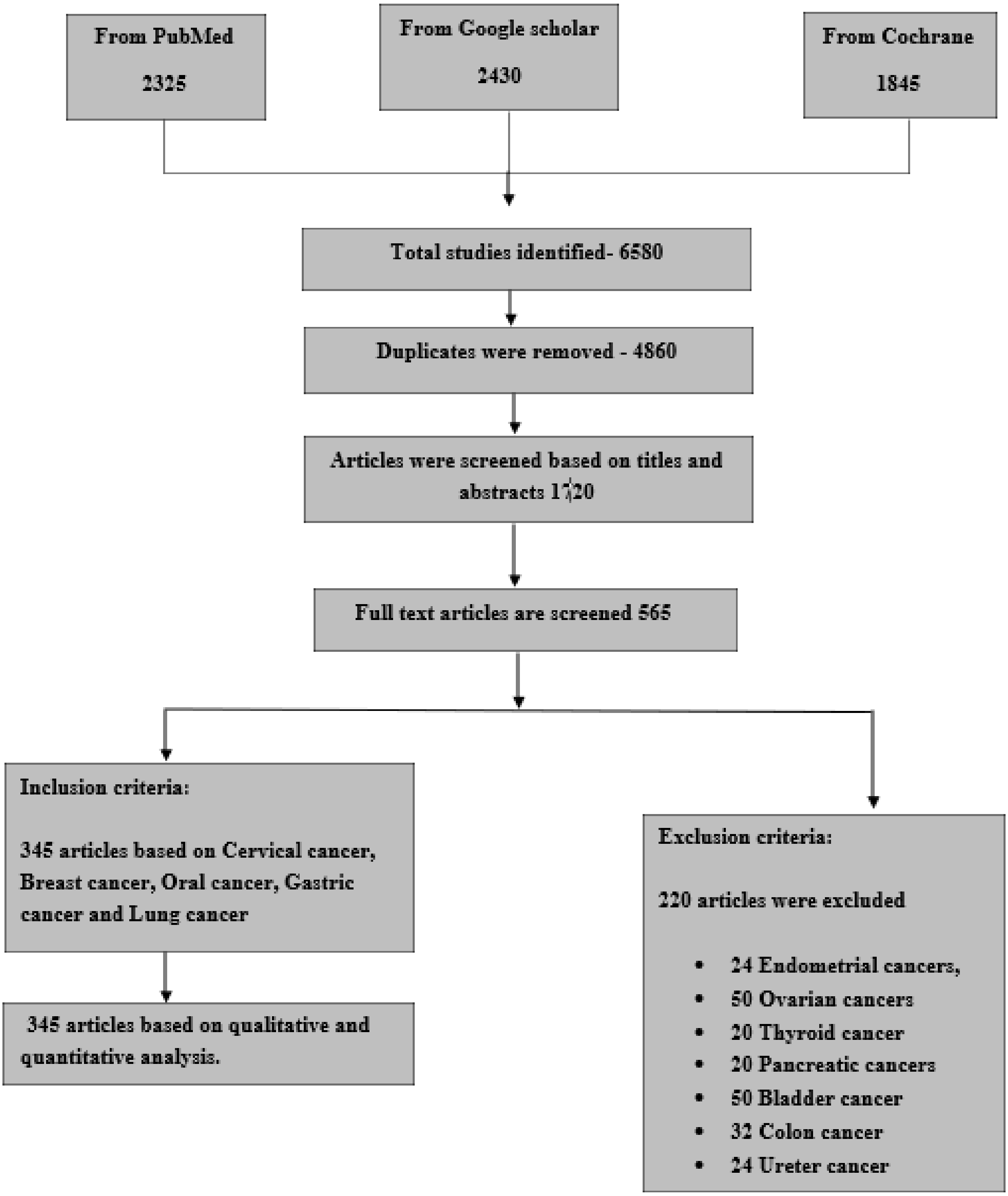


Figure 2: PRISMA Diagram

KEY WORDS:

Test accuracy, Sensitivity, specificity, true positive, true negative, false positive and false negative.

Study quality Assessment:

Critical Appraisal

Quality Assessment of this review. It includes studies in terms of risk of bias and concerns regarding applicability over four domains, (patient selection, index test(s), reference standard, and flow and timing), which are each rated in terms of risk of bias. A summary graphic may be helpful to convey the methodological quality of each study. Risk of bias graph and summary shows how published DTA systematic reviews have graphically summarized the methodology quality of the included studies.

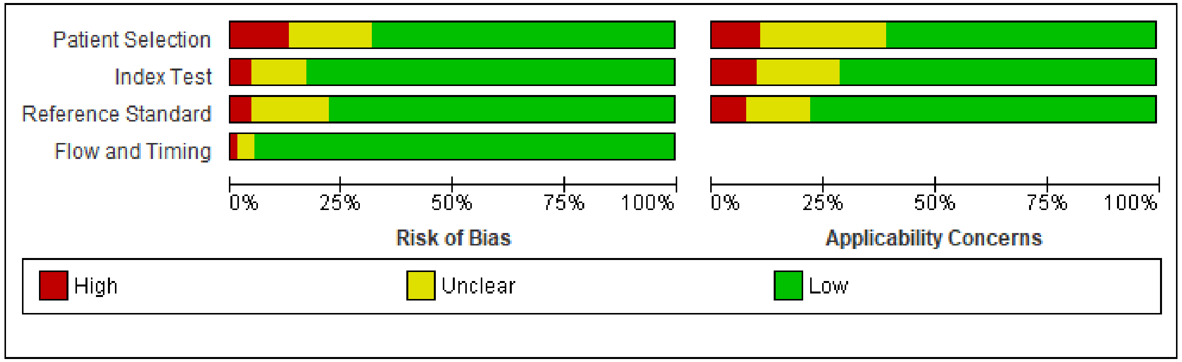


Figure 3: Risk of bias graph- Cervical cancer

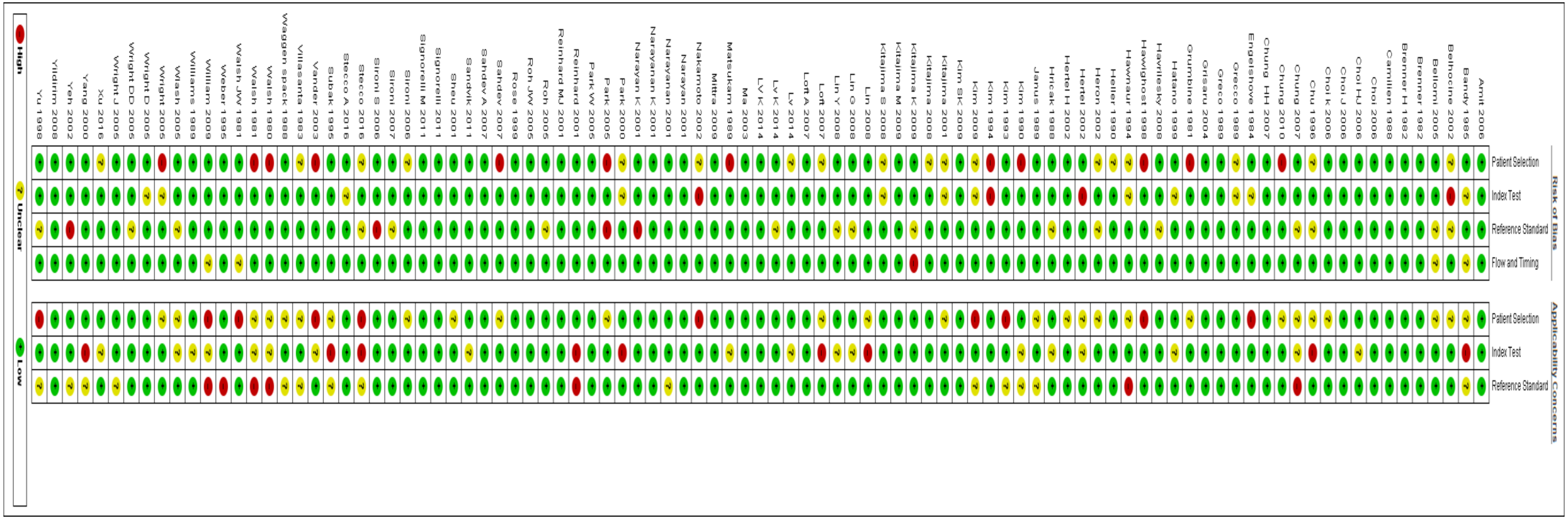


Figure 4: Risk of bias summary- Cervical cancer

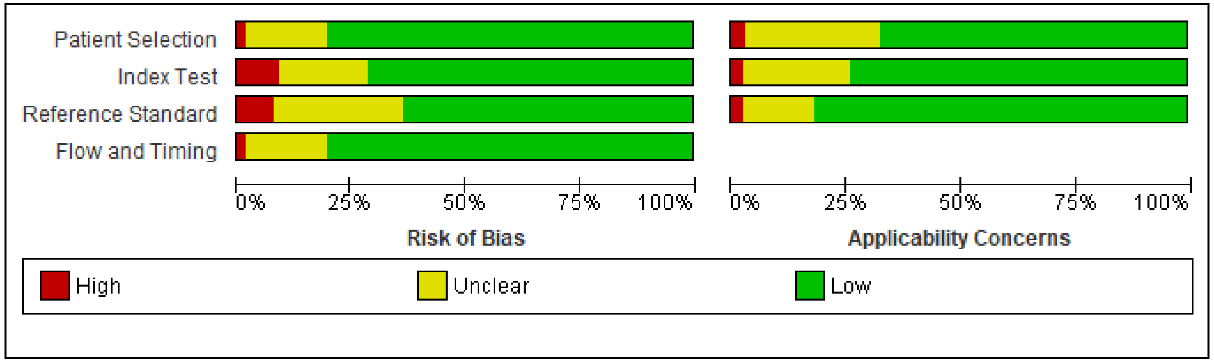


Figure 5: Risk of bias graph- Breast cancer

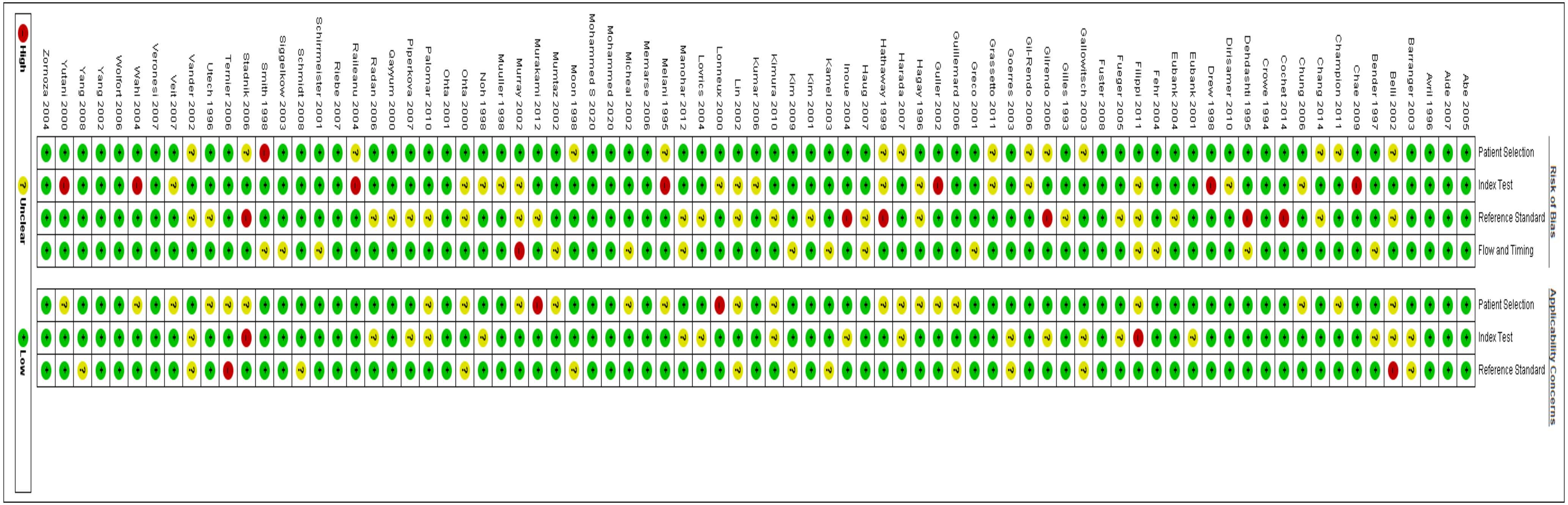


Figure 6: Risk of bias summary- Breast cancer

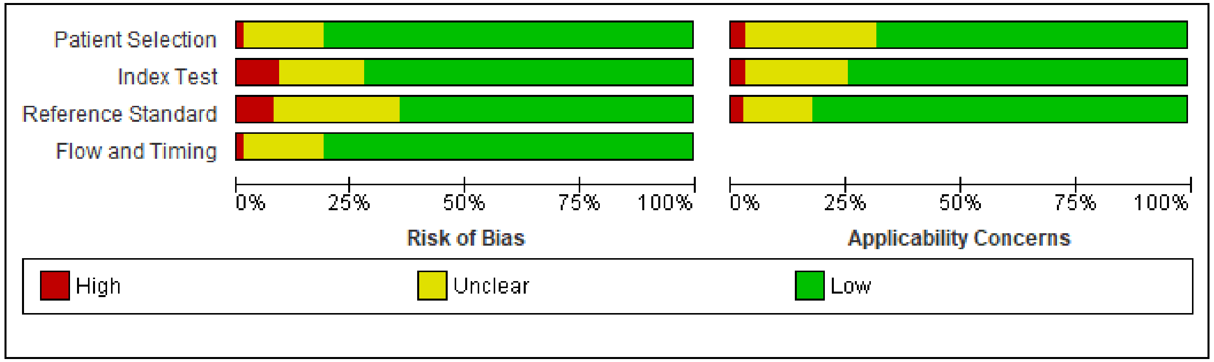


Figure 7: Risk of bias graph- Head and Neck cancer

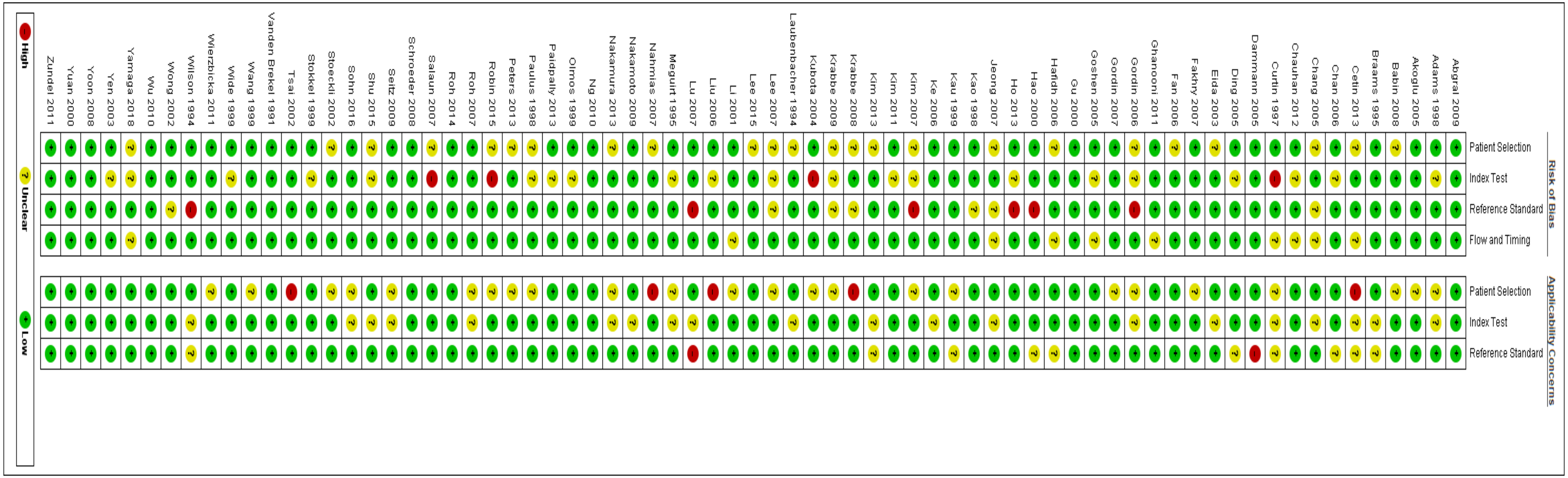


Figure 8: Risk of bias summary- Head and Neck cancer

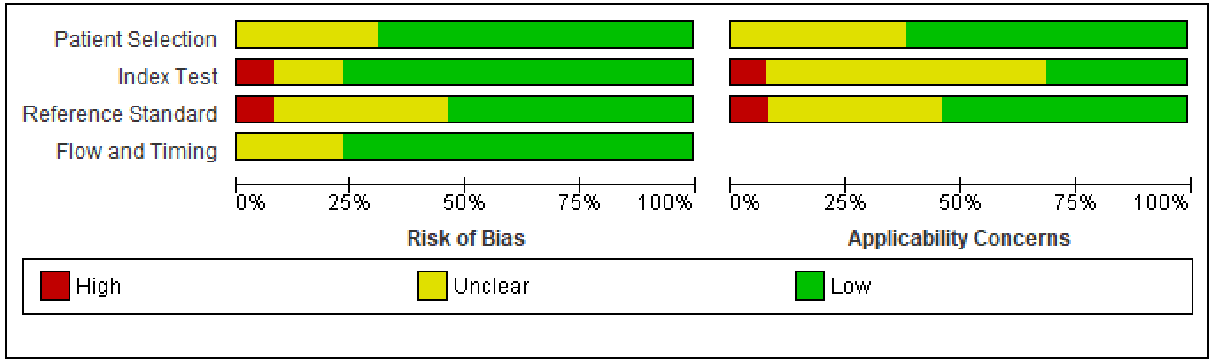


Figure 9: Risk of bias graph- Gastric cancer

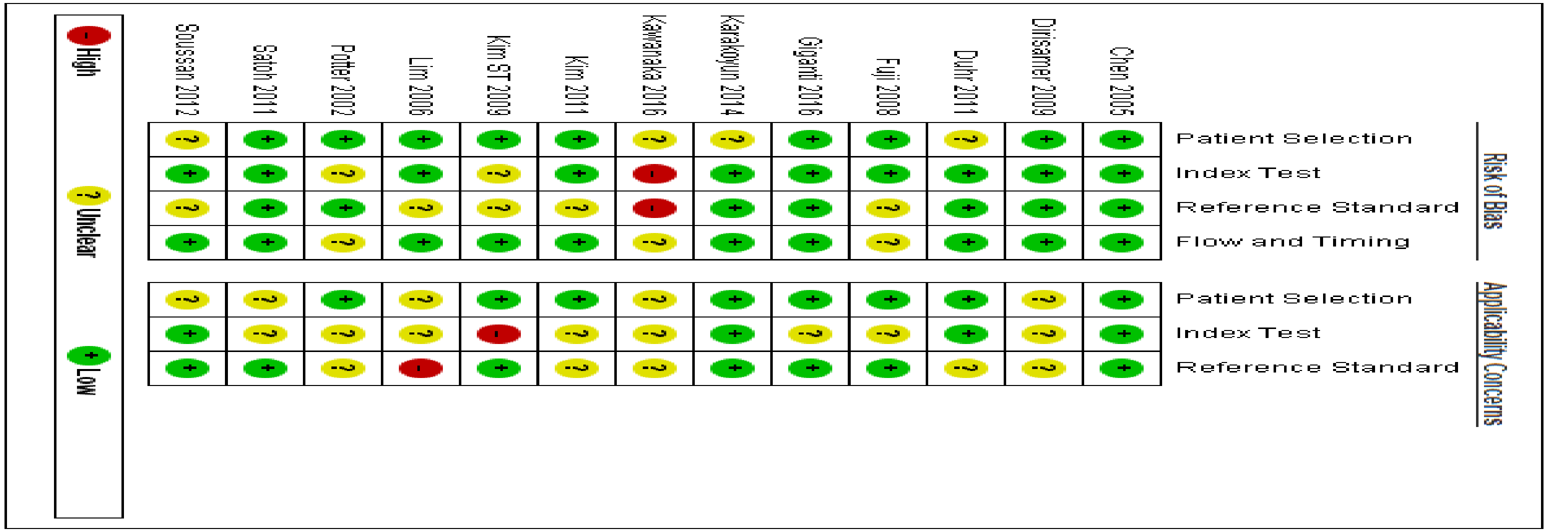


Figure 10: Risk of bias summary- Gastric cancer

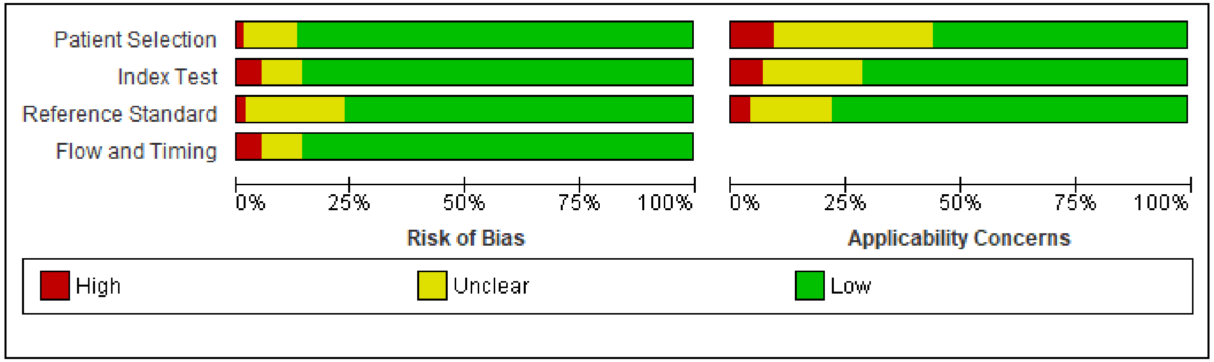


Figure 11: Risk of bias graph- Lung cancer

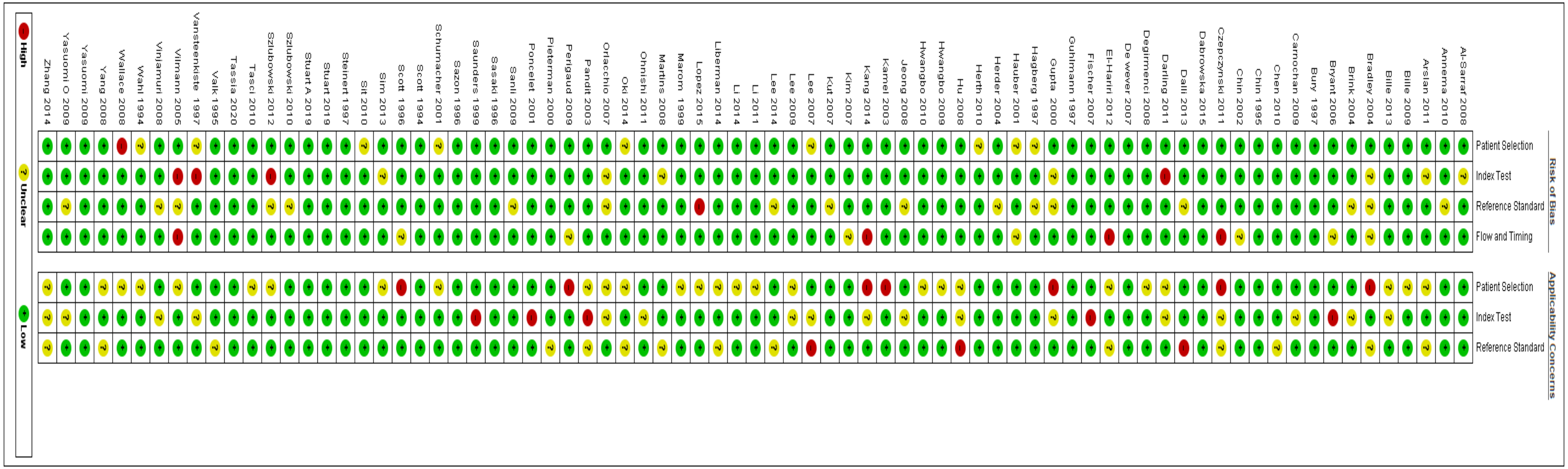


Figure 12: Risk of bias summary- Lung cancer

The analysis of risk was completed using Cochrane RevMan 5.0. This exercise is pivotal to knowing the quality of the data used.

Results

The results section includes information on study selection, study characteristics, risk of bias within studies, results of individual studies, synthesis of results, risk of bias across studies.

Study selection

A total of 6580 articles were identified by the search strategy of different databases like PubMed, Google scholar and Cochrane of which 4860 were removed based on duplicates, 1720 articles were removed based the title and abstract. The full texts of 565 articles were screened, of which 345 articles met the inclusion criteria and were included in this review and 345 articles were taken into consideration based on the qualitative and quantitative analysis.

Study Characteristics: Description of the included studies:

The study characteristics patients suffering with cervical, breast, head and neck, gastric cancer and lung for PET/CT, PET, MRI, and CT are included in the study. Total number of studies included in this systematic review and meta-analysis all together are 345 studies. All the included studies are retrospective and prospective study design, respectively. All the studies are clinically, methodologically, and statistically similar in their characteristics with same outcomes. The accuracy of PET/CT, PET, MRI, and CT were performed by meta-analysis through sensitivity and specificity which is represented by 2x2 table which shows the true positive, true negative, false positive and false negative values with the PPV, NPV and likelihood ratios with the overall accuracy of the device performance was given in the percentage for all five cancers such as cervical, breast, Head and neck gastric and lung cancer. The results of each individual study are presented. Meta-analysis was performed, the primary measures are pooled sensitivity and specificity, but, depending on the context, other diagnostic measures. Typically, reporting of the results includes information on the number of studies, number of patients and diagnostic measures can be calculated, such as the positive and negative predictive values, the positive and negative likelihood ratios are also reported in this study [28].

Forest Plots

The test result could be negative or above which it could be positive. With such a cutoff, results of a diagnostic test could be placed in a 2×2 table with the test result. Positive predictive values, Negative predictive values, positive likelihood ratios, and negative likelihood ratios are the approaches which are used to synthesize diagnostic test accuracy studies. The relationship between the sensitivity-specificity pair will define the appropriate approach to synthesizing outcomes. Meta-analysis could be used to assess DTAs of the same condition, in which case the performance between tests should be described together with each test’s individual performance.

PET/CT- Cervical cancer

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Amit 2006	6	0	1	4	0.86 [0.42, 1.00]	1.00 [0.40, 1.00]
Belhocine 2002	19	8	3	187	0.86 [0.65, 0.97]	0.96 [0.92, 0.98]
Choi 2006	19	9	14	112	0.58 [0.39, 0.75]	0.93 [0.86, 0.97]
Choi HJ 2006	10	4	3	5	0.77 [0.46, 0.95]	0.56 [0.21, 0.86]
Chung 2007	28	4	3	17	0.90 [0.74, 0.98]	0.81 [0.58, 0.95]
Chung 2009	7	1	10	16	0.41 [0.18, 0.67]	0.94 [0.71, 1.00]
Chung 2010	8	9	20	46	0.29 [0.13, 0.49]	0.84 [0.71, 0.92]
Crivellaro 2012	4	2	11	52	0.27 [0.08, 0.55]	0.96 [0.87, 1.00]
Grisaru 2004	10	0	0	2	1.00 [0.69, 1.00]	1.00 [0.16, 1.00]
Havrilesky 2003	12	2	2	13	0.86 [0.57, 0.98]	0.87 [0.60, 0.98]
Kim 2009	26	30	33	464	0.44 [0.31, 0.58]	0.94 [0.91, 0.96]
Kim SK 2009	14	14	16	35	0.47 [0.28, 0.66]	0.71 [0.57, 0.83]
Kitajima 2008	10	0	2	40	0.83 [0.52, 0.98]	1.00 [0.91, 1.00]
Kitajima 2009	12	1	11	1198	0.52 [0.31, 0.73]	1.00 [1.00, 1.00]
Kitajima 2012	14	6	22	158	0.39 [0.23, 0.57]	0.96 [0.92, 0.99]
Kitajima K 2009	6	3	6	30	0.50 [0.21, 0.79]	0.91 [0.76, 0.98]
Kitajima M 2009	11	2	11	729	0.50 [0.28, 0.72]	1.00 [0.99, 1.00]
Kitajima S 2008	23	2	2	25	0.92 [0.74, 0.99]	0.93 [0.76, 0.99]
Lin 2003	12	2	2	34	0.86 [0.57, 0.98]	0.94 [0.81, 0.99]
Loft 2007	21	7	1	50	0.95 [0.77, 1.00]	0.88 [0.76, 0.95]
Loft A 2007	15	1	0	104	1.00 [0.78, 1.00]	0.99 [0.95, 1.00]
Lv 2014	61	17	6	1079	0.91 [0.82, 0.97]	0.98 [0.98, 0.99]
LV K 2014	34	7	0	46	1.00 [0.90, 1.00]	0.87 [0.75, 0.95]
Ma 2003	38	0	0	66	1.00 [0.91, 1.00]	1.00 [0.95, 1.00]
Mittra 2009	22	2	1	5	0.96 [0.78, 1.00]	0.71 [0.29, 0.96]
Narayan 2001	10	1	2	11	0.83 [0.52, 0.98]	0.92 [0.62, 1.00]
Narayan K 2001	4	1	3	16	0.57 [0.18, 0.90]	0.94 [0.71, 1.00]
Park 2005	9	0	13	50	0.41 [0.21, 0.64]	1.00 [0.93, 1.00]
Park W 2005	6	0	8	22	0.43 [0.18, 0.71]	1.00 [0.85, 1.00]
Reinhard 2001	17	2	4	269	0.81 [0.58, 0.95]	0.99 [0.97, 1.00]
Reinhard MJ 2001	10	0	1	24	0.91 [0.59, 1.00]	1.00 [0.86, 1.00]
Roh 2005	14	12	23	385	0.38 [0.22, 0.55]	0.97 [0.95, 0.98]
Roh JW 2005	9	0	13	50	0.41 [0.21, 0.64]	1.00 [0.93, 1.00]
Rose 1999	11	0	0	5	1.00 [0.72, 1.00]	1.00 [0.48, 1.00]
Sandvik 2011	1	3	4	28	0.20 [0.01, 0.72]	0.90 [0.74, 0.98]
Signorelli 2011	10	4	30	862	0.25 [0.13, 0.41]	1.00 [0.99, 1.00]
Signorelli M 2011	9	4	19	127	0.32 [0.16, 0.52]	0.97 [0.92, 0.99]
Sironi 2006	13	3	5	1060	0.72 [0.47, 0.90]	1.00 [0.99, 1.00]
Sironi 2007	5	0	1	6	0.83 [0.36, 1.00]	1.00 [0.54, 1.00]
Sironi S 2006	11	1	4	31	0.73 [0.45, 0.92]	0.97 [0.84, 1.00]
Stecco 2016	7	3	1	16	0.88 [0.47, 1.00]	0.84 [0.60, 0.97]
Stecco A 2016	26	17	11	162	0.70 [0.53, 0.84]	0.91 [0.85, 0.94]
Wright 2005	12	8	14	84	0.46 [0.27, 0.67]	0.91 [0.84, 0.96]
Wright D 2005	2	1	3	84	0.40 [0.05, 0.85]	0.99 [0.94, 1.00]
Wright DD 2005	10	4	9	36	0.53 [0.29, 0.76]	0.90 [0.76, 0.97]
Wright J 2005	1	1	3	40	0.25 [0.01, 0.81]	0.98 [0.87, 1.00]
Xu 2016	19	8	4	20	0.83 [0.61, 0.95]	0.71 [0.51, 0.87]

PET-Cervical cancer

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Chang 2014	17	2	1	7	0.94 [0.73, 1.00]	0.78 [0.40, 0.97]
Havrilesky 2003	12	2	2	3	0.86 [0.57, 0.98]	0.60 [0.15, 0.95]
Kitajima 2008	20	6	5	21	0.80 [0.59, 0.93]	0.78 [0.58, 0.91]
Lai 2014	61	6	6	327	0.91 [0.82, 0.97]	0.98 [0.96, 0.99]
Ryu 2003	28	52	3	166	0.90 [0.74, 0.98]	0.76 [0.70, 0.82]
Sakurai 2006	43	3	4	4	0.91 [0.80, 0.98]	0.57 [0.18, 0.90]
Vander 2003	23	1	2	13	0.92 [0.74, 0.99]	0.93 [0.66, 1.00]
Yen 2004	84	8	10	448	0.89 [0.81, 0.95]	0.98 [0.97, 0.99]

CT-Cervical cancer

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Bandy 1985	9	3	3	29	0.75 [0.43, 0.95]	0.91 [0.75, 0.98]
Bellomi 2005	31	30	17	418	0.65 [0.49, 0.78]	0.93 [0.91, 0.95]
Brenner 1982	4	0	2	6	0.67 [0.22, 0.96]	1.00 [0.54, 1.00]
Brenner H 1982	4	1	2	13	0.67 [0.22, 0.96]	0.93 [0.66, 1.00]
Camilien 1988	3	1	9	38	0.25 [0.05, 0.57]	0.97 [0.87, 1.00]
Chu 1996	4	1	6	17	0.40 [0.12, 0.74]	0.94 [0.73, 1.00]
Engelshove 1984	3	4	1	2	0.75 [0.19, 0.99]	0.33 [0.04, 0.78]
Grumbine 1981	0	1	6	17	0.00 [0.00, 0.46]	0.94 [0.73, 1.00]
Heller 1990	31	8	30	184	0.51 [0.38, 0.64]	0.96 [0.92, 0.98]
Heron 2002	24	2	2	36	0.92 [0.75, 0.99]	0.95 [0.82, 0.99]
Hertel 2002	3	8	17	47	0.15 [0.03, 0.38]	0.85 [0.73, 0.94]
Kim 1993	7	11	22	158	0.24 [0.10, 0.44]	0.93 [0.89, 0.97]
Matsukam 1989	5	2	2	61	0.71 [0.29, 0.96]	0.97 [0.89, 1.00]
Park 2000	14	3	4	15	0.78 [0.52, 0.94]	0.83 [0.59, 0.96]
Park 2005	0	0	0	0	Not estimable	Not estimable
Subak 1995	3	3	2	29	0.60 [0.15, 0.95]	0.91 [0.75, 0.98]
Villasanta 1983	10	4	3	25	0.77 [0.46, 0.95]	0.86 [0.68, 0.96]
Walsh 1980	12	3	3	7	0.80 [0.52, 0.96]	0.70 [0.35, 0.93]
Walsh 1981	27	2	1	7	0.96 [0.82, 1.00]	0.78 [0.40, 0.97]
Walsh JW 1981	11	2	2	0	0.85 [0.55, 0.98]	0.00 [0.00, 0.84]
William 2009	10	2	1	7	0.91 [0.59, 1.00]	0.78 [0.40, 0.97]
Wlash 2005	12	3	3	7	0.80 [0.52, 0.96]	0.70 [0.35, 0.93]
Yang 2000	11	2	6	57	0.65 [0.38, 0.86]	0.97 [0.88, 1.00]

MRI-Cervical cancer

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Bellomi 2005	35	31	13	417	0.73 [0.58, 0.85]	0.93 [0.90, 0.95]
Choi 2004	8	14	6	198	0.57 [0.29, 0.82]	0.93 [0.89, 0.96]
Choi 2006	4	5	9	4	0.31 [0.09, 0.61]	0.44 [0.14, 0.79]
Choi HJ 2006	12	24	3	346	0.80 [0.52, 0.96]	0.94 [0.91, 0.96]
Choi J 2006	15	47	17	1830	0.47 [0.29, 0.65]	0.97 [0.97, 0.98]
Choi k 2006	10	9	23	112	0.30 [0.16, 0.49]	0.93 [0.86, 0.97]
Chung HH 2007	30	44	66	693	0.31 [0.22, 0.42]	0.94 [0.92, 0.96]
Chung 2007	24	10	6	59	0.80 [0.61, 0.92]	0.86 [0.75, 0.93]
Chung 2010	18	17	10	38	0.64 [0.44, 0.81]	0.69 [0.55, 0.81]
Grecco 1989	3	6	5	32	0.38 [0.09, 0.76]	0.84 [0.69, 0.94]
Greco 1989	3	6	5	32	0.38 [0.09, 0.76]	0.84 [0.69, 0.94]
Hatano 1999	1	0	0	34	1.00 [0.03, 1.00]	1.00 [0.90, 1.00]
Hawighost 1998	13	3	6	11	0.68 [0.43, 0.87]	0.79 [0.49, 0.95]
Hawnaur 1994	12	4	4	29	0.75 [0.48, 0.93]	0.88 [0.72, 0.97]
Hertel 2002	3	7	4	48	0.43 [0.10, 0.82]	0.87 [0.76, 0.95]
Hertel H 2002	0	1	6	60	0.00 [0.00, 0.46]	0.98 [0.91, 1.00]
Hricak 1988	9	2	2	44	0.82 [0.48, 0.98]	0.96 [0.85, 0.99]
Janus 1989	3	2	1	16	0.75 [0.19, 0.99]	0.89 [0.65, 0.99]
Kim 1990	3	1	12	44	0.20 [0.04, 0.48]	0.98 [0.88, 1.00]
Kim 1993	7	2	22	167	0.24 [0.10, 0.44]	0.99 [0.96, 1.00]
Kim 1994	23	2	14	223	0.62 [0.45, 0.78]	0.99 [0.97, 1.00]
Kim 2009	17	16	13	33	0.57 [0.37, 0.75]	0.67 [0.52, 0.80]
Kim SK 2009	32	38	27	456	0.54 [0.41, 0.67]	0.92 [0.90, 0.94]
Lin 2008	4	22	22	990	0.15 [0.04, 0.35]	0.98 [0.97, 0.99]
Lin G 2008	3	4	9	284	0.25 [0.05, 0.57]	0.99 [0.96, 1.00]
Lin Y 2008	2	2	5	41	0.29 [0.04, 0.71]	0.95 [0.84, 0.99]
Lv 2014	15	8	19	45	0.44 [0.27, 0.62]	0.85 [0.72, 0.93]
Lv K 2014	25	16	42	1080	0.37 [0.26, 0.50]	0.99 [0.98, 0.99]
Narayanan 2001	6	0	6	12	0.50 [0.21, 0.79]	1.00 [0.74, 1.00]
Narayanan K 2001	8	6	6	16	0.57 [0.29, 0.82]	0.73 [0.50, 0.89]
Park 2005	8	6	6	16	0.57 [0.29, 0.82]	0.73 [0.50, 0.89]
Park W 2005	12	10	10	40	0.55 [0.32, 0.76]	0.80 [0.66, 0.90]
Reinhard 2001	8	4	3	20	0.73 [0.39, 0.94]	0.83 [0.63, 0.95]
Reinhard MJ 2001	14	8	7	263	0.67 [0.43, 0.85]	0.97 [0.94, 0.99]
Sahdev 2007	12	15	32	1427	0.27 [0.15, 0.43]	0.99 [0.98, 0.99]
Sahdev A 2007	7	11	12	120	0.37 [0.16, 0.62]	0.92 [0.85, 0.96]
Sheu 2001	9	4	2	26	0.82 [0.48, 0.98]	0.87 [0.69, 0.96]
Stecco 2016	7	3	1	16	0.88 [0.47, 1.00]	0.84 [0.60, 0.97]
Stecco A 2016	33	15	4	164	0.89 [0.75, 0.97]	0.92 [0.87, 0.95]
Subak 1995	8	5	5	53	0.62 [0.32, 0.86]	0.91 [0.81, 0.97]
Waggen spack 1988	3	0	0	17	1.00 [0.29, 1.00]	1.00 [0.80, 1.00]
Weber 1995	18	1	3	15	0.86 [0.64, 0.97]	0.94 [0.70, 1.00]
Williams 1989	9	2	2	7	0.82 [0.48, 0.98]	0.78 [0.40, 0.97]
Yang 2000	12	6	5	53	0.71 [0.44, 0.90]	0.90 [0.79, 0.96]
Yu 1998	9	7	5	73	0.64 [0.35, 0.87]	0.91 [0.83, 0.96]

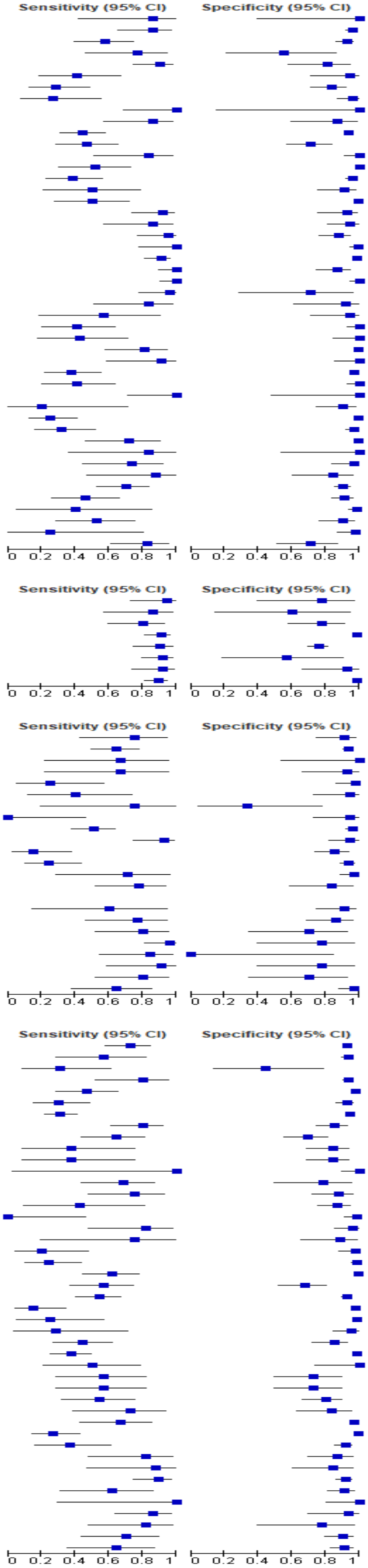


Figure 13: Forest Plot for Cervical cancer

The Diagnostic test accuracy is represented by the summary statistics and summary line from four sets of basic data, namely true positive (TP), false positive (FP), false negative (FN), and true negative (TN). Representative summary statistics are the sensitivity, specificity. Forest plot of sensitivity and specificity of detecting cervical cancer with PET with the 95 % CI for each population of the included studies. A total of 124 studies were included in this meta-analysis. Among them, 8 studies had reported the performance of PET, 49 studies had reported the performance of PET/CT, 45 studies had reported the performance of MRI and 22 studies had reported the performance of CT, respectively. After pooling all studies, of CT, MRI, PET and PET/CT Forest plot of sensitivity and specificity of *CT 0.62 (0.57, 0.67), 0.92 (0.57, 0.67), MRI 0.52 (0.49,0.55), 0.96 (0.95, 0.96) PET 0.90 (0.86,0.93) 0.93(0.91, 0.94)* and *PET/CT 0.65(0.62, 0.68) 0.97(0.97,0.98)* in detecting LN metastases cervical cancer Tumors staging like IA, IB II A, II B, III A and IV A in cervical cancer with 95 % CI for each population of the included studies.

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
CT	238	96	144	1180	0.62 [0.57, 0.67]	0.92 [0.91, 0.94]
MRI	517	446	480	9704	0.52 [0.49, 0.55]	0.96 [0.95, 0.96]
PET	288	80	33	989	0.90 [0.86, 0.93]	0.93 [0.91, 0.94]
PET-CT	670	210	358	7944	0.65 [0.62, 0.68]	0.97 [0.97, 0.98]

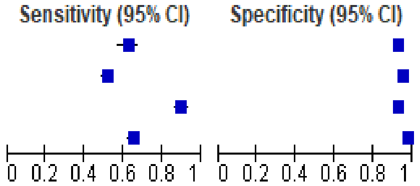


Figure 14: Cervical cancer Cumulative values

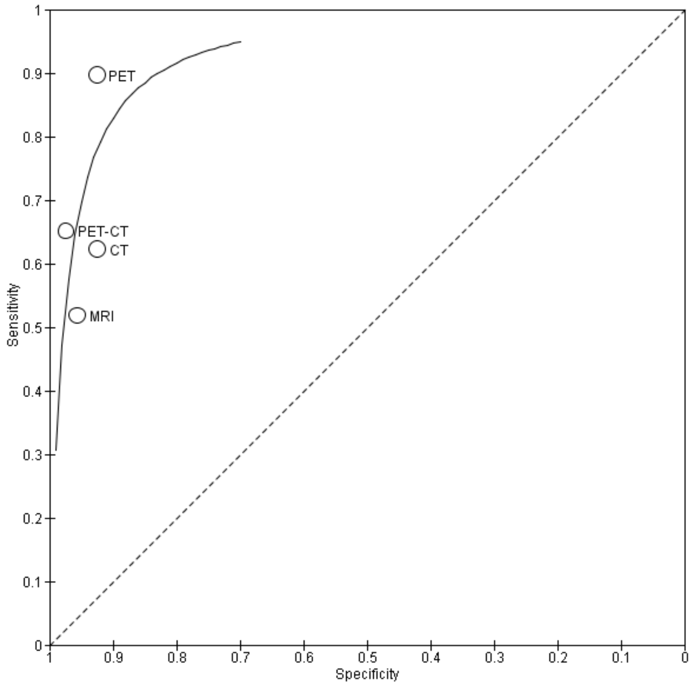
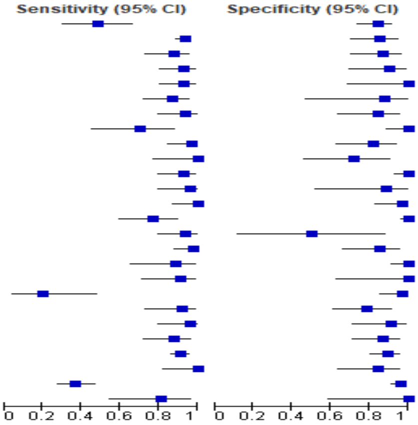


Figure 15: ROC Curve- Cumulative values for cervical cancer

The above ROC curve for cervical cancer shows PET has outperformed with higher pooled sensitivity (0.90 [95% CI: 0.86, 0.93] and specificity (0.93 [95% CI: 0.91, 0.94] when compared to PET/CT, MRI and CT.

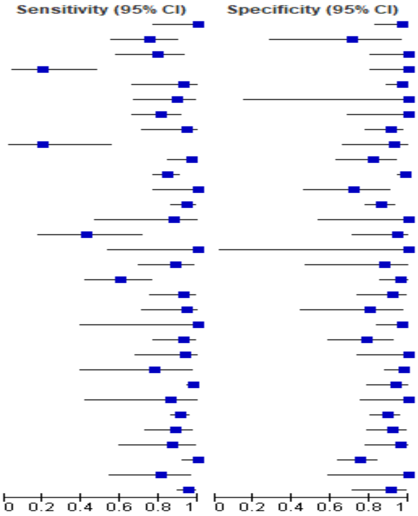
PET/CT-Breast cancer

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Chae 2009	16	12	17	63	0.48 [0.31, 0.66]	0.84 [0.74, 0.91]
Champion 2011	175	6	12	35	0.94 [0.89, 0.97]	0.85 [0.71, 0.94]
Chang 2014	35	4	5	27	0.88 [0.73, 0.96]	0.87 [0.70, 0.96]
Cochet 2014	39	2	3	19	0.93 [0.81, 0.99]	0.90 [0.70, 0.99]
Dirisamer 2010	39	0	3	10	0.93 [0.81, 0.99]	1.00 [0.69, 1.00]
Filippi 2011	33	1	5	7	0.87 [0.72, 0.96]	0.88 [0.47, 1.00]
Fueger 2005	31	4	2	21	0.94 [0.80, 0.99]	0.84 [0.64, 0.95]
Fuster 2008	14	0	6	32	0.70 [0.46, 0.88]	1.00 [0.89, 1.00]
Gallowitsch 2003	33	5	1	23	0.97 [0.85, 1.00]	0.82 [0.63, 0.94]
Goerres 2003	14	5	0	13	1.00 [0.77, 1.00]	0.72 [0.47, 0.90]
Grassetto 2011	37	0	3	49	0.93 [0.80, 0.98]	1.00 [0.93, 1.00]
Haug 2007	24	1	1	8	0.96 [0.80, 1.00]	0.89 [0.52, 1.00]
Kamel 2003	26	1	0	30	1.00 [0.87, 1.00]	0.97 [0.83, 1.00]
Kim 2009	27	0	8	102	0.77 [0.60, 0.90]	1.00 [0.96, 1.00]
Lonneux 2000	31	3	2	3	0.94 [0.80, 0.99]	0.50 [0.12, 0.88]
Manohar 2012	44	4	1	23	0.98 [0.88, 1.00]	0.85 [0.66, 0.96]
Mohammed 2020	16	0	2	42	0.89 [0.65, 0.99]	1.00 [0.92, 1.00]
Mohammed S 2020	20	0	2	8	0.91 [0.71, 0.99]	1.00 [0.63, 1.00]
Monzawa 2009	3	1	12	34	0.20 [0.04, 0.48]	0.97 [0.85, 1.00]
Moon 1998	22	7	2	26	0.92 [0.73, 0.99]	0.79 [0.61, 0.91]
Murakami 2012	24	2	1	20	0.96 [0.80, 1.00]	0.91 [0.71, 0.99]
Palomar 2010	29	5	4	32	0.88 [0.72, 0.97]	0.86 [0.71, 0.95]
Schmidt 2008	170	8	16	69	0.91 [0.86, 0.95]	0.90 [0.81, 0.95]
Veit 2007	19	4	0	21	1.00 [0.82, 1.00]	0.84 [0.64, 0.95]
Veronesi 2007	38	5	65	128	0.37 [0.28, 0.47]	0.96 [0.91, 0.99]
Wolfort 2006	13	0	3	7	0.81 [0.54, 0.96]	1.00 [0.59, 1.00]



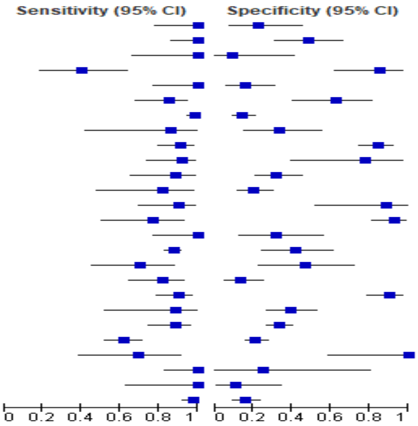
PET-Breast cancer

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Abe 2005	14	1	0	29	1.00 [0.77, 1.00]	0.97 [0.83, 1.00]
Aide 2007	21	2	7	5	0.75 [0.55, 0.89]	0.71 [0.29, 0.96]
Avril 1996	19	0	5	17	0.79 [0.58, 0.93]	1.00 [0.80, 1.00]
Barranger 2003	3	0	12	17	0.20 [0.04, 0.48]	1.00 [0.80, 1.00]
Bender 1997	13	2	1	58	0.93 [0.66, 1.00]	0.97 [0.88, 1.00]
Dehdashti 1995	17	0	2	2	0.89 [0.67, 0.99]	1.00 [0.16, 1.00]
Dirisamer 2010	34	0	8	10	0.81 [0.66, 0.91]	1.00 [0.69, 1.00]
Eubank 2004	16	4	1	40	0.94 [0.71, 1.00]	0.91 [0.78, 0.97]
Fehr 2004	2	1	8	13	0.20 [0.03, 0.56]	0.93 [0.66, 1.00]
Gallowitsch 2003	33	5	1	23	0.97 [0.85, 1.00]	0.82 [0.63, 0.94]
Gilrendo 2006	120	2	22	131	0.85 [0.77, 0.90]	0.98 [0.95, 1.00]
Goerres 2003	14	5	0	13	1.00 [0.77, 1.00]	0.72 [0.47, 0.90]
Greco 2001	68	13	4	82	0.94 [0.86, 0.98]	0.86 [0.78, 0.93]
Guillemard 2006	7	0	1	6	0.88 [0.47, 1.00]	1.00 [0.54, 1.00]
Guller 2002	6	1	8	16	0.43 [0.18, 0.71]	0.94 [0.71, 1.00]
Hathaway 1999	6	0	0	1	1.00 [0.54, 1.00]	1.00 [0.03, 1.00]
Haug 2007	23	1	3	7	0.88 [0.70, 0.98]	0.88 [0.47, 1.00]
Inoue 2004	21	2	14	44	0.60 [0.42, 0.76]	0.96 [0.85, 0.99]
Kamel 2003	25	2	2	23	0.93 [0.76, 0.99]	0.92 [0.74, 0.99]
Kim 2001	16	2	1	8	0.94 [0.71, 1.00]	0.80 [0.44, 0.97]
Lin 2002	4	1	0	31	1.00 [0.40, 1.00]	0.97 [0.84, 1.00]
Moon 1998	27	6	2	22	0.93 [0.77, 0.99]	0.79 [0.59, 0.92]
Noh 1998	14	0	1	12	0.93 [0.68, 1.00]	1.00 [0.74, 1.00]
Ohta 2001	7	1	2	42	0.78 [0.40, 0.97]	0.98 [0.88, 1.00]
Piperkova 2007	221	2	5	29	0.98 [0.95, 0.99]	0.94 [0.79, 0.99]
Raileanu 2004	6	0	1	13	0.86 [0.42, 1.00]	1.00 [0.75, 1.00]
Schmidt 2008	170	8	16	69	0.91 [0.86, 0.95]	0.90 [0.81, 0.95]
Siggelkow 2003	31	3	4	35	0.89 [0.73, 0.97]	0.92 [0.79, 0.98]
Smith 1998	13	1	2	22	0.87 [0.60, 0.98]	0.96 [0.78, 1.00]
Utech 1996	44	20	0	60	1.00 [0.92, 1.00]	0.75 [0.64, 0.84]
Wolfort 2006	13	0	3	7	0.81 [0.54, 0.96]	1.00 [0.59, 1.00]
Yang 2002	100	2	5	20	0.95 [0.89, 0.98]	0.91 [0.71, 0.99]



CT-Breast cancer

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Avril 1996	15	17	0	5	1.00 [0.78, 1.00]	0.23 [0.08, 0.45]
Chung 2006	25	18	0	17	1.00 [0.86, 1.00]	0.49 [0.31, 0.66]
Crowe 1994	9	10	0	1	1.00 [0.66, 1.00]	0.09 [0.00, 0.41]
Eubank 2001	8	3	12	17	0.40 [0.19, 0.64]	0.85 [0.62, 0.97]
Fuster 2008	14	32	0	6	1.00 [0.77, 1.00]	0.16 [0.06, 0.31]
Gallowitsch 2003	28	9	5	15	0.85 [0.68, 0.95]	0.63 [0.41, 0.81]
Gilrendo 2006	120	131	2	22	0.98 [0.94, 1.00]	0.14 [0.09, 0.21]
Guller 2002	6	16	1	8	0.86 [0.42, 1.00]	0.33 [0.16, 0.55]
Hagay 1996	42	11	4	61	0.91 [0.79, 0.98]	0.85 [0.74, 0.92]
Haug 2007	23	2	2	7	0.92 [0.74, 0.99]	0.78 [0.40, 0.97]
Kumar 2006	16	42	2	20	0.89 [0.65, 0.99]	0.32 [0.21, 0.45]
Lovrics 2004	9	63	2	16	0.82 [0.48, 0.98]	0.20 [0.12, 0.31]
Mohammed 2020	19	1	2	8	0.90 [0.70, 0.99]	0.89 [0.52, 1.00]
Mohammed S 2020	13	3	4	40	0.76 [0.50, 0.93]	0.93 [0.81, 0.99]
Ohta 2001	14	13	0	6	1.00 [0.77, 1.00]	0.32 [0.13, 0.57]
Piperkova 2007	198	18	28	13	0.88 [0.83, 0.92]	0.42 [0.25, 0.61]
Radan 2006	14	9	6	8	0.70 [0.46, 0.88]	0.47 [0.23, 0.72]
Schirrmeister 2001	27	45	6	7	0.82 [0.65, 0.93]	0.13 [0.06, 0.26]
Ternier 2006	47	5	5	46	0.90 [0.79, 0.97]	0.90 [0.79, 0.97]
Vander 2002	8	37	1	24	0.89 [0.52, 1.00]	0.39 [0.27, 0.53]
Veronesi 2007	38	128	5	65	0.88 [0.75, 0.96]	0.34 [0.27, 0.41]
Wahl 2004	66	159	40	43	0.62 [0.52, 0.71]	0.21 [0.16, 0.28]
Wolfort 2006	9	0	4	7	0.69 [0.39, 0.91]	1.00 [0.59, 1.00]
Yang 2008	20	3	0	1	1.00 [0.83, 1.00]	0.25 [0.01, 0.81]
Yutani 1999	8	16	0	2	1.00 [0.63, 1.00]	0.11 [0.01, 0.35]
Zornoza 2004	90	91	2	17	0.98 [0.92, 1.00]	0.16 [0.09, 0.24]



MRI-Breast cancer

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Belli 2002	22	2	0	16	1.00 [0.85, 1.00]	0.89 [0.65, 0.99]
Bender 1997	13	2	1	58	0.93 [0.66, 1.00]	0.97 [0.88, 1.00]
Drew 1998	63	3	0	39	1.00 [0.94, 1.00]	0.93 [0.81, 0.99]
Gilles 1993	14	1	0	11	1.00 [0.77, 1.00]	0.92 [0.62, 1.00]
Harada 2007	23	2	0	8	1.00 [0.85, 1.00]	0.80 [0.44, 0.97]
Hathaway 1999	6	0	0	1	1.00 [0.54, 1.00]	1.00 [0.03, 1.00]
Kimura 2010	2	0	0	8	1.00 [0.16, 1.00]	1.00 [0.63, 1.00]
Melani 1995	7	1	0	12	1.00 [0.59, 1.00]	0.92 [0.64, 1.00]
Memarse 2006	6	0	0	16	1.00 [0.54, 1.00]	1.00 [0.79, 1.00]
Micheal 2002	9	0	2	7	0.82 [0.48, 0.98]	1.00 [0.59, 1.00]
Mumtaz 1997	36	6	4	29	0.90 [0.76, 0.97]	0.83 [0.66, 0.93]
Murray 2002	10	17	0	20	1.00 [0.69, 1.00]	0.54 [0.37, 0.71]
Muuller 1998	10	2	0	55	1.00 [0.69, 1.00]	0.96 [0.88, 1.00]
Qayyum 2000	26	1	1	20	0.96 [0.81, 1.00]	0.95 [0.76, 1.00]
Riebe 2007	10	5	1	11	0.91 [0.59, 1.00]	0.69 [0.41, 0.89]
Stadnik 2006	5	1	0	4	1.00 [0.48, 1.00]	0.80 [0.28, 0.99]

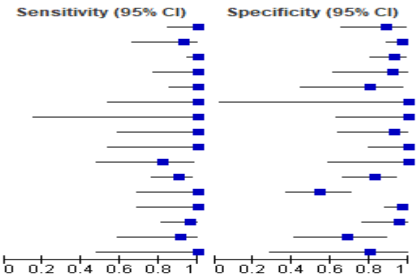


Figure 16: Forest Plot for Breast cancer

The Diagnostic test accuracy is represented by the summary statistics and summary line from four sets of basic data, namely true positive (TP), false positive (FP), false negative (FN), and true negative (TN). Representative summary statistics are the sensitivity, specificity. Forest plot of sensitivity and specificity of detecting cervical cancer with PET with the 95 % CI for each population of the included studies. A total of 99 studies were included in this meta-analysis. Among them, 32 studies had reported the performance of PET, 25 studies had reported the performance of PET/CT, 16 studies had reported the performance of MRI and 26 studies had reported the performance of CT, respectively. After pooling all studies, of CT, MRI, PET and PET/CT Forest plot of sensitivity and specificity of *CT 0.87 (0.85, 0.89), 0.35 (0.33,0.38) MRI 0.97 (0.94, 0.98), 0.88(0.84, 0.91) PET 0.89 (0.86,0.90) 0.91(0.89, 0.93) and PET/CT 0.86(0.83, 0.88) 0.91(0.89, 0.93)* in detecting local recurrences, lesion basis, distant metastases, and breast lesions in Breast cancer with 95 % CI for each population of the included studies.

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
CT	886	882	133	482	0.87 [0.85, 0.89]	0.35 [0.33, 0.38]
MRI	262	43	9	315	0.97 [0.94, 0.98]	0.88 [0.84, 0.91]
PET	1028	85	136	887	0.88 [0.86, 0.90]	0.91 [0.89, 0.93]
PET/CT	969	79	164	818	0.86 [0.83, 0.88]	0.91 [0.89, 0.93]

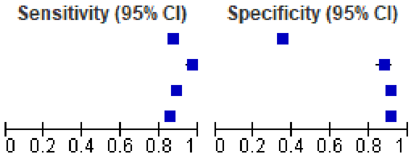


Figure 17: Breast cancer Cumulative values

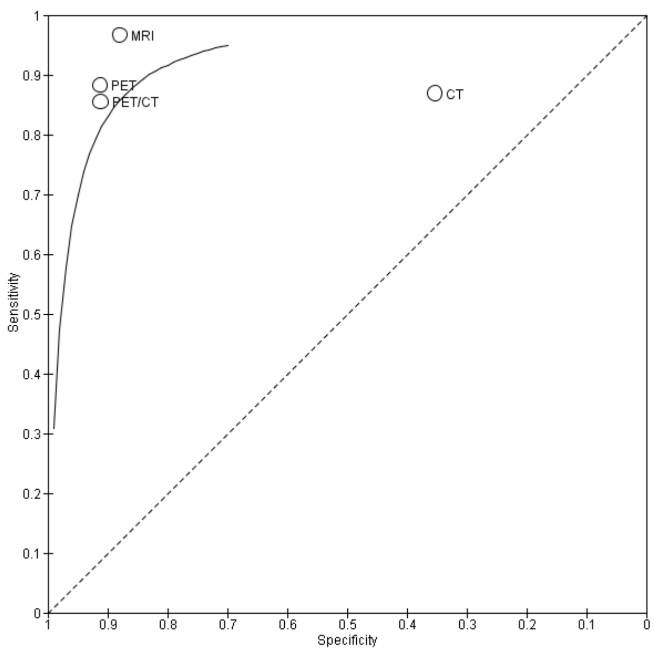
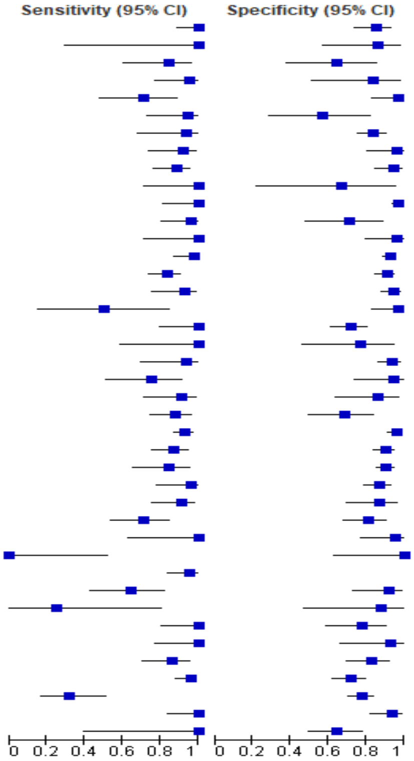


Figure 18: ROC Curve- Cumulative values for breast cancer

The above ROC curve for breast cancer shows MRI has outperformed with higher pooled sensitivity (0.97 [95% CI: 0.94, 0.98] and specificity (0.88 [95% CI: 0.84, 0.91] when compared to PET/CT, PET and CT.

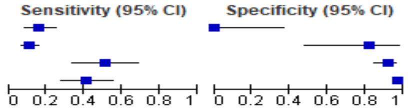
PET/CT-Head and neck cancer

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Abgral 2009	30	9	0	52	1.00 [0.88, 1.00]	0.85 [0.74, 0.93]
Babin 2008	3	2	0	12	1.00 [0.29, 1.00]	0.86 [0.57, 0.98]
cetin 2013	16	6	3	11	0.84 [0.60, 0.97]	0.65 [0.38, 0.86]
Chan 2006	21	2	1	10	0.95 [0.77, 1.00]	0.83 [0.52, 0.98]
Chauhan 2012	15	1	6	29	0.71 [0.48, 0.89]	0.97 [0.83, 1.00]
Fakhry 2007	17	6	1	8	0.94 [0.73, 1.00]	0.57 [0.29, 0.82]
Ghanooni 2011	14	17	1	87	0.93 [0.68, 1.00]	0.84 [0.75, 0.90]
Gordin 2006	23	1	2	25	0.92 [0.74, 0.99]	0.96 [0.80, 1.00]
Gordin 2007	46	3	6	52	0.88 [0.77, 0.96]	0.95 [0.85, 0.99]
Goshen 2005	11	2	0	4	1.00 [0.72, 1.00]	0.67 [0.22, 0.96]
Ho 2013	18	7	0	227	1.00 [0.81, 1.00]	0.97 [0.94, 0.99]
Jeong 2007	25	6	1	15	0.96 [0.80, 1.00]	0.71 [0.48, 0.89]
Kao 1998	11	1	0	24	1.00 [0.72, 1.00]	0.96 [0.80, 1.00]
Kim 2007	39	23	1	286	0.97 [0.87, 1.00]	0.93 [0.89, 0.95]
Kim 2011	74	13	15	126	0.83 [0.74, 0.90]	0.91 [0.85, 0.95]
Kim 2013	25	5	2	87	0.93 [0.76, 0.99]	0.95 [0.88, 0.98]
Krabbe 2008	4	1	4	29	0.50 [0.16, 0.84]	0.97 [0.83, 1.00]
Krabbe 2009	16	26	0	66	1.00 [0.79, 1.00]	0.72 [0.61, 0.81]
Kubota 2004	7	3	0	10	1.00 [0.59, 1.00]	0.77 [0.46, 0.95]
Lee 2007	15	5	1	74	0.94 [0.70, 1.00]	0.94 [0.86, 0.98]
Lee 2015	15	1	5	18	0.75 [0.51, 0.91]	0.95 [0.74, 1.00]
Li 2001	20	3	2	18	0.91 [0.71, 0.99]	0.86 [0.64, 0.97]
Nahmias 2007	37	10	5	22	0.88 [0.74, 0.96]	0.69 [0.50, 0.84]
Nakamura 2013	119	6	9	136	0.93 [0.87, 0.97]	0.96 [0.91, 0.98]
Ng 2010	48	12	7	112	0.87 [0.76, 0.95]	0.90 [0.84, 0.95]
Paidpally 2013	22	19	4	182	0.85 [0.65, 0.96]	0.91 [0.86, 0.94]
Robin 2015	22	12	1	81	0.96 [0.78, 1.00]	0.87 [0.79, 0.93]
Roh 2007	30	4	3	26	0.91 [0.76, 0.98]	0.87 [0.69, 0.96]
Roh 2014	27	10	11	43	0.71 [0.54, 0.85]	0.81 [0.68, 0.91]
Salaun 2007	8	1	0	21	1.00 [0.63, 1.00]	0.95 [0.77, 1.00]
Schroeder 2008	0	0	5	8	0.00 [0.00, 0.52]	1.00 [0.63, 1.00]
Seitz 2009	39	0	2	0	0.95 [0.83, 0.99]	Not estimable
Sohn 2016	16	2	9	22	0.64 [0.43, 0.82]	0.92 [0.73, 0.99]
Stoeckli 2002	1	1	3	7	0.25 [0.01, 0.81]	0.88 [0.47, 1.00]
Stokkel 1999	17	7	0	24	1.00 [0.80, 1.00]	0.77 [0.59, 0.90]
Tsai 2002	14	1	0	13	1.00 [0.77, 1.00]	0.93 [0.66, 1.00]
Wierzbicka 2011	31	8	5	39	0.86 [0.71, 0.95]	0.83 [0.69, 0.92]
Wong 2002	69	31	3	78	0.96 [0.88, 0.99]	0.72 [0.62, 0.80]
Yamaga 2018	10	39	21	135	0.32 [0.17, 0.51]	0.78 [0.71, 0.84]
Yen 2003	21	3	0	43	1.00 [0.84, 1.00]	0.93 [0.82, 0.99]
Zundel 2011	4	17	0	31	1.00 [0.40, 1.00]	0.65 [0.49, 0.78]



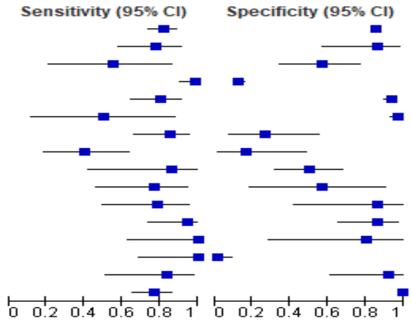
PET-Head and neck cancer

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Chang 2005	14	8	73	0	0.16 [0.09, 0.26]	0.00 [0.00, 0.37]
Liu 2006	21	2	170	9	0.11 [0.07, 0.16]	0.82 [0.48, 0.98]
Shu 2006	18	8	17	91	0.51 [0.34, 0.69]	0.92 [0.85, 0.96]
Shu-hang 2006	21	13	30	393	0.41 [0.28, 0.56]	0.97 [0.95, 0.98]



CT-Head and neck cancer

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Adams 1998	96	175	21	992	0.82 [0.74, 0.89]	0.85 [0.83, 0.87]
Akoglu 2005	21	2	6	12	0.78 [0.58, 0.91]	0.86 [0.57, 0.98]
Braams 1995	5	10	4	13	0.56 [0.21, 0.86]	0.57 [0.34, 0.77]
Curtin 1998	57	415	1	62	0.98 [0.91, 1.00]	0.13 [0.10, 0.16]
Dammann 2005	32	17	8	236	0.80 [0.64, 0.91]	0.93 [0.89, 0.96]
Eida 2003	3	5	3	162	0.50 [0.12, 0.88]	0.97 [0.93, 0.99]
Fan 2006	23	11	4	4	0.85 [0.66, 0.96]	0.27 [0.08, 0.55]
Hafidh 2006	8	10	12	2	0.40 [0.19, 0.64]	0.17 [0.02, 0.48]
Kau 1999	6	17	1	17	0.86 [0.42, 1.00]	0.50 [0.32, 0.68]
Ke 2006	10	3	3	4	0.77 [0.46, 0.95]	0.57 [0.18, 0.90]
Lu 2007	11	1	3	6	0.79 [0.49, 0.95]	0.86 [0.42, 1.00]
Mcguirt 1995	18	3	1	19	0.95 [0.74, 1.00]	0.86 [0.65, 0.97]
Paulus 1998	8	1	0	4	1.00 [0.63, 1.00]	0.80 [0.28, 0.99]
Peters 2012	10	56	0	1	1.00 [0.69, 1.00]	0.02 [0.00, 0.09]
Wu 2010	10	1	2	11	0.83 [0.52, 0.98]	0.92 [0.62, 1.00]
Yoon 2009	57	2	17	326	0.77 [0.66, 0.86]	0.99 [0.98, 1.00]



MRI-Head and neck cancer

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Adams 1998	94	250	23	917	0.80 [0.72, 0.87]	0.79 [0.76, 0.81]
Akoglu 2005	16	1	11	13	0.59 [0.39, 0.78]	0.93 [0.66, 1.00]
Braams 1995	5	6	10	134	0.33 [0.12, 0.62]	0.96 [0.91, 0.98]
Curtin 1998	53	382	5	95	0.91 [0.81, 0.97]	0.20 [0.16, 0.24]
Dammann 2005	37	14	3	239	0.93 [0.80, 0.98]	0.94 [0.91, 0.97]
Ding 2005	132	27	34	255	0.80 [0.73, 0.85]	0.90 [0.86, 0.94]
Gu 2000	8	3	1	50	0.89 [0.52, 1.00]	0.94 [0.84, 0.99]
Hafidh 2006	11	10	9	2	0.55 [0.32, 0.77]	0.17 [0.02, 0.48]
Hao 2000	30	2	11	38	0.73 [0.57, 0.86]	0.95 [0.83, 0.99]
Kau 1999	2	17	1	15	0.67 [0.09, 0.99]	0.47 [0.29, 0.65]
Laubenbacher 1994	13	7	5	9	0.72 [0.47, 0.90]	0.56 [0.30, 0.80]
Nakamoto 2009	16	2	4	30	0.80 [0.56, 0.94]	0.94 [0.79, 0.99]
Olmos 1999	22	11	2	27	0.92 [0.73, 0.99]	0.71 [0.54, 0.85]
Seitz 2009	20	1	0	4	1.00 [0.83, 1.00]	0.80 [0.28, 0.99]
VandenBrekel 1991	87	13	42	415	0.67 [0.59, 0.75]	0.97 [0.95, 0.98]
Wang 1999	23	0	15	130	0.61 [0.43, 0.76]	1.00 [0.97, 1.00]
Wide 1999	18	11	9	34	0.67 [0.46, 0.83]	0.76 [0.60, 0.87]
Wilson 1994	17	16	0	18	1.00 [0.80, 1.00]	0.53 [0.35, 0.70]
Yoon 2009	57	2	17	326	0.77 [0.66, 0.86]	0.99 [0.98, 1.00]
Yuan 2000	12	1	2	9	0.86 [0.57, 0.98]	0.90 [0.55, 1.00]

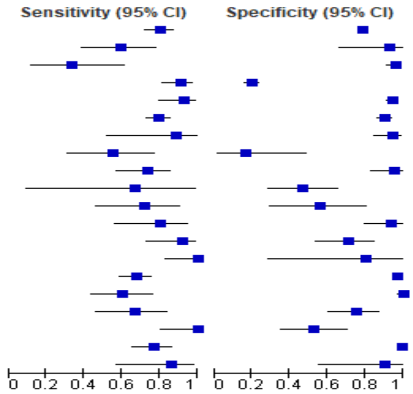


Figure 19: Forest Plot for Head and neck cancer

The Diagnostic test accuracy is represented by the summary statistics and summary line from four sets of basic data, namely true positive (TP), false positive (FP), false negative (FN), and true negative (TN). Representative summary statistics are the sensitivity, specificity. Forest plot of sensitivity and specificity of detecting cervical cancer with PET with the 95 % CI for each population of the included studies. A total of 81 studies were included in this meta-analysis. Among them, 4 studies had reported the performance of PET, 41 studies had reported the performance of PET/CT, 20 studies had reported the performance of MRI and 16 studies had reported the performance of CT, respectively. After pooling all studies, of CT, MRI, PET and PET/CT Forest plot of sensitivity and specificity of *CT 0.81(0.77,0.85), 0.72(0.70, 0.74) MRI 0.77(0.74,0.79), 0.78(0.77,0.79) PET 0.20 (0.16, 0.25) 0.94(0.92, 0.96) and PET/CT 0.84(0.82,0.86) 0.88(0.86,0.89)* in detecting Lymph node metastasis, detection of recurrence in patients and detecting neck levels I, II, and III with head and neck cancer Head and neck cancer with 95 % CI for each population of the included studies.

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
CT	375	729	86	1871	0.81 [0.77, 0.85]	0.72 [0.70, 0.74]
MRI	673	776	204	2760	0.77 [0.74, 0.79]	0.78 [0.77, 0.79]
PET	74	31	290	493	0.20 [0.16, 0.25]	0.94 [0.92, 0.96]
PET/CT	1000	326	192	2292	0.84 [0.82, 0.86]	0.88 [0.86, 0.89]

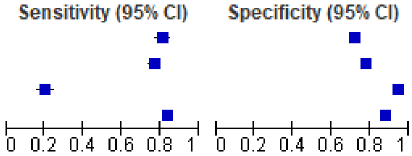


Figure 20: Head and Neck cancer Cumulative values

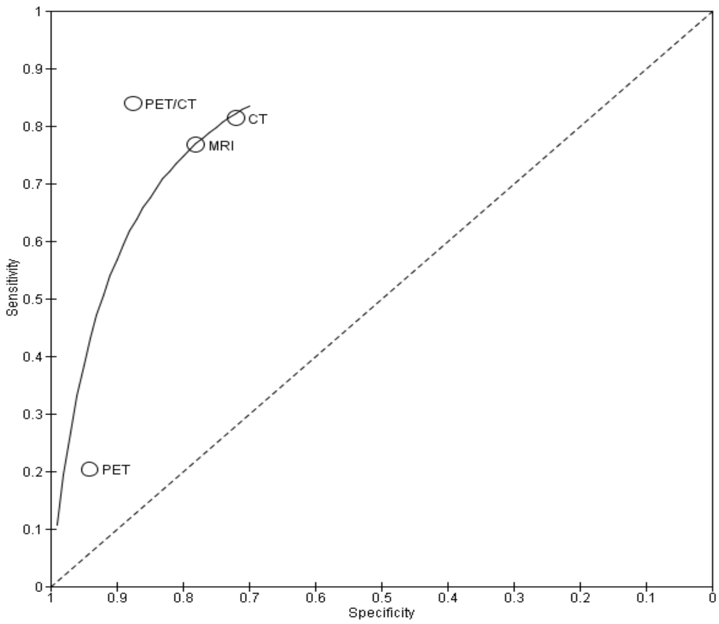
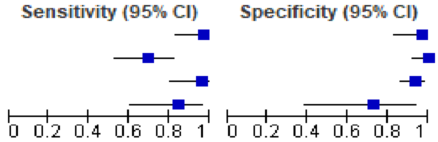


Figure 21: ROC Curve- Cumulative values for Head and Neck cancer

The above ROC curve for head and neck cancer shows PET/CT has outperformed with higher pooled sensitivity (0.84 [95% CI: 0.84, 0.86] and specificity (0.88 [95% CI: 0.86, 0.89] when compared to MRI, PET and CT.

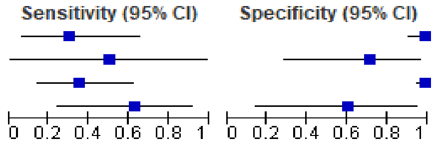
PET/CT-Gastric cancer

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Dirisamer 2009	30	1	1	30	0.97 [0.83, 1.00]	0.97 [0.83, 1.00]
Kawanaka 2016	29	0	13	44	0.69 [0.53, 0.82]	1.00 [0.92, 1.00]
Satoh2011	25	5	1	76	0.96 [0.80, 1.00]	0.94 [0.86, 0.98]
Soussan 2012	16	3	3	8	0.84 [0.60, 0.97]	0.73 [0.39, 0.94]



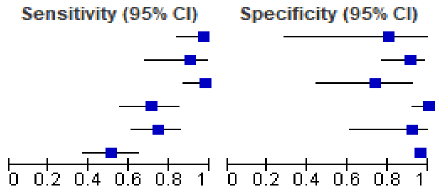
PET-Gastric cancer

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Chen 2005	3	1	7	57	0.30 [0.07, 0.65]	0.98 [0.91, 1.00]
Kim 2011	1	2	1	5	0.50 [0.01, 0.99]	0.71 [0.29, 0.96]
Lim 2006	6	1	11	94	0.35 [0.14, 0.62]	0.99 [0.94, 1.00]
Potter 2002	5	2	3	3	0.63 [0.24, 0.91]	0.60 [0.15, 0.95]



CT-Gastric cancer

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Duhr 2011	31	1	1	4	0.97 [0.84, 1.00]	0.80 [0.28, 0.99]
Giganti 2016	18	3	2	32	0.90 [0.68, 0.99]	0.91 [0.77, 0.98]
Karakoyun 2014	39	4	1	11	0.97 [0.87, 1.00]	0.73 [0.45, 0.92]
Kawanaka 2016	30	0	12	44	0.71 [0.55, 0.84]	1.00 [0.92, 1.00]
Kim 2011	44	1	15	11	0.75 [0.62, 0.85]	0.92 [0.62, 1.00]
Kim SJ 2009	27	17	26	428	0.51 [0.37, 0.65]	0.96 [0.94, 0.98]



MRI-Gastric cancer

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Fuji 2008	13	1	2	10	0.87 [0.60, 0.98]	0.91 [0.59, 1.00]
Satoh2011	20	16	4	90	0.83 [0.63, 0.95]	0.85 [0.77, 0.91]
Soussan 2012	16	2	3	9	0.84 [0.60, 0.97]	0.82 [0.48, 0.98]

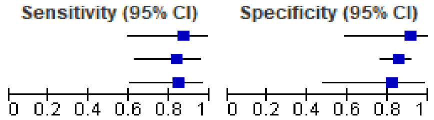


Figure 22: Forest Plot for Gastric Cancer

The Diagnostic test accuracy is represented by the summary statistics and summary line from four sets of basic data, namely true positive (TP), false positive (FP), false negative (FN), and true negative (TN). Representative summary statistics are the sensitivity, specificity. Forest plot of sensitivity and specificity of detecting cervical cancer with PET with the 95 % CI for each population of the included studies. A total of 17 studies were included in this meta-analysis. Among them, 4 studies had reported the performance of PET, 4 studies had reported the performance of PET/CT, 3 studies had reported the performance of MRI and 7 studies had reported the performance of CT, respectively. After pooling all studies, of CT, MRI, PET and PET/CT Forest plot of *sensitivity and specificity of CT 0.77(0.71,0.82), 0.95(0.93,0.97) MRI 0.84(0.73,0.93), 0.850.78,0.91() PET 0.41(0.25,0.58) 0.96(0.92,0.99) and PET/CT 0.85(0.77,0.91) 0.95 (0.90, 0.98)* in detecting recurrent gastric cancer and Peritoneal metastases in Gastric cancer with 95 % CI for each population of the included studies.

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
CT	189	26	57	530	0.77 [0.71, 0.82]	0.95 [0.93, 0.97]
MRI	49	19	9	109	0.84 [0.73, 0.93]	0.85 [0.78, 0.91]
PET	15	6	22	159	0.41 [0.25, 0.58]	0.96 [0.92, 0.99]
PET/CT	100	9	18	158	0.85 [0.77, 0.91]	0.95 [0.90, 0.98]

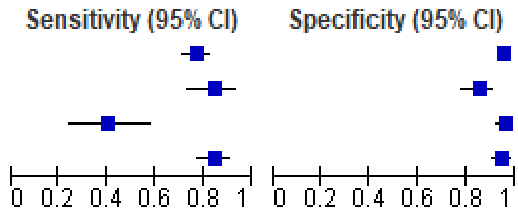


Figure 23: Gastric cancer Cumulative values

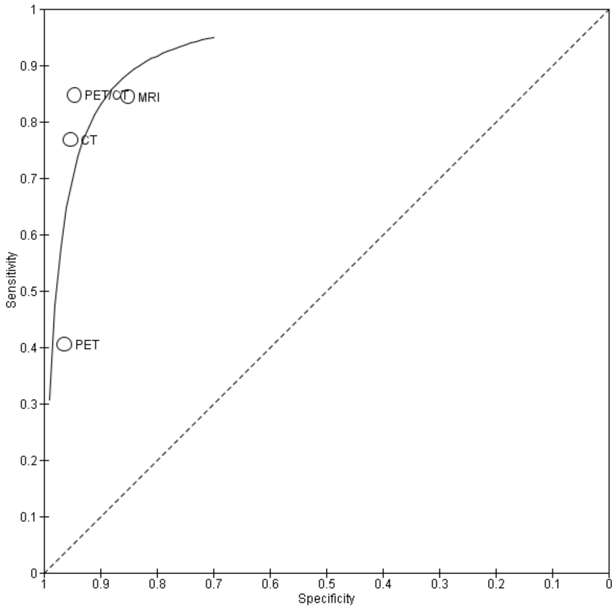
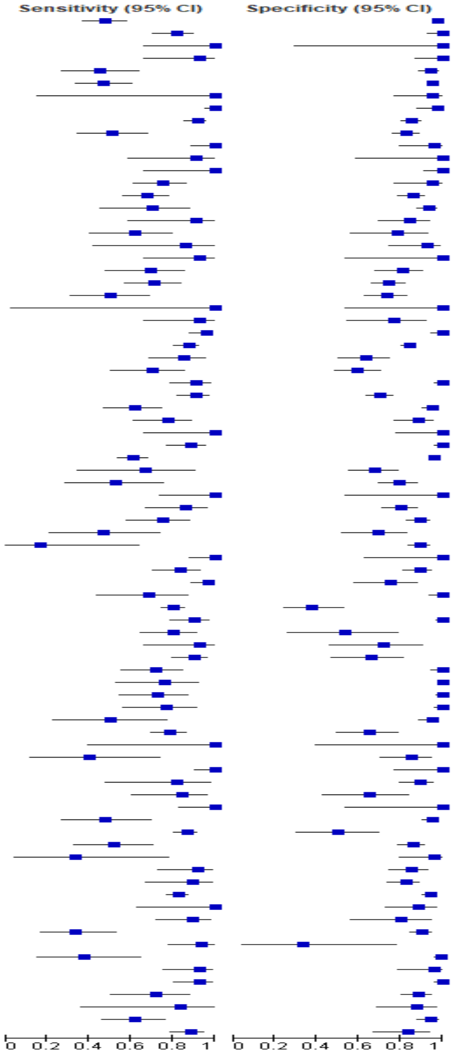


Figure 24: ROC Curve- Cumulative values for Gastric cancer

The above ROC curve for gastric cancer shows PET/CT has outperformed with higher pooled sensitivity (0.85 [95% CI: 0.77, 0.91] and specificity (0.95 [95% CI: 0.90, 0.98] when compared to MRI, PET and CT.

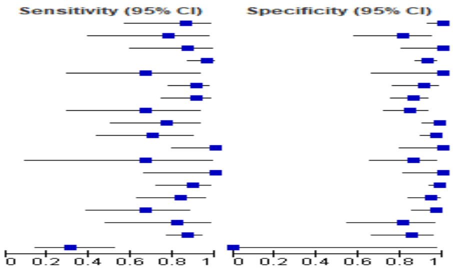
PET/CT-Lung Cancer

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Al-Sarraf 2008	48	20	53	842	0.48 [0.37, 0.58]	0.98 [0.96, 0.99]
Annema 2010	58	0	13	52	0.82 [0.71, 0.90]	1.00 [0.93, 1.00]
Arslan 2011	9	0	0	3	1.00 [0.66, 1.00]	1.00 [0.29, 1.00]
Azad 2010	13	0	1	27	0.93 [0.66, 1.00]	1.00 [0.87, 1.00]
Bille 2009	14	7	17	121	0.45 [0.27, 0.64]	0.95 [0.89, 0.98]
Bille 2013	28	13	32	280	0.47 [0.34, 0.60]	0.96 [0.93, 0.98]
Bradley 2004	2	1	0	21	1.00 [0.16, 1.00]	0.95 [0.77, 1.00]
Brink 2004	76	1	0	43	1.00 [0.95, 1.00]	0.98 [0.88, 1.00]
Bryant 2006	131	33	12	195	0.92 [0.86, 0.96]	0.86 [0.80, 0.90]
Carnochan 2009	19	27	18	130	0.51 [0.34, 0.68]	0.83 [0.76, 0.88]
Chen 2010	31	1	0	24	1.00 [0.89, 1.00]	0.96 [0.80, 1.00]
Chin 2002	10	0	1	7	0.91 [0.59, 1.00]	1.00 [0.59, 1.00]
Czepczynski 2011	9	0	0	42	1.00 [0.66, 1.00]	1.00 [0.92, 1.00]
Dabrowska 2015	37	1	12	21	0.76 [0.61, 0.87]	0.95 [0.77, 1.00]
Dalli 2013	54	18	26	111	0.68 [0.56, 0.78]	0.86 [0.79, 0.92]
Darling 2011	14	8	6	121	0.70 [0.46, 0.88]	0.94 [0.88, 0.97]
De wever 2007	10	6	1	33	0.91 [0.59, 1.00]	0.85 [0.69, 0.94]
Degirmenci 2008	16	5	10	18	0.62 [0.41, 0.80]	0.78 [0.56, 0.93]
El-Hariri 2012	6	2	1	24	0.86 [0.42, 1.00]	0.92 [0.75, 0.99]
Fischer 2007	13	0	1	6	0.93 [0.66, 1.00]	1.00 [0.54, 1.00]
Fischer 2011	18	10	8	43	0.69 [0.48, 0.86]	0.81 [0.68, 0.91]
Gunluoglu 2011	35	30	14	89	0.71 [0.57, 0.83]	0.75 [0.66, 0.82]
Harders 2012	15	22	15	62	0.50 [0.31, 0.69]	0.74 [0.63, 0.83]
Hauber 2001	1	0	0	6	1.00 [0.03, 1.00]	1.00 [0.54, 1.00]
Herder 2004	13	5	1	17	0.93 [0.66, 1.00]	0.77 [0.55, 0.92]
Herth 2010	68	0	3	68	0.96 [0.88, 0.99]	1.00 [0.95, 1.00]
Hu 2008	117	72	17	378	0.87 [0.80, 0.92]	0.84 [0.80, 0.87]
Hu 2011	29	25	5	43	0.85 [0.69, 0.95]	0.63 [0.51, 0.75]
Hwangbo 2009	21	35	9	52	0.70 [0.51, 0.85]	0.60 [0.49, 0.70]
Hwangbo 2010	41	0	4	98	0.91 [0.79, 0.98]	1.00 [0.96, 1.00]
Iskender 2012	63	65	6	152	0.91 [0.82, 0.97]	0.70 [0.63, 0.76]
Jeon 2010	32	8	20	150	0.62 [0.47, 0.75]	0.95 [0.90, 0.98]
Jeong 2008	31	7	9	53	0.78 [0.62, 0.89]	0.88 [0.77, 0.95]
Kamel 2003	9	0	0	15	1.00 [0.66, 1.00]	1.00 [0.78, 1.00]
Kang 2014	52	0	7	89	0.88 [0.77, 0.95]	1.00 [0.96, 1.00]
Kim 2007	110	21	70	473	0.61 [0.54, 0.68]	0.96 [0.94, 0.97]
Koksal 2013	8	22	4	47	0.67 [0.35, 0.90]	0.68 [0.56, 0.79]
Kuo 2012	10	17	9	66	0.53 [0.29, 0.76]	0.80 [0.69, 0.88]
Kut 2007	12	0	0	6	1.00 [0.74, 1.00]	1.00 [0.54, 1.00]
Lee 2007	24	19	4	79	0.86 [0.67, 0.96]	0.81 [0.71, 0.88]
Lee 2009	27	16	9	130	0.75 [0.58, 0.88]	0.89 [0.83, 0.94]
Lee 2011	7	12	8	27	0.47 [0.21, 0.73]	0.69 [0.52, 0.83]
Lee 2012	1	16	5	138	0.17 [0.00, 0.64]	0.90 [0.84, 0.94]
Lee 2014	29	0	0	8	1.00 [0.88, 1.00]	1.00 [0.63, 1.00]
Li 2010	41	12	8	97	0.84 [0.70, 0.93]	0.89 [0.82, 0.94]
Li 2011	58	9	2	27	0.97 [0.88, 1.00]	0.75 [0.58, 0.88]
Li 2012	13	0	6	61	0.68 [0.43, 0.87]	1.00 [0.94, 1.00]
Li 2014	199	31	49	19	0.80 [0.75, 0.85]	0.38 [0.25, 0.53]
Liberman 2014	47	0	5	114	0.90 [0.79, 0.97]	1.00 [0.97, 1.00]
Lopez 2015	32	7	8	8	0.80 [0.64, 0.91]	0.53 [0.27, 0.79]
Martins 2008	13	5	1	13	0.93 [0.66, 1.00]	0.72 [0.47, 0.90]
Morikawa 2009	55	11	6	21	0.90 [0.80, 0.96]	0.66 [0.47, 0.81]
Ohnishi 2011	28	0	11	71	0.72 [0.55, 0.85]	1.00 [0.95, 1.00]
Ohno 2011	16	0	5	229	0.76 [0.53, 0.92]	1.00 [0.98, 1.00]
Oki 2014	24	0	9	113	0.73 [0.54, 0.87]	1.00 [0.97, 1.00]
Orlacchio 2007	20	0	6	100	0.77 [0.56, 0.91]	1.00 [0.96, 1.00]
Ose 2012	7	5	7	93	0.50 [0.23, 0.77]	0.95 [0.88, 0.98]
Ozkan 2011	84	16	23	30	0.79 [0.70, 0.86]	0.65 [0.50, 0.79]
Pandit 2003	4	0	0	4	1.00 [0.40, 1.00]	1.00 [0.40, 1.00]
Perigaud 2009	4	6	6	35	0.40 [0.12, 0.74]	0.85 [0.71, 0.94]
Plathow 2008	38	0	0	14	1.00 [0.91, 1.00]	1.00 [0.77, 1.00]
Sanli 2009	9	7	2	60	0.82 [0.48, 0.98]	0.90 [0.80, 0.96]
Saydam 2012	16	8	3	15	0.84 [0.60, 0.97]	0.65 [0.43, 0.84]
Schumacher 2001	20	0	0	6	1.00 [0.83, 1.00]	1.00 [0.54, 1.00]
Shin 2008	11	8	12	153	0.48 [0.27, 0.69]	0.95 [0.90, 0.98]
Sim 2013	137	14	21	14	0.87 [0.80, 0.92]	0.50 [0.31, 0.69]
Sit 2010	15	18	14	110	0.52 [0.33, 0.71]	0.86 [0.79, 0.91]
Sommer 2012	2	1	4	24	0.33 [0.04, 0.78]	0.96 [0.80, 1.00]
Subedi 2009	22	10	2	57	0.92 [0.73, 0.99]	0.85 [0.74, 0.93]
Tasci 2010	17	19	2	89	0.89 [0.67, 0.99]	0.82 [0.74, 0.89]
Tassia 2020	197	18	41	280	0.83 [0.77, 0.87]	0.94 [0.91, 0.96]
Toba 2010	8	4	0	30	1.00 [0.63, 1.00]	0.88 [0.73, 0.97]
Tournoy 2007	25	4	3	16	0.89 [0.72, 0.98]	0.80 [0.56, 0.94]
Uruga 2011	10	15	20	137	0.33 [0.17, 0.53]	0.90 [0.84, 0.94]
Uskul 2009	28	4	2	2	0.93 [0.78, 0.99]	0.33 [0.04, 0.78]
Usuda 2013	6	1	10	143	0.38 [0.15, 0.65]	0.99 [0.96, 1.00]
Vinjamuri 2008	25	1	2	23	0.93 [0.76, 0.99]	0.96 [0.79, 1.00]
Wallace 2008	39	0	3	96	0.93 [0.81, 0.99]	1.00 [0.96, 1.00]
Yang 2008	18	11	7	86	0.72 [0.51, 0.88]	0.89 [0.81, 0.94]
Yang 2010	5	3	1	22	0.83 [0.36, 1.00]	0.88 [0.69, 0.97]
Yi 2008	28	6	17	99	0.62 [0.47, 0.76]	0.94 [0.88, 0.98]
Zhang 2014	68	6	9	30	0.88 [0.79, 0.95]	0.83 [0.67, 0.94]



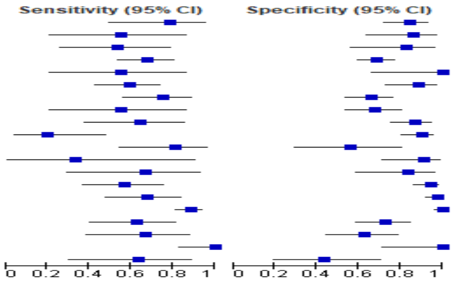
PET-Lung cancer

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Bury 1997	12	0	2	52	0.86 [0.57, 0.98]	1.00 [0.93, 1.00]
Chin 1995	7	4	2	17	0.78 [0.40, 0.97]	0.81 [0.58, 0.95]
Guhlmann 1997	13	0	2	17	0.87 [0.60, 0.98]	1.00 [0.80, 1.00]
Gupta 2000	51	8	2	107	0.96 [0.87, 1.00]	0.93 [0.87, 0.97]
Hagberg 1997	6	0	3	9	0.67 [0.30, 0.93]	1.00 [0.66, 1.00]
Marom 1999	40	3	4	31	0.91 [0.78, 0.97]	0.91 [0.76, 0.98]
Pieterman 2000	29	10	3	60	0.91 [0.75, 0.98]	0.86 [0.75, 0.93]
Poncelet 2001	6	8	3	44	0.67 [0.30, 0.93]	0.85 [0.72, 0.93]
Sasaki 1996	13	1	4	53	0.76 [0.50, 0.93]	0.98 [0.90, 1.00]
Saunders 1999	12	2	5	65	0.71 [0.44, 0.90]	0.97 [0.90, 1.00]
Sazon 1996	16	0	0	16	1.00 [0.79, 1.00]	1.00 [0.79, 1.00]
Scott 1994	2	3	1	19	0.67 [0.09, 0.99]	0.86 [0.65, 0.97]
Scott 1996	9	0	0	18	1.00 [0.66, 1.00]	1.00 [0.81, 1.00]
Steinert 1997	25	1	3	83	0.89 [0.72, 0.98]	0.99 [0.94, 1.00]
Valk 1995	20	3	4	49	0.83 [0.63, 0.95]	0.94 [0.84, 0.99]
Vansteenkiste 1997	10	1	5	34	0.67 [0.38, 0.88]	0.97 [0.85, 1.00]
Wahl 1994	9	3	2	13	0.82 [0.48, 0.98]	0.81 [0.54, 0.96]
Yasuomi 2009	61	4	9	23	0.87 [0.77, 0.94]	0.85 [0.66, 0.96]
Yasuomi O 2009	8	1	18	0	0.31 [0.14, 0.52]	0.00 [0.00, 0.97]



CT-Lung cancer

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Bury 1997	11	8	3	44	0.79 [0.49, 0.95]	0.85 [0.72, 0.93]
Chin 1995	5	3	4	18	0.56 [0.21, 0.86]	0.86 [0.64, 0.97]
Guhlmann 1997	8	3	7	14	0.53 [0.27, 0.79]	0.82 [0.57, 0.96]
Gupta 2000	36	36	17	79	0.68 [0.54, 0.80]	0.69 [0.59, 0.77]
Hagberg 1997	5	0	4	9	0.56 [0.21, 0.86]	1.00 [0.66, 1.00]
Marom 1999	26	4	18	30	0.59 [0.43, 0.74]	0.88 [0.73, 0.97]
Pieterman 2000	24	24	8	46	0.75 [0.57, 0.89]	0.66 [0.53, 0.77]
Poncelet 2001	5	17	4	36	0.56 [0.21, 0.86]	0.68 [0.54, 0.80]
Sasaki 1996	11	7	6	47	0.65 [0.38, 0.86]	0.87 [0.75, 0.95]
Saunders 1999	3	7	12	62	0.20 [0.04, 0.48]	0.90 [0.80, 0.96]
Sazon 1996	13	7	3	9	0.81 [0.54, 0.96]	0.56 [0.30, 0.80]
Scott 1994	1	2	2	20	0.33 [0.01, 0.91]	0.91 [0.71, 0.99]
Scott 1996	6	3	3	15	0.67 [0.30, 0.93]	0.83 [0.59, 0.96]
Steinert 1997	16	5	12	79	0.57 [0.37, 0.76]	0.94 [0.87, 0.98]
Szlubowski 2010	19	2	9	90	0.68 [0.48, 0.84]	0.98 [0.92, 1.00]
Szlubowski 2012	106	0	14	94	0.88 [0.81, 0.93]	1.00 [0.96, 1.00]
Valk 1995	15	14	9	38	0.63 [0.41, 0.81]	0.73 [0.59, 0.84]
Vansteenkiste 1997	10	13	5	22	0.67 [0.38, 0.88]	0.63 [0.45, 0.79]
Vilmann 2005	20	0	0	11	1.00 [0.83, 1.00]	1.00 [0.72, 1.00]
Wahl 1994	7	9	4	7	0.64 [0.31, 0.89]	0.44 [0.20, 0.70]



MRI-Lung cancer

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Stuart 2019	26	9	26	126	0.50 [0.36, 0.64]	0.93 [0.88, 0.97]
Stuart A 2019	28	6	24	129	0.54 [0.39, 0.68]	0.96 [0.91, 0.98]
Tassia 2020	61	21	21	162	0.74 [0.64, 0.83]	0.89 [0.83, 0.93]
Yasuomi 2009	61	4	9	23	0.87 [0.77, 0.94]	0.85 [0.66, 0.96]
Yasuomi O 2009	8	1	18	0	0.31 [0.14, 0.52]	0.00 [0.00, 0.97]

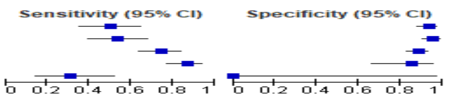


Figure 25: Forest Plot for Lung cancer

The Diagnostic test accuracy is represented by the summary statistics and summary line from four sets of basic data, namely true positive (TP), false positive (FP), false negative (FN), and true negative (TN). Representative summary statistics are the sensitivity, specificity. Forest plot of sensitivity and specificity of detecting cervical cancer with PET with the 95 % CI for each population of the included studies. A total of 125 studies were included in this meta-analysis. Among them, 18 studies had reported the performance of PET, 82 studies had reported the performance of PET/CT, 5 studies had reported the performance of MRI and 20 studies had reported the performance of CT, respectively. After pooling all studies, of CT, MRI, PET and PET/CT Forest plot of sensitivity and specificity of *CT 0.71 (0.66, 0.75), 0.82 (0.80,0.85) MRI 0.65(0.59,0.71), 0.91(0.89,0.94) PET 0.83 (0.79, 0.86) 0.93 (0.91 0.95) and PET/CT 0.78(0.77, 0.80) 0.90(0.89, 0.90)* in detecting mediastinal lymph node metastases, detecting stage IIIb, local T and N stage, M-stage lung cancer, solitary pulmonary nodule in lung cancer with 95 % CI for each population of the included studies.

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
CT	347	164	144	770	0.71 [0.66, 0.75]	0.82 [0.80, 0.85]
MRI	184	41	98	440	0.65 [0.59, 0.71]	0.91 [0.89, 0.94]
PET	349	52	72	710	0.83 [0.79, 0.86]	0.93 [0.91, 0.95]
PET/CT	2788	817	765	7021	0.78 [0.77, 0.80]	0.90 [0.89, 0.90]

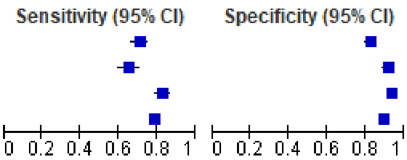


Figure 26: Lung cancer Cumulative values

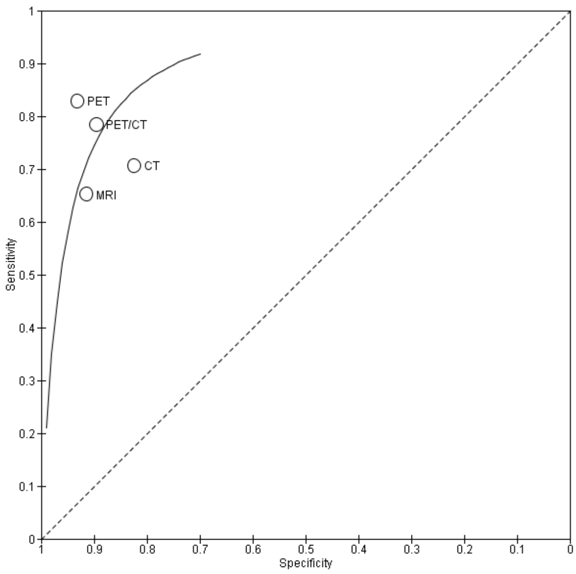


Figure 27: ROC Curve- Cumulative values for Lung cancer

The above ROC curve for lung cancer shows PET has outperformed with higher pooled sensitivity (0.83 [95% CI: 0.79, 0.86] and specificity (0.93 [95% CI: 0.91, 0.95] when compared to MRI, PET/ CT and CT.

Conclusion

This meta-analysis evaluated the published literature for which oncological conditions PET /CT is likely to be shown to be diagnostically accurate compared to other available diagnostic modalities PET, CT and MRI on five different cancers cervical, breast, head and neck, gastric and lung cancer. Diagnosis and detection of different cancers by PET, PET/CT, CT and MRI varies based on the region, recurrence and different stages of cancer. The forest plot was plotted for all five different cancers with a total of 345 studies and their sensitivity and specificity was calculated. The pooled data for the cervical cancer with a sensitivity and specificity of CT 0.62 (0.57, 0.67), 0.92 (0.57, 0.67), MRI 0.52 (0.49,0.55), 0.96 (0.95, 0.96) PET 0.90 (0.86,0.93) 0.93(0.91, 0.94) and PET/CT 0.65(0.62, 0.68) 0.97(0.97,0.98) in detecting LN metastases cervical cancer Tumor staging like IA, IB II A, II B, III A and IV A in cervical cancer. The pooled data for the Breast cancer with a sensitivity and specificity of CT 0.87 (0.85, 0.89), 0.35 (0.33,0.38) MRI 0.97 (0.94, 0.98), 0.88(0.84, 0.91) PET 0.89 (0.86,0.90) 0.91(0.89, 0.93) and PET/CT 0.86(0.83, 0.88) 0.91(0.89, 0.93) in detecting local recurrences, lesion basis, distant metastases and breast lesions in breast cancer. The pooled data for the head and neck cancer with a sensitivity and specificity of CT 0.81(0.77,0.85), 0.72(0.70, 0.74) MRI 0.77(0.74,0.79), 0.78(0.77,0.79) PET 0.20 (0.16, 0.25) 0.94(0.92, 0.96) and PET/CT 0.84(0.82,0.86) 0.88(0.86,0.89) in detecting lymph node metastasis, detection of recurrence in patients and detecting neck levels I, II, and III with head and neck cancer. The pooled data for the gastric cancer with a sensitivity and specificity of CT 0.77(0.71,0.82), 0.95(0.93,0.97) MRI 0.84(0.73,0.93), 0.850.78,0.91() PET 0.41(0.25,0.58) 0.96(0.92,0.99) and PET/CT 0.85(0.77,0.91) 0.95 (0.90, 0.98) in detecting recurrent gastric cancer and peritoneal metastases in gastric cancer. The pooled data for the lung cancer with a sensitivity and specificity of CT 0.71 (0.66, 0.75), 0.82 (0.80,0.85) MRI 0.65(0.59,0.71), 0.91(0.89,0.94) PET 0.83 (0.79, 0.86) 0.93 (0.91 0.95) and PET/CT 0.78(0.77, 0.80) 0.90(0.89, 0.90) in detecting mediastinal lymph node Metastases, detecting stage III b, local T and N stage, M-stage lung cancer, solitary pulmonary nodule in lung cancer.

These findings have clinical implication in terms of providing useful information not only to radiologists in interpreting images but also choosing the imaging modality for the management of suspected cancer patients.

Chapter – III

Cost effectiveness model

Cancer is emerging as a serious public health concern in India as a repercussion of the continuous demographic and epidemiological shift. According to the research, cancer is predominantly reported among the elderly, as well as females of reproductive age. Cancer treatment is one of the highest out-of-pocket costs of any disease. The average out-of-pocket cost for inpatient treatment in private hospitals is almost three times that of public facilities. Furthermore, around 40% of cancer hospitalization cases are financed primarily by borrowings, asset sales, and contributions from friends and family. The spiraling expense of cancer detection and treatment has placed a significant financial strain on afflicted families. In this study, we compare PET/CT versus CT to evaluate the cost effectiveness diagnostic modality to diagnose the top five cancers in India.

Objectives:

The objective of this economic evaluation is to evaluate the cost effectiveness of diagnosis of top five cancer in India with PET/CT compared to CT.

PICO Components

P - Population: Patients with high risk for diagnosing with breast cancer, lung cancer, oral cancer, gastric cancer and cervical cancer.

I - Intervention: PET/CT as diagnostic tool

C - Comparator: Computed Tomography (CT)

O - Outcome: Incremental costs, Incremental QALY, Incremental cost effectiveness ratio (ICER)

Time Horizon: Lifetime

Perspective: Societal Perspective

Methods

The cost effectiveness analysis (CEA) specifically aims to compare and analyze cost and health related ramifications of different modalities/interventions together. It serves as a tool for assessment of the value of new and existing medical technologies, their healthcare benefits concerning the incremental costs. Cost effective analysis paves the way for priority setting and the necessary earmarking of healthcare interventions.

A cost-effectiveness analysis was carried out to evaluate the cost-effectiveness of PET/CT vs CT as a diagnostics modality in patients with high risk of top five cancers in India namely, Breast cancer, Lung cancer, Oral cancer, Gastric cancer and Cervical cancer. Cost and Quality Adjusted Life Years (QALYs) were chosen as outcomes and individuals with high risk aged between 30 and 80 are considered to be eligible for diagnosis. A deterministic and probabilistic Markov model was developed with a cohort of 1,000 patients. We chose a cycle length of one year and ran the model for 50 cycles (i.e., 50 years). Cost effectiveness of PET/CT was assessed from societal perspective with time horizon of 5 years, 10 years and lifetime. Direct medical cost, Direct Non-Medical cost and Indirect cost were calculated and depicted as mean along with its standard error and distribution type. Costs are presented in IN Rupees. The costs and Quality Adjusted Life Years (QALYs) were discounted by 3% per year.

Design of the model:

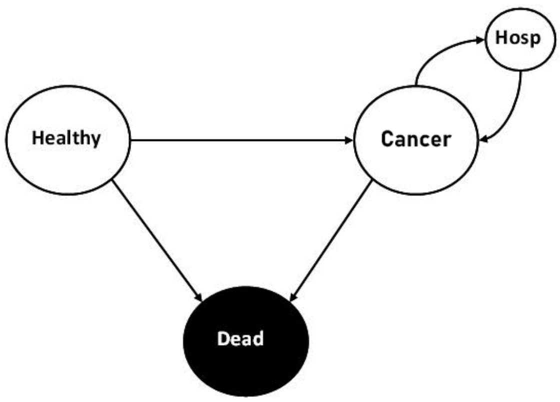


Figure 28: Markov Model Structure

Since cancer is a non-communicable disease, we used a cohort-based Markov model. Figure 28 illustrates the natural history component of our model with three states: healthy, cancer stage with hospitalization and death.

Cancer diagnosis requires a thorough physical examination and history assessment along with diagnostic testing. Diagnostic test could be done in an invasive (blood tests, biopsy, etc.) or a non-invasive way (CT or PET/CT). A PET/CT or CT scan can show cross section of your bones, organs, and soft tissues more distinct than an x-ray would.

The model, and its calculations were performed in Microsoft Excel. Data for cost effectiveness analysis were derived from primary data and literature. In circumstances of lack of data availability, an expert's opinion was taken into consideration.

Quantifying the model's parameters

The data used for the model and their sources are shown in Table 1. PUBMED, GOOGLE SCHOLAR and WEB OF SCIENCE were used to identify HTA's, Economic evaluation and costing data relevant to India. When relevant data were unattainable in the published literature or datasets, we considered the opinion of experts. In this model we incorporated hospitalization cost, physician consultation fees, cost of scan with consumables, cost of the device per patient, room rent per day, productivity loss of patients due to early death caused by cancer, doctor salary per patients, nurse salary per patient and technical staff salary per patient. Foreign exchange rate was used for conversion of foreign currency to IN Rupees and local costs were adjusted as per local inflation rates. For natural history component of our model, we used incidence rates and mortality rates extracted from literature.

Several probabilities like Probability of dying healthy (natural death), Probability of developing cancer, Probability of hospitalization with cancer and Probability of dying due to cancer, which were calculated from incidence rates and the mortality rates were incorporated in this model.

We first extracted age-specific cancer incidence data for all of India's top five cancers, after which we calculated the percentage of incidence by age followed by, calculating the cumulative probabilities utilizing age and incidence percentage. The probability of dying from cancer was calculated using WHO cancer death rates. We considered the odds of developing cancer as a reference for the probability of hospitalization with cancer. Only when the cancer has progressed to the third or fourth stage, or when the patient reaches the age of 50, will the patient be admitted to the hospital. Weighted average method was done to average five probabilities into one after assessing the probabilities for all cancer (Annexure 1). The gamma distribution was adopted as the input parameter for all costs and length of stay (LOS). In contrast, beta and normal distributions were used for utility weights and hazardous ratio, respectively.

We first extracted the age wise cancer incidence data for all the top five cancers in India. Which was then followed by calculating the percentage of incidence age wise. Later on, we estimated the cumulative probabilities based on the age and the incidence percentage. Similarly, Probability of dying due to cancer was estimated using the age wise cancer mortality rates extracted from WHO. For Probability of hospitalization with cancer we used the probabilities of developing cancer as reference. After estimating the probabilities for all the cancers, we used weighted average method to average five probabilities into one probability. (Annexure 1) Gamma distribution was used as the input parameter for all the costs and length of stay (LOS), beta distribution for utility weights were used and for hazard ratios the input parameter used was normal.

Table 6: Model Input Parameters

	Model Value	Mean	Standard Error	Alpha	Beta	Distribution Type	Formula	Source
PET/CT								
Direct Cost								
Diagnostic Cost								
Device cost/patient	2348.00	2348	234.8	100	23.48	Gamma	2484.60	Primary data
Consultation fees	150.00	150	15	100	1.5	Gamma	119.91	Central Government Health Scheme (CGHS)
PET/CT scan with FDG	8777.00	8777	877.7	100	87.77	Gamma	8957.97	Primary data
Technical staff salary/patient/day	30.00	30	3	100	0.3	Gamma	32.03	Cost Database, PGIMER
Total diagnostic cost PET/CT	**11305.00**	**11305**	**1130.5**	**100**	**113.05**	**Gamma**	**12559.00**	
Hospitalization cost								
Doctor salary/patient/day	100.00	100	10	100	1	Gamma	90.39	Cost Database, PGIMER
Nurse salary/patient/day	50.00	50	5	100	0.5	Gamma	51.26	Cost Database, PGIMER
Room with bed/day	4000.00	4000	400	100	40	Gamma	4024.83	Central Government Health Scheme (CGHS)
Total hosp for LOS PET/CT	**4150.00**	**4150**	**415**	**100**	**41.5**	**Gamma**	**4503.32**	
Indirect Cost								

Productivity lost due to early death								
Daily wage lost	460.00	460	23	400	1.15	Gamma	469.14	tradingeconomics.com
Total Indirect cost	**460.00**	**460**	**23**	**400**	**1.15**	**Gamma**	**446.08**	
CT								
Direct cost								
Consultation and Diagnostic cost								
Device cost/patient	171.00	171	17.1	100	1.71	Gamma	142.81	Primary Data
Consultation fees	150.00	150	15	100	1.5	Gamma	141.44	Central Government Health Scheme (CGHS)
CT Scan with Contrast	2200.00	2200	220	100	22	Gamma	2162.99	Central Government Health Scheme (CGHS) Primary data
Technical staff salary/patient/day	30.00	30	3	100	0.3	Gamma	30.23	Cost Database, PGIMER
Total diagnostic cost CT	**2551.00**	**2551**	**255.1**	**100**	**25.51**	**Gamma**	**2168.66**	
Hospitalization cost								
Doctor salary/patient/day	100.00	100	10	100	1	Gamma	115.91	Cost Database, PGIMER
Nurse salary/patient/day	50.00	50	5	100	0.5	Gamma	46.90	Cost Database, PGIMER
Room with bed/day	4000.00	4000	400	100	40	Gamma	4468.56	Central Government Health Scheme (CGHS)
Total hosp for LOS CT	**4150.00**	**4150**	**415**	**100**	**41.5**	**Gamma**	**3611.31**	
Indirect Cost								
Productivity lost due to early death								
Daily wage lost	460.00	460	23	400	1.15	Gamma	453.69	tradingeconomics.com
Total Indirect cost	**460.00**	**460**	**23**	**400**	**1.15**	**Gamma**	**469.89**	
Mean annual wage	**140000.00**	**140000**	**7000**	**400**	**350**	**Gamma**	**126496.55**	Ministry of Labour and Employment
Length of stay	**2.00**	**2**	**0.1**	**400**	**0.005**	**Gamma**	**1.96**	HTA on PET/CT National Health Systems Resource Centre
utility healthy CT	**0.85**	**0.85**	**0.085**	**14.15**	**2.50**	**Beta**	**0.76**	HTA on PET/CT National Health Systems Resource Centre
utility disease CT	**0.50**	**0.5**	**0.05**	**49.50**	**49.50**	**Beta**	**0.46**	HTA on PET/CT National Health Systems Resource Centre
utility hosp CT	**0.20**	**0.2**	**0.02**	**79.80**	**319.20**	**Beta**	**0.17**	HTA on PET/CT National Health Systems Resource Centre
Diagnostic Proportion	**0.10**	**0.1**	**0.01**	**89.90**	**809.10**	**Beta**	**0.11**	
Utility healthy	**0.95**	**0.95**	**0.095**	**4.05**	**0.21**	**Beta**	**1.00**	HTA on PET/CT National Health Systems Resource Centre
Utility disease	**0.60**	**0.6**	**0.06**	**39.40**	**26.27**	**Beta**	**0.59**	HTA on PET/CT National Health Systems Resource Centre
Utility hospitalization	**0.20**	**0.2**	**0.02**	**79.80**	**319.20**	**Beta**	**0.23**	HTA on PET/CT National Health Systems Resource Centre
Discount rate	**3%**	**3%**						
Retirement age	**65.00**	**65.00**						India Stat

A cost-effectiveness study yields QALYs (Quality Adjusted Life Years), which represent both the quality and quantity of life linked with various health issues. QALYs are calculated using the length of life and quality of life, or utility ratings, for each health condition. The utilities are scored from 0 to 1, 0 indicating death and 1 indicating perfect health.

Incremental cost effectiveness ratio (ICER) is the difference in cost between two possible interventions (PET/CT and CT), divided by the difference in their effect.

$$ICER = C_{PET/CT\ screening} - C_{No\ screening} / E_{PET/CT\ screening} - E_{No\ Screening}$$

-where, C is cost and E is the effectiveness.

The GDP per capita was believed to be the cost-effectiveness threshold. To estimate the likelihood of PET/CT's potential to be a cost-effective screening tool, various degrees of willingness to pay were incorporated in the model.

Sensitivity Analysis:

Sensitivity analysis is performed to assess the input parameter's uncertainty and robustness of a model. For a probabilistic sensitivity analysis (PSA), several input model parameters from each range are chosen randomly and incorporated in the model to generate outcomes (cost and health result). To account for the heterogeneity, a Monte Carlo Stimulation with 1,000 repetitions were also carried out. A cost-effectiveness plane was plotted incorporating the PSA results (Figure 3) The proportion of outcomes that fall favorably (i.e., are regarded cost-effective) in respect to a specific cost-effectiveness threshold is a major output of a PSA. A cost-effectiveness acceptability curve might be used to illustrate this.

Sensitivity analysis were conducted examine model sensitivity to different parameters. A number of input model parameters is randomly sampled from each range in a probabilistic sensitivity analysis (PSA), and the model is 'run' to create outputs (cost and health result) that are saved. In addition, a Monte Carlo Simulation with 1,000 repetitions was performed to account for heterogeneity. The results obtained from PSA were plotted on the cost-effectiveness plane. The proportion of outcomes that fall favorably (cost-effective) in respect to a specific cost-effectiveness threshold is a major output of a PSA. A cost-effectiveness acceptability curve might be used to illustrate this. PSA findings were presented using a scatter plot of incremental cost effectiveness and cost effectiveness acceptability curves.

Net monetary benefit:

NMB or net monetary benefit, is a summary statistic that indicates the worth of an intervention in monetary terms. This is calculated when a willingness to pay threshold for a unit benefit, in this case QALY, is known.

The use of NMB scales both health outcomes and resource consumption to costs, allowing comparisons to be conducted without the need of ratios (as in ICERs).

(Incremental Benefit x Threshold) – Incremental cost

The difference in NMB between alternative interventions is measured by incremental NMB, with a positive incremental NMB indicating that the intervention is more cost-effective than the alternative at the specified willingness-to-pay level.

Threshold Analysis:

The threshold for India was calculated to be ₹1,46,000. If the ICER value falls in quadrant 1 and quadrant 3, we accept or reject the intervention based on the threshold value. If the ICER is less than the threshold then we accept, else reject.

Whereas, if the ICER value falls on quadrant 4 we accept (Dominates) the intervention as its less costly and more effective and if it falls on quadrant 2, we completely reject (Dominated) as its more expensive and the outcomes is less. Since some of the PSA values are on the 2nd and 4th quadrant, WTP analysis was conducted to understand the exact cost where PET/CT is cost-effective as diagnostic modality.

Results:

Cost – effectiveness results:

Base case results:

Table 1 displays the base-case results of model analyses, which revealed that PET/CT as diagnostic modality gains 4.19, 6.42 and 6.99 QALYs, in the time horizon of 5 years, 10 years and lifetime respectively. The ICER for PET/CT compared to CT were 617; 1,783 and 2,337 respectively for different time horizons.

Table 3: Base-case analysis results for QALYs and ICERs

Time Horizon	Diagnostic Techniques	QALYs	Cost	ICER
5 years	PET/CT	4.19	₹ 8,36,904	617
	CT	3.74	₹ 8,36,625	
10 years	PET/CT	6.42	₹ 59,30,657	1,783
	CT	5.69	₹ 59,29,359	
Lifetime	PET/CT	6.99	₹ 3,03,89,268	2,337
	CT	6.18	₹ 3,03,87,377	

PSA Results:

Figure 2 represents the results obtained from probabilistic model. A Monte Carlo simulation of 1000 iteration was performed to deal with the uncertainty of the variables that affect the outcomes. The ICER values obtained from PSA are all somewhere close to the base-case lifetime horizon ICER value. From the graph, it is clearly visible QALY gained from PET/CT diagnostic is high compared to that of CT.

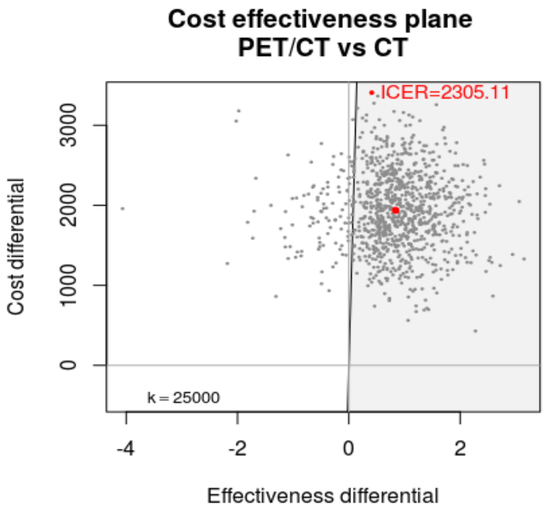


Figure 29: ICER Scatter Plot

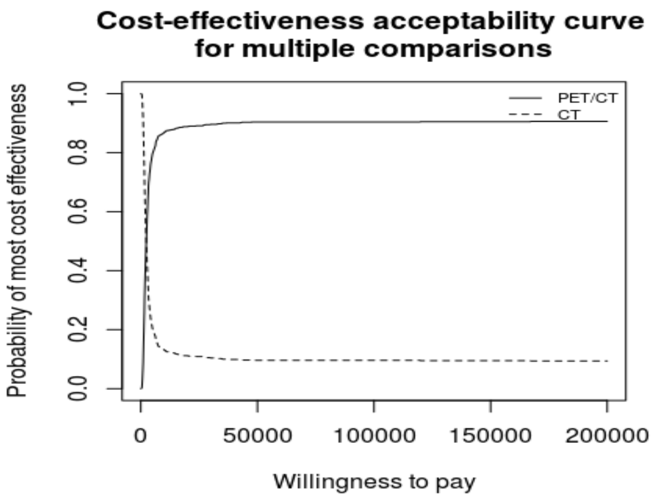
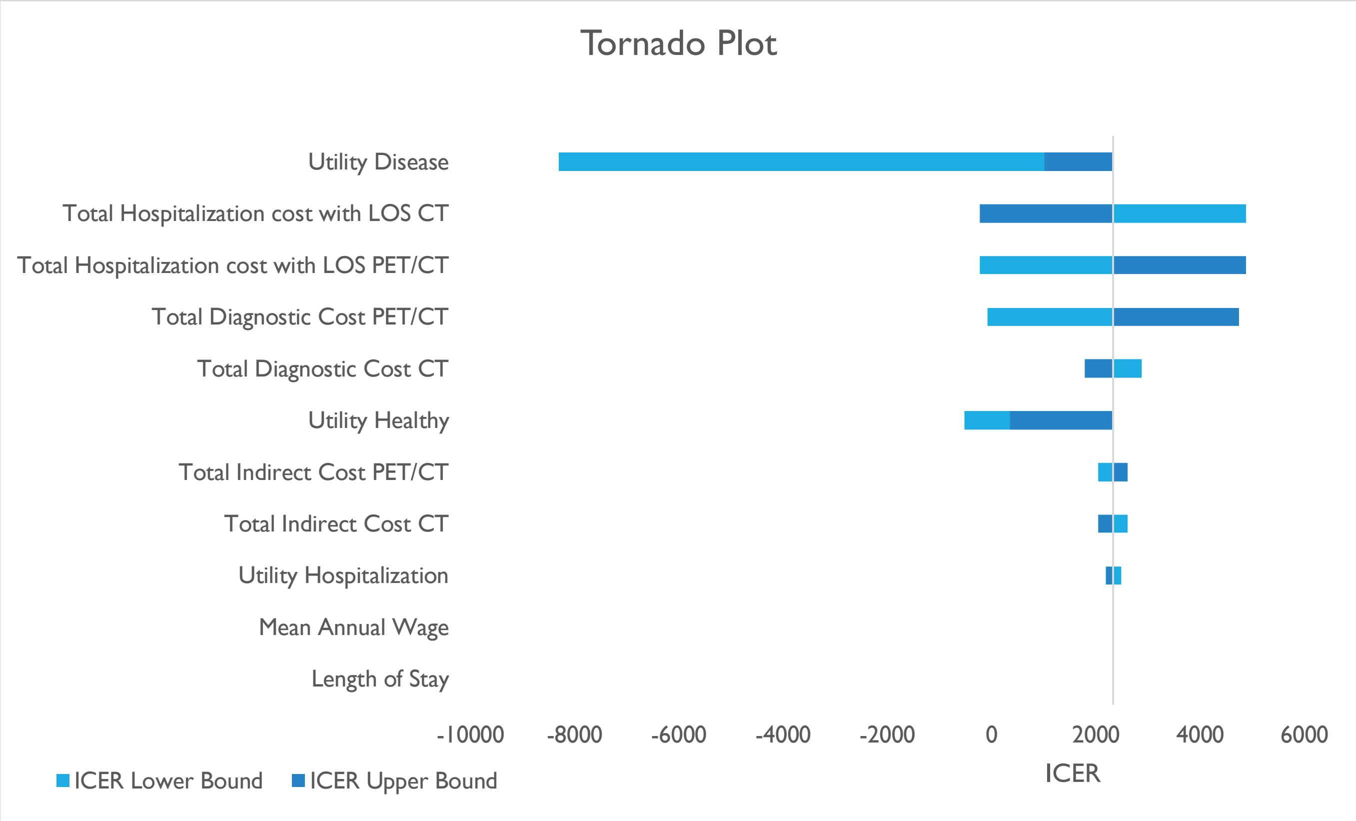


Figure 30: Cost Effectiveness Acceptability Curve

Figure 3 shows the probability of diagnosing with PET/CT being cost effective with respect to willingness to pay. Up to the willingness to pay of ₹ 9,000, CT is cost-effective. When the willingness to pay is high, patients opt for better interventions that give better outcomes. Here, in our study, when the WTP is greater than 9,000, PET/CT is almost 80% cost effective. When the WTP gets higher the probability of PET/CT being cost effective also increases. The net monetary benefit for diagnosing lung cancer with PET/CT is higher compared to that of CT.

The main result of this study was that diagnosing lung cancer with PET/CT was cost-effective compared to CT among high-risk patients. The ICER values obtained from PSA are all somewhere close to the base-case lifetime horizon ICER value. From the graph, it is clearly visible QALY gained from PET/CT diagnostic is high compared to that of CT. Since the incremental net monetary benefit is higher for diagnosing Lung cancer with PET/CT, it is a cost-effective modality for high-risk patient.

OWSA Results



Our one way sensitivity analysis reveals that the uncertainty in the utility of diseased patient, Total hospitalization cost with Length of stay for PET/CT and CT, Total diagnostic cost for PET/CT and CT and utility of health population have the greatest impact on the ICER.

Conclusion

Total cost of establishing PET/ CT scan facility without cyclotron was calculated to be INR 17.08 Cr (USD 2,339,048.75). Proposing more units would cost the government a huge sum of money where there is no data regarding the utilization levels of the existing units. The cost of performing PET/ CT scans can decrease if the number of examinations increase over the time. Various strategies can be adopted in order to cut down the capital and operational cost of setting up the facilities, which in turn can decrease the unit cost of PET/ CT scan. The total cost of setting up of cyclotron facility was calculated to be INR 58.63 Cr (USD 8,026,734.1). This model thus proposes additional 04 Cyclotrons units to meet the current demand via phase wise implementation, which is still very less than that is required.

Besides, there are currently 88 units of PET/ CT in the South zone, of which 13 alone belongs to Kerala. Wherein East, North East and Central zones have less than that of Kerala each. It is concluded from the study that setting up of additional PET/ CT units in Kerala is not suggested, rather focusing on other areas where there is dire need of development in PET/ CT infrastructure would upbring the current scenario in India.

Discussion

Cancer treatment delay is a problem in health systems worldwide. The impact of delay on mortality can now be quantified for prioritisation and modelling. Even a four-week delay of cancer treatment is associated with increased mortality across surgical, systemic treatment, and radiotherapy indications for cancers. Policies focused on minimising system level delays to cancer treatment initiation could improve population level survival outcomes. (379)

India has very limited PET/CT scanners and cyclotrons when the number of cancer cases is taken into account. Approximately 10 lakhs new cancer cases were registered on the year 2018. Uttar Pradesh with population of 19,98,12,341 people had the highest number of newly registered cases, that is 1,57,852, in the year 2018. Currently there are only 279 PET/ CT scanners in India, which is very less than that is required and essential.

There are inequities in the distribution and access to nuclear medicine and diagnostic imaging across the globe. Launched in 2019, the IAEA Medical Imaging and Nuclear Medicine resources database, IMAGINE, presents interactive maps on every country's availability of medical imaging equipment and human resources. According to this database the population served by 1 PET/ CT scanner in High Income Countries (HICs) is approximately 6,01,000, 34,84,000 in Upper Middle-Income Countries (UMICs) and 1,00,00,000 in Lower Middle-Income Countries (LMICs) and 16,66,67,000 in Low Income Countries (LICs).

Addressing the inequities in the distribution and access to the nuclear medicine and diagnostic imaging is still existing as a challenge for the country. If the norms are defined as 1 PET/ CT scanner per 5 lakh population then, we are currently way behind in meeting the demand. We have currently 279 PET/ CT units, and need additional 2224 units to meet the standards. In case of 1 PET/ CT scanner per 10,00,000 population, we would require additional 972 units to meet the norms. Whereas in case of 1 PET/ CT scanner per 1,00,00,000 population, then we have surplus units in running. Proposing more than 1000 units would cost the government a huge sum of money where there is no data regarding the utilization levels of the existing units. An additional 13 units of PET/CTs and 4 Cyclotrons units can be set up to meet the current demand, which is still very less than that is required.

Factors limiting Growth of PET in India-

Costs & Infrastructure

High operational and capital costs is a challenge to Indian Healthcare system. Limited availability of the radiotracer FDG currently creates high-cost barriers for cancer-care programs integrating PET technology. The costs of FDG (18F-fluorodeoxyglucose), a critical component of PET imaging, vary widely. Much of the difference in cost can be attributed to variable distance from the cyclotron facility to the PET clinic. FDG loses one-half of its activity every two hours (approximately) from the time it is produced. Therefore, facilities that have to purchase FDG from other states have to pay for a large amount of FDG in order to have sufficient radioactivity remaining to perform PET exams by the time it reaches the PET facility. FDG costs are also high because availability in India is low. At present, there are only 20 cyclotrons producing FDG for oncologic PET imaging across India. Because there are so few PET facilities in India, the amounts of FDG produced are relatively small and there is no cost reduction due to large volume production.

Therefore, a well-functioning PET infrastructure in India would require a cyclotron network that makes FDG easily available to PET centers in every state.

Education and Training

The final category of constraints limiting the full adoption of PET in India is the education and training of health care professionals. As there is a shortage of human resource in all areas of nuclear medicine. This demand will increase with growing numbers of PET facilities and cyclotron installations. Deployment and uptake of PET technology is limited by the number of trained, qualified personnel ranging from people to perform synthesis and to formulate and certify radiopharmaceuticals to imaging specialists and cyclotron operators. Additionally, support personnel for regulatory oversight, operations and maintenance, training, and so on are in short supply. Physician groups, cancer patients and the general public are uneducated about the utilization and benefits of PET technology in cancer care. Majority of undergraduate medical students receive anywhere little knowledge of nuclear medicine education. This statistic is higher in other countries. Doctors tend to use PET imaging at the end of the diagnostic pathway, and this may prevent cost-effective care. Medical literature suggests that PET imaging can result in substantial healthcare savings if it is used as an initial tool in the diagnostic pathway of an oncology patient, rather than a last resort. It can eliminate the need for further tests or procedures in as many as 90% of cases (390), change treatment strategies in as many as 50% of cases and improve decision-making by physicians in 83% of cases (391-392). Yet many doctors continue to view PET imaging as a diagnostic tool to be used when all other means have failed. Cancer patients and the general public – A lack of knowledge among cancer patients and the general public may also be a limiting factor to the expansion of PET imaging. Approximately, general public at some point may be impacted by cancer through illness or the illness of a family member or friend. Yet very few are aware of the potential benefits of PET in determining the most appropriate management of their cancer. Coordinated policy action at the level of the healthcare system would obviate some of these concerns.

Time for national strategy

Most PET scanners are situated in population-dense cities and it is difficult to justify the cost and operation of a PET scanner in small cities, even though they may serve a large geographic area. Geography also makes it difficult to transport FDG over long distances. Regulation of FDG is viewed as a major hurdle to the efficient use of PET resources. India does not have a national approach or national policies for the use of PET as a clinical tool for cancer care. There has not been a coordinated approach to implementing a national strategy for the focused translation of PET technology from research purposes to the clinical care of cancer (e.g., developing a PET network or developing national PET policies and indications for use). Although we can explore possibilities for the conversion of existing SPECT into PET as SPECT isotope Tc-99m has long shelf life than FDG, moreover we can save huge amount of money as well.

To provide financial assistance to poor patients a new scheme for cancer care has been formulated under Ministry of Health & Family Welfare. The Umbrella Scheme of Rashtriya Arogya Nidhi (RAN) will have three components namely (i) Rashtriya Arogya Nidhi (RAN), (ii) Health Minister's Cancer Patients Fund (HMCPF) and (iii) Scheme for financial assistance for patients suffering from specified rare diseases. Financial assistance under the scheme of Rashtriya Arogya

Nidhi (RAN) for the treatment to the eligible poor population covering PET investigations for cancer and cardiology (393). Even Health Ministers cancer patient fund within RAN for the Cancer Patients is approved plan allocation for National cancer control Programme (NCCP) as mandated in the 11th five-year plan. (394). The financial assistance to the cancer patient up to Rs. 2,00,000/- (Rs. 5,00,000/- in emergency cases), would be processed by the concerned Regional Cancer Canters (RCC) (394). Interestingly! government of India has taken many steps to facilitate health insurance in India. Nevertheless! A visionary approach coupled with a timely strategy based on expected future cancer burden in the country needs to be adopted to address the anticipated increase in PET-CT imaging requirements.

Recommendation

At this time, the early detection of cancer and precursor lesions represents a largely unmet potential to decrease morbidity and mortality from malignancies. We need to focus on cancer awareness, initial detection, diagnosis, and availability and affordability of treatment in all sorts of cancers. Early diagnosed cancers are treatable and cost effective to treat, and the patient goes back to lead a normal routine life. Equal distribution of nuclear medicine facilities, particularly the human resource, and health-care equipment will address the demand of cancer care facilities. As we know, multimodality imaging has been widely adopted by the scientific community as a way to gain a more comprehensive understanding of the effects of diseases and treatments.

The PET– CT revolution has initiated a new way of looking at physiology and morphology simultaneously, and the new class of PET–MR which are radiation free systems are broadening the horizon of opportunities for applications in healthcare. An integrated PET-CT has been documented to have improved image interpretations in 49% of the patients and 30% of the sites. PET-CT have an incremental value in terms of baseline preoperative staging, restaging, and evaluation of suspected recurrence. The studies published in the last decade have shown overwhelming scientific evidence of PET-CT having an accuracy ranging from 84% to 93% in comparison to 63–64% of CT alone. (396-397) PET-CT has had a major impact in an otherwise blind area of detecting unknown primary Tumor where otherwise no single imaging modality was successful. The continued introduction of new detector technologies, hybrid imaging, and advanced algorithms for image reconstruction and analysis we propose an evaluation of the existing SPECT imaging facilities for possible conversion into PET as the only difference is the detector which is possible according to literature. In India at present, we have 194 SPECT facilities, which can be converted into PET by changing a detector. This way we can save huge amount of money making this intervention a cost-effective intervention.

Moreover, in India the public sector accounts for only around 20 percent of the total healthcare expenditure, representing around 1% of the GDP (398). Since healthcare in India is dominated by the private sectors, government can have a PPP (Public Private Partnership) with the private sectors to fulfil the demands by providing treatment and covering almost all the population for good and reasonable price.

PPP’s in Healthcare can be classified in the key areas such as:

- Infrastructure development
- Management and Operations

- Capacity building and training
- Financing Mechanism
- IT infrastructure development for Networking and Data Transfer
- Materials Management

One of the main challenges faced in India is the out-of-pocket expenditures, which are very high and covering them through insurance is still low compared to the population.

Discussion on number of PET- CT units-

- States having maximum number of PET-CT units are in Maharashtra-48 States & union territory having only one PET-CT unit Manipur, Tripura, Uttarakhand, Jharkhand, Puducherry.
- States and union territory not even having one PET-CT unit are-Himachal Pradesh, Arunachal Pradesh, Goa, Mizoram, Meghalaya, Nagaland, Sikkim, Andaman & Nicobar Islands, Dadra and Nagar Haveli, Lakshadweep, and Ladakh.
- In Kerala we have 13 PET-CT units and is not suggestive of adding another PET-CT unit for Kerala, rather recommend it for states having higher cancer incidence and lesser PET-CT units.

Public Private Partnership Model for Service Delivery only for PET- CT

- PET-CT diagnostic service can be provided in Public Private Partnership model across India following National Free Diagnostic Scheme (section radiology services).
- It will help to - Provide accessible, affordable and quality PET-CT diagnostic service in all public health facilities up to district hospitals. Leading to reduction of direct cost for PET-CT scan causing a remarkable impact on out-of- pocket expenditure by general public.
- Utilizing the capacity of private service providers in supporting government to provide PET-CT scan will lead to strengthening PET-CT diagnostic service network across the country.
- Cost of PET-CT scans are conducted for around Rs 11,000 - 15,000 in private sector which are suggested to be included free of cost under PMJAY scheme.

Cyclotron

- We suggest cyclotron should be under public sector as –
- If the cost of raw material for PET-CT is maintained the cost for PET-CT scan will also be maintained otherwise if it is under private sector the cost might increase according to market fluctuations.
- Private companies are more interested in installation of PET-CT units as they will get return on investment soon, unlike the case of cyclotron.
- We need to focus on even distribution of cyclotron units across the country, as the shelf life of the radioisotopes used for PET-CT is very less

Limitations

The increasing use of other diagnostic modalities has led to concerns about the potential overutilization of PET. There is a perception that CT and MRI are overused modalities in private sector and utilized in cases when there is little evidence to support their need. Consequently, there are concerns that PET imaging will follow this path, even though PET has a far more restricted number of indications. While it is beyond the scope of this report to evaluate the use of CT and MRI, this perception (or misperception) suggests it may be time for governments to develop a systematic approach to assess the proper utilization of CT and MRI, rather than limit the expansion, and utilization, of PET technology in clinical care. Governments should consider the merits of PET technology based on its own capabilities, not on the possible overuse of other technologies.

Appendix- 1

PET/CT- Cervical cancer

S.no	Study - PET/CT-Cervical cancer	TP	FP	FN	TN	PPV	NPV	LR+	LR-	Total	Over all accuracy
1	Belhocine 2002 [29]	19	8	3	187	0.7	0.98	21	0.14	217	94.9
2	Choi 2006 [30]	19	9	14	112	0.67	0.88	7.74	0.45	154	85
3	Chung 2009 [31]	7	1	10	16	0.87	0.61	7	0.6	34	48.5
4	Chung 2010 [32]	8	9	20	46	0.47	0.69	1.74	0.85	83	65
5	Crivellaro 2012 [33]	4	2	11	52	0.66	0.82	7.2	0.76	69	81.1
6	Havrilesky 2003 [34]	12	2	2	13	0.85	0.86	6.42	0.16	29	86.2
7	Kim 2009 [35]	26	30	33	464	0.46	0.93	7.25	0.59	553	88.6
8	Kitajima 2009 [36]	12	1	11	1198	0.92	0.99	625.5	0.47	1222	99
9	Kitajima 2012 [37]	14	6	22	158	0.7	0.87	10.6	0.63	200	86
10	Lin 2003 [38]	12	2	2	34	0.85	0.94	15.4	0.15	50	92
11	Loft 2007 [39]	21	7	1	50	0.75	0.98	7.77	0.05	79	89.8
12	Lv 2014 [40]	61	17	6	1079	0.78	0.99	58.6	0.09	1163	98
13	Narayan 2001 [41]	10	1	2	11	0.9	0.84	10	0.18	24	87.5
14	Reinhard 2001 [42]	17	2	4	269	0.89	0.98	109.6	0.19	292	95.8
15	Roh 2005 [43]	14	12	23	385	0.53	0.94	12.5	0.64	434	91.9
16	Sandvik 2011 [44]	1	3	4	28	0.25	0.87	2.06	0.88	36	80.5
17	Signorelli 2011 [45]	10	4	30	862	0.71	0.96	54.1	0.75	906	96.2
18	Sironi 2006 [46]	13	3	5	1060	0.81	0.99	255.9	0.27	1081	99.2
19	Stecco 2016 [47]	7	3	1	16	0.7	0.94	5.54	0.14	27	85.1
20	Wright 2005 [48]	12	8	14	84	0.6	0.85	5.3	0.58	118	81.3
21	Xu 2016 [49]	19	8	4	20	0.7	0.83	2.89	0.24	51	76.4
22	Yeh 2002 [50]	10	2	1	29	0.83	0.96	14	0.09	42	92.8
23	Yildirim 2008 [51]	2	2	2	10	0.5	0.83	3	0.6	16	75
24	LV K 2014 [52]	34	7	0	46	0.82	1	7.57	0	87	91.9
25	Narayan K 2001 [53]	4	1	3	16	0.8	0.84	9.71	0.45	24	83.3
26	Park W 2005 [54]	6	0	8	22	1	0.73	0	0.57	36	77.7
27	Park 2005 [54]	9	0	13	50	1	0.79	0	0.59	72	81.9
28	Reinhard MJ 2001 [42]	10	0	1	24	1	0.96	0	0.09	35	97.14
29	Kim SK 2009 [35]	14	14	16	35	0.5	0.68	1.63	0.74	79	74.6
30	Choi HJ 2006 [30]	10	4	3	5	0.71	0.62	1.73	0.41	22	68.1
31	Loft A 2007 [39]	15	1	0	104	0.93	1	10.5	0	120	99.1
32	Ma 2003 [55]	38	0	0	66	1	1	0	0	104	100
33	Signorelli M 2011 [45]	9	4	19	127	0.69	0.86	10.5	0.69	159	85.5
34	Roh JW 2005 [43]	9	0	13	50	1	0.79	0	0.5	72	81.9
35	Sironi S 2006 [46]	11	1	4	31	0.91	0.88	23.4	0.27	47	89.3
36	Wright J 2005 [48]	1	1	3	40	0.5	0.93	10.25	0.76	45	91.1
37	Wright D 2005 [48]	2	1	3	84	0.66	0.9		0.6	90	95.5
38	Wright DD 2005 [48]	10	4	9	36	0.71	0.8	5.26	0.52	59	77.9
39	Stecco A 2016 [47]	26	17	11	162	0.6	0.93	7.39	0.32	216	87.03
40	Rose 1999 [56]	11	0	0	5	1	1	0	0	16	100
41	Kitajima K 2009 [36]	6	3	6	30	0.66	0.83	5.5	0.55	45	80
42	Kitajima M 2009 [36]	11	2	11	729	0.84	0.98	182.7	7.5	753	98.2
43	Kitajima 2008 [57]	10	0	2	40	1	0.9	0	0.16	52	96.1
44	Amit 2006 [58]	6	0	1	4	1	0.8	0	0.14	11	90.9
45	Chung 2007 [59]	28	4	3	17	0.87	0.85	4.74	0.11	52	86.5
46	Grisaru 2004 [60]	10	0	0	2	1	1	0	0	12	100
47	Kitajima S 2008 [57]	23	2	2	25	0.92	0.92	12.4	0.08	52	92.3
48	Mittra 2009 [61]	22	2	1	5	0.91	0.83	3.34	0.06	30	90
49	Sironi 2007 [62]	5	0	1	6	1	0.85	0	0.16	12	91.6
	Cumulative	**670**	**210**	**358**	**7944**	**0.75**	**0.95**	**25.6**	**0.37**	**9182**	**93.80%**

PET- Cervical cancer

S.no	Study- PET-Cervical cancer	TP	FP	FN	TN	PPV	NPV	LR+	LR-	Total	Over all accuracy
1	Chang 2014 [63]	17	2	1	7	0.89	0.87	4.25	0.07	27	88.8
2	Kitajima 2008 [64]	20	6	5	21	0.76	0.8	3.6	0.25	52	78.8
3	Vander 2003 [65]	23	1	2	13	0.95	0.86	12.8	0.08	39	92.3
4	Havrilesky 2003 [34]	12	2	2	3	0.85	0.6	2.14	0.23	19	78.9
5	Ryu 2003 [66]	28	52	3	166	0.35	0.98	3.78	0.12	249	77.9
6	Sakurai 2006 [67]	43	3	4	4	0.93	0.5	2.13	0.14	54	88.8
7	Lai 2014 [68]	61	6	6	327	0.91	0.98	50.5	0.09	400	97
8	Yen 2004 [69]	84	8	10	448	0.91	0.97	50.9	0.1	550	96.7
	Cumulative	**288**	**80**	**33**	**989**	**0.78**	**0.96**	**11.9**	**0.11**	**1390**	**91.80%**

CT- Cervical cancer

S.no	Study-CT-Cervical cancer	TP	FP	FN	TN	PPV	NPV	LR+	LR-	Total	Over all accuracy
1	Bandy 1985 [70]	9	3	3	29	0.75	0.9	8	0.27	44	86.3
2	Bellomi 2005 [71]	31	30	17	418	0.58	0.96	9.6	0.37	496	90.5
3	Camilien 1988 [72]	3	1	9	38	0.75	0.8	9.75	0.76	51	80.3
4	Chu 1996 [73]	4	1	6	17	0.8	0.73	7.2	0.63	28	75
5	Engelshove 1984 [74]	3	4	1	2	0.42	0.66	1.12	0.75	10	50
6	Heller 1990 [75]	31	8	30	184	0.79	0.85	12.1	0.51	253	84.9
7	Heron 2002 [76]	24	2	2	36	0.92	0.94	17.5	0.08	64	93.7
8	Hertel 2002 [77]	3	8	17	47	0.3	0.84	1.96	0.85	67	76.1
9	Kim 1993 [78]	7	11	22	158	0.38	0.87	3.7	0.81	198	83.3
10	Matsukam 1989 [79]	5	2	2	61	0.71	0.96	22.5	0.29	70	94.2
11	Subak 1995 [80]	3	3	2	29	0.5	0.93	6.4	0.4	37	86.4
12	Villasanta 1983 [81]	10	4	3	25	0.71	0.89	5.57	0.26	42	83.3
13	Walsh 1980 [82]	12	3	3	7	0.8	0.7	2.66	0.28	25	76
14	William 2009 [83]	10	2	1	7	0.83	0.87	4	0.11	20	85
15	Wlash 2005 [84]	12	3	3	7	0.8	0.7	2.66	0.28	25	76
16	Yang 2000 [85]	11	2	6	57	0.78	0.9	12.9	0.35	77	88.3
17	Park 2000 [86]	14	3	4	15	0.82	0.78	4.66	0.26	36	80.5
18	Walsh 1981 [87]	27	2	1	7	0.93	0.87	4.33	0.04	37	91.8
19	Grumbine 1981 [88]	0	1	6	17	0	0.73	0	1.05	24	70.8
20	Walsh JW 1981 [87]	11	2	2	0	0.84	0	0.84	0	15	73.3
21	Brenner 1982 [89]	4	0	2	6	1	1.75	0	0.33	12	83.3
22	Brenner H 1982 [89]	4	1	2	13	0.8	0.86	9.33	0.35	20	85
	Cumulative	**238**	**96**	**144**	**1180**	**0.72**	**0.88**	**8.24**	**0.4**	**1721**	**82%**

MRI- Cervical cancer

S.no	Study- MRI-Cervical cancer	TP	FP	FN	TN	PPV	NPV	LR+	LR-	Total	Over all accuracy
1	Bellomi 2005 [90]	35	31	13	417	0.53	0.96	10.5	0.2	496	91.1
2	Choi 2004 [91]	8	14	6	198	0.36	0.97	8.6	0.4	226	91.1
3	Choi 2006 [92]	4	5	9	4	0.44	0.3	0.55	1.55	22	36.3
4	Chung 2007 [93]	24	10	6	59	0.7	0.9	5.5	0.2	99	53.5
5	Chung 2010 [94]	18	17	10	38	0.51	0.79	2.07	0.51	83	67.4
6	Grecco 1989 [95]	3	6	5	32	0.33	0.86	2.37	0.74	44	79.5
7	Hawighost 1998 [96]	13	3	6	11	0.81	0.64	3.19	0.4	33	72.7
8	Hawnaur 1994 [97]	12	4	4	29	0.75	0.87	6.18	0.28	49	83.6
9	Hertel 2002 [98]	3	7	4	48	0.3	0.92	3.36	0.65	62	82.2
10	Hricak 1988 [99]	9	2	2	44	0.81	0.95	18.8	0.19	57	92.9
11	Janus 1989 [100]	3	2	1	16	0.6	0.94	6.75	0.28	22	86.3
12	Kim 1990 [101]	3	1	12	44	0.75	0.78	9	0.81	60	78.3
13	Kim 1993 [102]	7	2	22	167	0.77	0.88	20.3	0.76	198	87.8
14	Kim 1994 [103]	23	2	14	223	0.92	0.94	69.9	0.3	262	93.8
15	Kim 2009 [35]	17	16	13	33	0.51	0.71	1.73	0.64	79	63.2
16	Lin 2008 [104]	4	22	22	990	0.15	0.97	7.07	0.86	1038	95.7
17	Lv 2014 [40]	15	8	19	45	0.65	0.7	2.9	0.6	87	68.9
18	Park 2005 [54]	8	6	6	16	0.57	0.72	2.09	0.5	36	66.6
19	Reinhard 2001 [42]	8	4	3	20	0.66	0.86	4.36	0.32	35	80
20	Sahdev 2007 [105]	12	15	32	1427	0.44	0.97	26.2	0.73	1486	96.8
21	Sheu 2001 [106]	9	4	2	26	0.69	0.92	6.13	0.2	41	85.3
22	Stecco 2016 [47]	7	3	1	16	0.7	0.94	5.54	0.14	27	85.1
23	Subak 1995 [80]	8	5	5	53	0.61	0.91	7.13	0.42	71	85.9
24	Yang 2000 [107]	12	6	5	53	0.66	0.91	6.94	0.32	76	85.5
25	Yu 1998 [108]	9	7	5	73	0.56	0.93	7.3	0.39	94	87.2
26	Hertel H 2002 [98]	0	1	6	60	0	0.9	0	1	67	89.5
27	Chung HH 2007 [93]	30	44	66	693	0.4	0.91	5.23	0.73	833	86.7
28	Greco 1989 [95]	3	6	5	32	0.33	0.86	2.37	0.74	46	69.5
29	Lv K 2014 [40]	25	16	42	1080	0.6	0.96	25.5	0.63	1163	95
30	Narayanan 2001 [53]	6	0	6	12	1	0.66	0	0.5	24	75
31	Narayanan K 2001 [53]	8	6	6	16	0.57	0.72	2.09	0.58	36	66.6
32	Park W 2005 [54]	12	10	10	40	0.54	0.8	2.72	0.56	72	72.2
33	Reinhard MJ 2001 [42]	14	8	7	263	0.63	0.97	22.5	0.34	292	94.8
34	Sahdev A 2007 [105]	7	11	12	120	0.38	0.9	4.38	0.68	150	84.6
35	Waggen spack 1988 [109]	3	0	0	17	1	1	0	0	20	100
36	Kim SK 2009 [35]	32	38	27	456	0.45	0.94	7.05	0.49	553	88.2
37	Choi k 2006 [30]	10	9	23	112	0.52	0.82	4.07	0.75	154	79.2
38	Stecco A 2016 [47]	33	15	4	164	0.68	0.97	10.64	0.11	216	91.2
39	Choi HJ 2006 [91]	12	24	3	346	0.33	0.99	12.3	0.21	385	92.9
40	Choi J 2006 [91]	15	47	17	1830	0.24	0.99	18.7	0.54	1909	96.6
41	Lin G 2008 [104]	3	4	9	284	0.42	0.96	18	0.76	300	95.6
42	Lin Y 2008 [104]	2	2	5	41	0.5	0.89	6.14	0.74	50	86
43	Hatano 1999 [110]	1	0	0	34	1	1	0	0	35	100
44	Weber 1995 [111]	18	1	3	15	0.94	0.83	13.71	0.15	37	89.1
45	Williams 1989 [83]	9	2	2	7	0.81	0.77	3.68	0.23	20	80
	Cumulative	**517**	**446**	**480**	**9704**	**0.54**	**0.95**	**11.8**	**0.5**	**11145**	**92%**

Appendix-II

1. PET/CT-Breast cancer

S.no	STUDY - PET/CT Breast cancer	TP	FP	FN	TN	PPV	NPV	LR+	LR-	Total	Over all accuracy %
1	Chae 2009 [159]	16	12	17	63	0.57	0.78	3.03	0.61	108	21.2
2	Champion 2011 [160]	175	6	12	35	0.96	0.74	6.39	0.07	228	92.1
3	Chang 2014 [161]	35	4	5	27	0.89	0.84	6.78	0.14	71	87.3
4	Cochet 2014 [162]	39	2	3	19	0.95	0.86	9.75	0.07	63	92
5	Dirisamer 2010 [163]	39	0	3	10	1	0.76	0	0.07	52	94.2
6	Filippi 2011 [164]	33	1	5	7	0.97	0.58	6.94	0.15	46	86.9
7	Fueger 2005 [165]	31	4	2	21	0.88	0.91	5.87	0.07	58	89.6
8	Fuster 2008 [123]	14	0	6	32	1	0.84	0	0.3	52	88.4
9	Gallowitsch 2003 [124]	33	5	1	23	0.86	0.95	5.43	0.03	62	90.3
10	Goerres 2003 [166]	14	5	0	13	0.73	1	3.6	0	32	84.3
11	Grassetto 2011 [167]	37	0	3	49	1	0.94	0	0.07	89	100
12	Haug 2007 [128]	24	1	1	8	0.96	0.88	8.64	0.04	34	94.1
13	Kamel 2003 [168]	26	1	0	30	0.96	1	31	0	57	98.6
14	Kim 2009 [169]	27	0	8	102	1	0.9	0	0.2	137	94.1
15	Lonneux 2000 [170]	31	3	2	3	0.91	0.6	1.87	0.12	39	87.1
16	Manohar 2012 [171]	44	4	1	23	0.91	0.95	6.6	0.02	72	93
17	Moon 1998 [172]	22	7	2	26	0.75	0.92	4.32	0.1	57	84.2
18	Murakami 2012 [173]	24	2	1	20	0.92	0.95	10.56	0.04	47	93.6
19	Palomar 2010 [174]	29	5	4	32	0.85	0.88	6.5	0.14	70	87.1
20	Schmidt 2008 [175]	170	8	16	69	0.95	0.81	8.79	0.09	263	90.8
21	Veit 2007 [176]	19	4	0	21	0.82	1	6.25	0	44	90.9
22	Veronesi 2007 [137]	38	5	65	128	0.88	0.66	9.81	0.65	236	70.3
23	Wolfort 2006 [139]	13	0	3	7	1	0.7	0	0.18	23	86.9
24	Mohammed 2020	16	0	2	42	1	0.95	0	0.11	60	96
25	Mohammed S 2020	20	0	2	8	1	0.85	0	0.09	30	93.3
	Cumulative	**969**	**79**	**164**	**818**	**0.92**	**0.83**	**9.71**	**0.15**	**2030**	**88**

2. PET-Breast cancer

S.no	STUDY - PET Breast cancer	TP	FP	FN	TN	PPV	NPV	LR+	LR-	Total	Over all accuracy %
1	Abe 2005 [177]	14	1	0	29	0.93	1	3	0	44	97.7
2	Aide 2007 [178]	21	2	7	5	0.91	0.41	2.62	0.35	35	74.2
3	Avril 1996 [119]	19	0	5	17	1	0.77	0	0.2	41	87.8
4	Barranger 2003 [179]	3	0	12	17	1	0.58	0	0.8	32	62.5
5	Bender 1997 [144]	13	2	1	58	0.86	0.98	27.8	0.07	74	95.5
6	Dehdashti 1995 [180]	17	0	2	2	1	0.5	0	0.1	21	90.4
7	Dirisamer 2010 [163]	34	0	8	10	1	0.55	0	0.19	52	84.6
8	Eubank 2004 [122]	16	4	1	40	0.8	0.97	10.35	0.06	61	91.8
9	Fehr 2004 [181]	2	1	8	13	0.66	0.61	2.8	0.86	24	62.5
10	Gallowitsch 2003 [124]	33	5	1	23	0.86	0.95	5.43	0.03	62	90.3
11	Gilrendo 2006 [125]	120	2	22	131	0.98	0.85	56.1	0.15	275	91.2
12	Goerres 2003 [166]	14	5	0	13	0.73	1	3.6	0	32	84.3
13	Greco 2001 [182]	68	13	4	82	0.83	0.95	6.9	0.06	167	89.8
14	Guillemard 2006 [183]	7	0	1	6	1	0.85	0	0.12	14	92.8
15	Guller 2002 [126]	6	1	8	16	0.85	0.66	7.28	0.6	31	70.9
16	Hathaway 1999 [148]	6	0	0	1	1	1	0	0	7	100
17	Haug 2007 [127]	23	1	3	7	0.95	0.7	7.07	0.13	34	88.2
18	Inoue 2004 [184]	21	2	14	44	0.91	0.75	13.8	0.41	81	80.2
19	Kamel 2003 [168]	25	2	2	23	0.92	0.92	11.5	0.08	52	92.3
20	Kim 2001 [185]	16	2	1	8	0.88	0.88	4.7	0.07	27	88.8
21	Lin 2002 [186]	4	1	0	31	0.8	1	31	0	36	97.2
22	Moon 1998 [172]	27	6	2	22	0.81	0.91	4.34	0.08	57	85.9
23	Noh 1998 [187]	14	0	1	12	1	0.9	0	0.06	27	96.2
24	Ohta 2001 [188]	7	1	2	42	0.87	0.95	33.4	0.22	52	94.2
25	Piperkova 2007 [132]	221	2	5	29	0.99	0.85	15.1	0.02	257	97.2
26	Raileanu 2004 [189]	6	0	1	13	1	0.92	0	1.42	20	95
27	Schmidt 2008 [175]	170	8	16	69	0.95	0.81	8.79	0.09	263	90.8
28	Siggelkow 2003 [190]	31	3	4	35	0.91	0.89	11.2	0.12	73	90.4
29	Smith 1998 [191]	13	1	2	22	0.92	0.91	19.9	0.13	38	92.1
30	Utech 1996 [192]	44	20	0	60	0.68	1	4	0	124	83.8
31	Wolfort 2006 [139]	13	0	3	7	1	0.7	0	0.18	23	86.9
32	Yang 2002 [193]	100	2	5	20	0.98	0.8	10.47	0.05	127	94.4
	Cumulative	**1028**	**85**	**136**	**887**	**0.92**	**0.86**	**10.09**	**0.12**	**2136**	**90.1**

3. CT-Breast cancer

S.no	STUDY - CT Breast cancer	TP	FP	FN	TN	PPV	NPV	LR+	LR-	Total	Over all accuracy %
1	Avril 1996 [119]	15	17	0	5	0.46	1	1.29	0	37	54.05
2	Chung 2006 [120]	25	18	0	17	0.58	1	1.94	0	60	70
3	Crowe 1994 [121]	9	10	0	1	0.47	1	1.1	0	20	50
4	Eubank 2001 [122]	8	3	12	17	0.72	0.58	2.66	0.7	40	62.5
5	Fuster 2008 [123]	14	32	0	6	0.3	1	1.18	0	52	38.4
6	Gallowitsch 2003 [124]	28	9	5	15	0.75	0.75	2.26	0.24	57	75.4
7	Gil-Rendo 2006 [125]	120	131	2	22	0.47	0.91	1.14	0.11	275	51.6
8	Guller 2002 [126]	6	16	1	8	0.27	0.88	1.28	0.42	31	11.8
9	Hagay 1996 [127]	42	11	4	61	0.79	0.93	5.97	0.1	118	87.2
10	Haug 2007 [128]	23	2	2	7	0.92	0.77	4.14	0.1	34	88.2
11	Kumar 2006 [129]	16	42	2	20	0.27	0.9	1.31	0.34	80	45
12	Lovrics 2004 [130]	9	63	2	16	0.12	0.88	1.02	0.89	90	27.7
13	Ohta 2000 [131]	14	13	0	6	0.51	1	1.46	0	33	60.6
14	Piperkova 2007 [132]	198	18	28	13	0.91	0.31	1.5	0.29	257	82.1
15	Radan 2006 [133]	14	9	6	8	0.6	0.57	1.32	0.63	37	59.4
16	Schirrmeister 2001 [134]	27	45	6	7	0.37	0.53	0.94	1.35	85	40
17	Ternier 2006 [135]	47	5	5	46	0.9	0.9	9.21	0.1	103	59.4
18	Vander 2002 [136]	8	37	1	24	0.17	0.96	1.46	0.28	70	45.7
19	Veronesi 2007 [137]	38	128	5	65	0.22	0.92	1.33	0.34	236	42.7
20	Wahl 2004 [138]	66	159	40	43	0.29	0.51	0.79	1.77	308	35.3
21	Wolfort 2006 [139]	9	0	4	7	1	0.63	0	0.3	20	80
22	Yang 2008 [140]	20	3	0	1	0.86	1	1.33	0	24	41.6
23	Yutani 1999 [141]	8	16	0	2	0.33	1	1.12	0	26	38.4
24	Zornoza 2004 [142]	90	91	2	17	0.49	0.89	1.16	0.13	200	53.5
25	Mohammed 2020	19	1	2	8	0.95	0.8	8.14	0.1	30	90
26	Mohammed S 2020	13	3	4	40	0.81	0.9	10.9	0.25	60	88.3
	Cumulative	**886**	**882**	**133**	**482**	**0.5**	**0.78**	**1.34**	**0.66**	**2383**	**57.4**

4. MRI-Breast cancer

S.no	STUDY - MRI Breast cancer	TP	FP	FN	TN	PPV	NPV	LR+	LR-	Total	Over all accuracy %
1	Belli 2002 [143]	22	2	0	16	0.91	1	9	0	40	95
2	Bender 1997 [144]	13	2	1	58	0.86	0.98	27.8	0.07	74	95.9
3	Drew 1998 [145]	63	3	0	39	0.95	1	14	0	105	97.1
4	Gilles 1993 [146]	14	1	0	11	0.93	1	12	0	26	96.1
5	Harada 2007 [147]	23	2	0	8	0.92	1	5	0	33	93.9
6	Hathaway 1999 [148]	6	0	0	1	1	1	0	0	7	100
7	Kimura 2010 [149]	2	0	0	8	1	1	0	0	10	100
8	Melani 1995 [150]	7	1	0	12	0.87	1	13	0	20	95
9	Memarse 2006 [151]	6	0	0	16	1	1	0	0	22	100
10	Micheal 2002 [152]	9	0	2	7	1	0.7	0	0.18	18	88.8
11	Mumtaz 1997 [153]	36	6	4	29	0.85	0.87	5.25	0.12	75	86.6
12	Murray 2002 [154]	10	17	0	20	0.37	1	2.17	0	47	63.8
13	Muuller 1998 [155]	10	2	0	55	0.83	1	28.5	0	67	97.1
14	Qayyum 2000 [156]	26	1	1	20	0.96	0.95	20.2	0.03	48	95.8
15	Stadnik 2006 [157]	5	1	0	4	0.83	1	5	0	10	90
16	Riebe 2007 [158]	10	5	1	11	0.66	0.91	2.9	0.13	27	77.7
	Cumulative	**262**	**43**	**9**	**315**	**0.85**	**0.97**	**8.04**	**0.03**	**629**	**91.7**

Appendix-III

PET/CT- Head and Neck cancer

S.no	STUDY - PET/CT Head and neck cancer	TP	FP	FN	TN	PPV	NPV	LR+	LR-	Total	Over all accuracy %
1	Abgral 2009 [222]	30	9	0	52	0.76	1	6.77	0	91	90.1
2	Babin 2008 [223]	3	2	0	12	0.6	1	7	0	17	88.2
3	Cetin 2013 [224]	16	6	3	11	0.72	0.78	2.38	0.24	36	75
4	Chan 2006 [225]	21	2	1	10	0.91	0.9	5.72	0.05	34	91.1
5	Chauhan 2012 [226]	15	1	6	29	0.93	0.82	21.4	0.29	51	86.2
6	Fakhry 2007 [227]	17	6	1	8	0.73	0.88	2.2	0.09	32	78.1
7	Ghanooni 2011 [228]	14	17	1	87	0.45	0.98	5.7	0.07	119	84.8
8	Gordin 2006 [229]	23	1	2	25	0.95	0.92	23.9	0.08	51	94.1
9	Gordin 2007 [230]	46	3	6	52	0.93	0.89	16.2	0.12	107	91.5
10	Goshen 2005 [231]	11	2	0	4	0.84	1	3	0	17	88.2
11	Ho 2013 [232]	18	7	0	227	0.72	1	33.4	0	252	97.2
12	Jeong 2007 [233]	25	6	1	15	0.8	0.93	3.36	0.05	47	85.1
13	Kao 1998 [234]	11	1	0	24	0.91	1	25	0	36	97.2
14	Kim 2007 235	39	23	1	286	0.62	0.99	13	0.02	349	93.1
15	Kim 2011 [236]	74	13	15	126	0.85	0.89	8.89	0.18	228	87.7
16	Kim 2013 [237]	25	5	2	87	0.83	0.97	17	0.07	119	94.1
17	Krabbe 2008 [238]	4	1	4	29	0.8	0.87	15	0.51	38	86.8
18	Krabbe 2009 [239]	16	26	0	66	0.38	1	3.53	0	108	75.9
19	Kubota 2004 [240]	7	3	0	10	0.7	1	4.33	0	20	85
20	Lee 2007 [241]	15	5	1	74	0.75	0.98	14.8	0.06	95	93.6
21	Lee 2015 [242]	15	1	5	18	0.93	0.78	14.2	0.26	39	84.6
22	Li 2001 [243]	20	3	2	18	0.86	0.9	6.36	0.1	43	88.3
23	Nahmias 2007 [244]	37	10	5	22	0.78	0.81	2.81	0.17	74	79.7
24	Nakamura 2013 [245]	119	6	9	136	0.95	0.93	22	0.07	270	94.4
25	Ng 2010 [246]	48	12	7	112	0.8	0.94	9.01	0.14	179	89.3
26	Paidpally 2013 [247]	22	19	4	182	0.53	0.97	8.95	0.16	227	89.8
27	Robin 2015 [248]	22	12	1	81	0.64	0.98	7.41	0.04	116	88.7
28	Roh 2007 [249]	30	4	3	26	0.88	0.89	6.81	0.1	63	88.8
29	Roh 2014 [250]	27	10	11	43	0.72	0.79	3.76	0.35	91	76.9
30	Salaun 2007 [251]	8	1	0	21	0.88	1	22	0	30	96.6
31	Schroeder 2008 [252]	0	0	58	7	0	0.61	0	1	13	53.8
32	Seitz 2009 [216]	39	0	2	0	1	0	0	0	41	95.1
33	Sohn 2016 [253]	16	2	9	22	0.88	0.7	7.68	0.39	49	77.5
34	Stoeckli 2002 [254]	1	1	3	7	0.5	0.7	2	0.85	12	66.6
35	Stokkel 1999 [255]	17	7	0	24	0.7	1	4.42	0	48	85.4
36	Tsai 2002 [256]	14	1	0	13	0.93	1	14	0	28	96.4
37	Wierzbicka 2011 [257]	31	8	5	39	0.79	0.88	5.05	0.16	83	84.3
38	Wong 2002 [258]	69	31	3	78	0.69	0.96	3.36	0.05	181	81.2
39	Yamaga 2018 [2259]	10	39	21	135	0.2	0.86	1.43	0.87	205	70.7
40	Yen 2003 [260]	21	3	0	43	0.87	1	15.3	0	67	95.5
41	Zundel 2011 [261]	4	17	0	31	0.19	1	2.82	0	52	67.3
	Cumulative	**1000**	**326**	**192**	**2292**	**29.9**	**36.5**	**391.95**	**6.54**	**3758**	**87.6**

Appendix -IV

1. PET- Head and Neck cancer

S.no	STUDY - PET Head and neck cancer	TP	FP	FN	TN	PPV	NPV	LR+	LR-	Total	Over all accuracy %
1	Chang 2005 [262]	14	8	73	0	0.63	0	0.16	0	95	14.7
2	Liu 2006 [263]	21	2	170	9	0.91	0.05	0.6	1.08	202	14.8
3	Shu-hang 2006 [264]	21	13	30	393	0.61	0.92	12.8	0.6	457	88.6
4	Shu 2006 [264]	18	8	17	91	0.69	0.84	6.36	0.52	134	81.3
	Cumulative	**74**	**31**	**290**	**493**	**2.84**	**1.81**	**19.92**	**2.2**	**888**	**64%**

2. CT- Head and Neck cancer

S.no	STUDY - CT Head and neck cancer	TP	FP	FN	TN	PPV	NPV	LR+	LR-	Total	Over all accuracy %
1	Adams 1998 [194]	96	175	21	992	0.35	0.97	5.47	0.21	1284	84.7
2	Akoglu 2005 [195]	21	2	6	12	0.91	0.66	5.44	0.25	41	80.4
3	Braams 1995 [196]	5	10	4	13	0.33	0.76	1.27	0.78	32	56.2
4	Curtin 1998 [197]	57	415	1	62	0.12	0.98	1.12	0.13	535	22.2
5	Dammann 2005 [198]	32	17	8	236	0.65	0.96	11.09	0.21	293	91.4
6	Eida 2003 [199]	3	5	3	162	0.37	0.98	16.7	0.51	173	95.3
7	Fan 2006 [200]	23	11	4	4	0.67	0.5	1.16	0.55	42	64.2
8	Hafidh 2006 [201]	8	10	12	2	0.44	0.14	0.48	3.6	32	31.2
9	Kau 1999 [202]	6	17	1	17	0.26	0.94	1.71	0.28	41	56.9
10	Ke 2006 [203]	10	3	3	4	0.76	0.57	1.79	0.4	20	70
11	Lu 2007 [204]	11	1	3	6	0.91	0.66	5.5	0.25	21	80.9
12	Mcguirt 1995 [205]	18	3	1	19	0.85	0.95	6.94	0.06	41	90.2
13	Paulus 1998 [206]	8	1	0	4	0.88	1	5	0	13	92.3
14	Peters 2012 [207]	10	56	0	1	0.15	1	1.01	0	67	16.4
15	Wu 2010 [208]	10	1	2	11	0.9	0.84	10	0.18	24	87.5
16	Yoon 2009 [209]	57	2	17	326	0.96	0.95	126	0.23	402	95.2
	Cumulative	**375**	**729**	**86**	**1871**	**9.51**	**12.86**	**200.68**	**7.64**	**3061**	**73.3**

3. MRI- Head and Neck cancer

S.no	STUDY - MRI Head and neck cancer	TP	FP	FN	TN	PPV	NPV	LR+	LR-	Total	Over all accuracy %
1	Adams 1998 [194]	94	250	23	917	0.27	0.97	3.75	0.25	1284	78.7
2	Akoglu 2005 [195]	16	1	11	13	0.94	0.54	8.29	0.43	41	70.7
3	Braams 1995 [196]	5	6	10	134	0.45	0.93	7.77	0.69	155	89.6
4	Curtin 1997 [197]	53	382	5	95	0.12	0.95	1.14	0.43	535	27.6
5	Dammann 2005 [198]	37	14	3	239	0.72	0.98	16.7	0.07	293	94.1
6	Ding 2005 [210]	132	27	34	255	0.83	0.88	8.3	0.22	448	86.3
7	Gu 2000 [211]	8	3	1	50	0.72	0.98	15.7	0.11	62	93.5
8	Hafidh 2006 [201]	11	10	9	2	0.52	0.18	0.66	2.7	32	40.6
9	Hao 2000 [212]	30	2	11	38	0.93	0.77	14.6	0.28	81	83.9
10	Kau 1999 [202]	2	17	1	15	0.1	0.93	1.25	0.71	35	48.5
11	Laubenbacher 1994 [213]	13	7	5	9	0.65	0.64	1.65	0.49	34	64.7
12	Nakamoto 2009 [214]	16	2	4	30	0.88	0.88	12.8	0.21	52	88.4
13	Olmos 1999 [215]	22	11	2	27	0.66	0.93	3.16	0.11	62	79
14	Seitz 2009 [216]	20	1	0	4	0.95	1	5	0	25	96
15	VandenBrekel 1991 [217]	87	13	42	415	0.87	0.9	22.2	0.33	557	90.1
16	Wang 1999 [218]	23	0	15	130	1	0.89	0	0.39	168	91.07
17	Wide 1999 [219]	18	11	9	34	0.62	0.79	2.72	0.44	72	72.2
18	Wilson 1994 [220]	17	16	0	18	0.51	1	2.12	0	51	68.6
19	Yoon 2009 [209]	57	2	17	326	0.96	0.95	126	0.23	402	95.2
20	Yuan 2000 [221]	12	1	2	9	0.92	0.81	8.57	0.15	24	87.5
	Cumulative	**673**	**776**	**204**	**2760**	**13.62**	**16.9**	**262.38**	**8.24**	**4413**	**77.7**

Appendix-VI

1. PET/CT-Gastro Cancer (GC)

S.no	STUDY - PET/CT GI cancer	TP	FP	FN	TN	PPV	NPV	LR+	LR-	Total	Over all accuracy %
1	Dirisamer 2009 [272]	30	1	1	30	0.96	0.96	30	0.03	62	96.7
2	Kawanaka 2016 [273]	29	0	13	44	1	0.77	0	0.3	86	84.8
3	Satoh [270]	25	5	1	76	0.83	0.98	15.5	0.04	107	94.3
4	Soussan [271]	16	3	3	8	0.84	0.72	3.08	0.21	30	80
	Cumulative	**100**	**9**	**18**	**158**	**3.63**	**3.43**	**48.58**	**0.58**	**285**	**90.5**

PET- Gastric cancer

S.no	STUDY - PET GI cancer	TP	FP	FN	TN	PPV	NPV	LR+	LR-	Total	Over all accuracy %
1	Chen 2005 [265]	3	1	7	57	0.75	0.89	17.4	0.71	68	88.2
2	Kim 2011 [266]	1	2	1	5	0.33	0.83	1.75	0.7	9	66.6
3	Lim 2006 [267]	6	1	11	94	0.85	0.89	33.5	0.65	112	89.2
4	Potter 2002 [268]	5	2	3	3	0.71	0.5	1.56	0.62	13	61.5
	Cumulative	**15**	**6**	**22**	**159**	**2.64**	**3.11**	**54.21**	**2.68**	**202**	**86.1**

2. CT- Gastric cancer

S.no	STUDY - CT GI cancer	TP	FP	FN	TN	PPV	NPV	LR+	LR-	Total	Over all accuracy %
1	Duhr 2011 [274]	31	1	1	4	0.96	0.8	4.84	0.03	37	94.5
2	Giganti 2016 [275]	18	3	2	32	0.85	0.94	10.5	0.1	55	90.9
3	Karakoyun 2014 [276]	39	4	1	11	0.9	0.91	3.65	0.03	55	90.9
4	Kawanaka 2016 [273]	30	0	12	44	1	0.78	0	0.28	86	86.4
5	Kim 2011 [266]	44	1	15	11	0.97	0.42	8.94	0.27	71	77.4
7	Kim SJ 2009 [277]	27	17	26	428	0.61	0.94	13.33	0.51	498	91.3
	Cumulative	**189**	**26**	**57**	**530**	**5.29**	**4.79**	**41.26**	**1.22**	**802**	**89.6**

3. MRI- Gastric cancer

S.no	STUDY - MRI GI cancer	TP	FP	FN	TN	PPV	NPV	LR+	LR-	Total	Over all accuracy %
1	Fuji 2008 [269]	13	1	2	10	0.92	0.83	9.53	0.14	26	88.4
2	Satoh 2011 [270]	20	16	4	90	0.55	0.95	5.52	0.19	130	84.6
3	Soussan 2012 [271]	16	2	3	9	0.88	0.75	4.63	0.19	30	83.3
	Cumulative	**49**	**19**	**9**	**109**	**2.35**	**2.53**	**19.68**	**0.52**	**186**	**84.9**

Appendix-VI

PET/CT- Lung cancer

	STUDY - PET/CT - Lung Cance	TP	FP	FN	TN	PPV	NPV	LR+	LR-	Total	Over all accuracy
1	Annema 2010 [273]	58	0	13	52	1	0.8	0	0.18	123	89.4
2	Herth 2010 [274]	68	0	3	68	1	0.95	0	0.04	139	97.8
3	Hwangbo 2009 [275]	41	0	4	98	1	0.96	0	0.08	143	97.2
4	Kang 2014 [276]	52	0	7	89	1	0.92	0	0.11	148	95.2
5	Lee 2014 [277]	29	0	0	8	1	1	0	0	37	100
6	Liberman 2014 [278]	47	0	5	114	1	0.95	0	0.09	166	96.9
7	Ohnishi 2011 [279]	28	0	11	71	1	0.86	0	0.28	110	90
8	Oki 2014 [280]	24	0	9	113	1	0.92	0	0.27	146	93.8
9	Wallace 2008 [281]	39	0	3	96	1	0.96	0	0.07	138	97.8
10	Schumacher 2001 [282]	20	0	0	6	1	1	0	0	26	100
11	Hauber 2001 [283]	1	0	0	6	1	1	0	0	7	100
12	Chin 2002 [284]	10	0	1	7	1	0.87	0	0.09	18	94.4
13	Kamel 2003 [285]	9	0	0	15	1	1	0	0	24	100
14	Pandit 2003 [286]	4	0	0	4	1	1	0	0	8	100
15	Bradley 2004 [287]	2	1	0	21	0.66	1	22	0	24	95.8
16	Brink 2004 [288]	76	1	0	43	0.98	1	44	0	120	99.1
17	Kut 2007 [289]	12	0	0	6	1	1	0	0	18	100
18	Fischer 2007 [290]	13	0	1	6	1	0.85	0	0.07	20	95
19	Vinjamuri 2008 [291]	25	1	2	23	0.96	0.92	22.2	0.07	51	100
20	Arslan 2011 [292]	9	0	0	3	1	1	0	0	12	83.3
21	Orlacchio 2007 [293]	20	0	6	100	1	0.94	0	0.23	126	95.2
22	Herder 2004 [294]	13	5	1	17	0.72	0.94	4.08	0.09	36	83.3
23	Degirmenci 2008 [295]	16	5	10	18	0.76	0.64	2.83	0.49	49	69.3
24	Martins 2008 [296]	13	5	1	13	0.72	0.92	3.34	0.09	32	81.2
25	Sim 2013 [297]	137	14	21	14	0.9	0.4	1.73	0.26	186	81.1
26	Dalli 2013 [298]	54	18	26	111	0.75	0.81	4.83	0.37	209	78.9
27	Zhang 2014 [299]	68	6	9	30	0.91	0.76	5.29	0.14	113	86.7
28	Jeong 2007 [300]	31	7	9	53	0.81	0.85	6.64	0.25	100	73.1
29	Li 2014 [301]	199	31	49	19	0.86	0.27	1.29	0.51	298	88.5
30	Li 2011 [302]	58	9	2	27	0.86	0.93	3.86	0.04	96	88.5
31	Lopez 2015 [303]	32	7	8	8	0.82	0.5	1.71	0.37	55	72.7
32	Dabrowska 2015 [304]	37	1	12	21	0.97	0.63	16.6	0.25	71	81.6
33	Tasci 2010 [305]	17	19	2	89	0.47	0.97	5.08	0.12	127	83.4
34	Li 2010 [306]	41	12	8	97	0.77	0.92	7.6	0.18	158	87.3
35	Sit 2010 [307]	15	18	14	110	0.45	0.88	3.67	0.56	157	79.6
36	Hwangbo 2009 [275]	21	35	9	52	0.37	0.85	1.74	0.5	117	25.6
37	Bille 2009 [308]	14	7	17	121	0.66	0.87	8.25	0.58	159	84.9
38	Perigaud 2009 [309]	4	6	6	35	0.4	0.85	2.73	0.7	51	76.4
39	Sanli 2009 [310]	9	7	2	60	0.56	0.96	7.83	0.2	78	88.4
40	Lee 2009 [311]	27	16	9	130	0.62	0.93	6.84	0.28	182	86.2
41	Al-Sarraf 2008 [312]	48	20	53	842	0.7	0.94	20.48	0.53	963	10.4
42	Yang 2008 [313]	18	11	7	86	0.62	0.92	6.34	0.31	122	85.2
43	Hu 2008 [314]	117	72	17	378	0.61	0.95	5.45	0.15	584	84.7
44	Kim 2007 [315]	110	21	70	473	0.83	0.87	14.37	0.4	674	86.4
45	Lee 2007 [316]	24	19	4	79	0.55	0.95	4.42	0.17	126	81.7
46	Bryant 2006 [317]	131	33	12	195	0.79	0.94	6.32	0.09	371	87.8
47	Tassia 2020 [318]	197	18	41	280	0.91	0.87	13.7	0.18	536	88.9
48	Bille 2013 [319]	28	13	32	280	0.68	0.89	10.51	0.55	353	87.2
49	Carnochan 2009 [320]	19	27	18	130	0.41	0.87	2.98	0.58	194	76.8
50	Chen 2010 [321]	31	1	0	24	0.96	1	25	0	56	98.2
51	Czepczynski 2011 [322]	9	0	0	42	1	1	0	0	51	100
52	Darling 2011 [323]	14	8	6	121	0.63	0.95	11.28	0.31	149	90.6
53	De wever 2007 [324]	10	6	1	33	0.62	0.97	5.9	0.1	50	86
54	El-Hariri 2012 [325]	6	2	1	24	0.75	0.96	11.14	0.15	33	90.9
55	Fischer 2011 [326]	18	10	8	43	0.64	0.84	3.66	0.37	79	77.2
56	Gunluoglu 2011 [327]	35	30	14	89	0.53	0.86	2.83	0.38	168	73.8
57	Harders 2012 [328]	15	22	15	62	0.4	0.8	1.9	0.67	114	67.5
58	Hu 2011 [329]	29	25	5	43	0.53	0.89	2.32	0.23	102	70.5
59	Iskender 2012 [330]	63	65	6	152	0.49	0.96	3.04	0.12	286	75.1
60	Jeon 2010 [331]	32	8	20	150	0.8	0.88	12.15	0.4	210	86.6
61	Koksal 2013 [332]	8	22	4	47	0.26	0.92	2.09	0.48	81	55.5
62	Kuo 2012 [333]	10	17	9	66	0.37	0.88	2.56	0.59	102	74.5
63	Lee 2011 [334]	7	12	8	27	0.36	0.77	1.51	0.77	54	62.9
64	Lee 2012 [335]	1	16	5	138	0.05	0.96	1.6	0.93	160	86.8
65	Li 2010 [336]	41	12	8	97	0.77	0.92	7.6	0.18	158	87.3
66	Li 2012 [337]	13	0	6	61	1	0.91	0	0.31	80	92.5
67	Morikawa 2009 [338]	55	11	6	21	0.83	0.77	2.62	0.14	93	81.7
68	Ohno 2011 [339]	16	0	5	229	1	0.97	0	0.23	250	98
69	Ose 2012 [340]	7	5	7	93	0.58	0.93	9.8	0.52	112	12.5
70	Ozkan 2011 [341]	84	16	23	30	0.84	0.56	2.25	0.32	153	74.5
71	Plathow 2008 [342]	38	0	0	14	1	1	0	0	52	100
72	Saydam 2012 [343]	16	8	3	15	0.66	0.83	2.42	0.24	42	73.8
73	Shin 2008 [344]	11	8	12	153	0.57	0.92	9.62	0.54	184	89.1
74	Sommer 2012 [345]	2	1	4	24	0.66	0.85	8.33	0.69	31	83.8
75	Subedi 2009 [346]	22	10	2	57	0.68	0.96	6.14	0.09	91	86.8
76	Toba 2010 [347]	8	4	0	30	0.66	1	8.5	0	42	90.4
77	Tournoy 2007 [348]	25	4	3	16	0.86	0.84	4.46	0.13	48	85.4
78	Uruga 2011 [349]	10	15	20	137	0.4	0.87	3.37	0.73	182	80.7
79	Uskul 2009 [350]	28	4	2	2	0.87	0.5	1040	0.2	36	83.3
80	Usuda 2013 [351]	6	1	10	143	0.85	0.93	54	0.62	160	93.1
81	Yang 2008 [313]	5	3	1	22	0.62	0.95	6.94	0.18	31	87
82	Yi 2008 [352]	28	6	17	99	0.82	0.85	10.8	0.4	150	84.6
		2788	**817**	**765**	**7021**	**0.77**	**0.9**	**7.52**	**0.24**	**11391**	**86.1**

PET- Lung cancer

	STUDY - PET - Lung Cancer	TP	FP	FN	TN	PPV	NPV	LR+	LR-	Total	Over all accuracy
1	Scott 1994 [353]	2	3	1	19	0.4	0.95	4.88	0.38	25	84
2	Wahl 1994 [354]	9	3	2	13	0.75	0.86	4.36	0.22	27	100
3	Chin 1995 [355]	7	4	2	17	0.63	0.89	4.08	0.27	30	80
4	Valk 1995 [356]	20	3	4	49	0.86	0.92	14.4	0.17	76	90.7
5	Scott 1996 [357]	9	0	0	18	1	1	0	0	27	100
6	Sazon 1996 [358]	16	0	0	16	1	1	0	0	32	100
7	Sasaki 1996 [359]	13	1	4	53	0.92	0.92	41.2	0.23	71	92.9
8	Vansteenkiste 1997 [360]	10	1	5	34	0.9	0.87	23.3	0.34	50	88
9	Steinert 1997 [361]	25	1	3	83	0.96	0.96	75	0.1	112	96.4
10	Guhlmann 1997 [362]	13	0	2	17	1	0.89	0	0.13	32	93.7
11	Hagberg 1997 [363]	6	0	3	9	1	0.75	0	0.33	18	83.3
12	Bury 1997 [364]	12	0	2	52	1	0.96	0	0.14	66	96.9
13	Saunders 1999 [365]	12	2	5	65	0.85	0.92	23.6	0.3	90	85.5
14	Marom 1999 [366]	40	3	4	31	0.93	0.88	10.3	0.09	78	91
15	Pieterman 2000 [367]	29	10	3	60	0.74	0.95	6.34	0.1	102	87.2
16	Gupta 2000 [368]	51	8	2	107	0.86	0.98	13.8	0.04	168	94
17	Poncelet 2001 [369]	6	8	3	44	0.42	0.93	4.33	0.39	61	81.9
18	Yasuomi 2009 [370]	61	4	9	23	0.93	0.71	5.88	0.15	97	86.5
	Yasuomi O 2009 [370]	8	1	18	0	0.88	0	0.3	0	27	29.6
	Cummulative	**349**	**52**	**72**	**710**	**0.87**	**0.9**	**12.14**	**0.18**	**1183**	**89.5**

CT- Lung cancer

S.no	STUDY - CT - Lung Cancer	TP	FP	FN	TN	PPV	NPV	LR+	LR-	Total	Over all accuracy
1	Szlubowski 2010 [371]	19	2	9	90	0.9	0.9	31.2	0.32	120	90.8
2	Szlubowski 2012 [372]	106	0	14	94	1	0.87	0	0.11	214	93.4
3	Vilmann 2005 [373]	20	0	0	11	1	1	0	0	31	100
4	Scott 1994 [353]	1	2	2	20	0.33	0.9	3.66	0.73	25	84
5	Wahl 1994 [354]	7	9	4	7	0.43	0.63	1.13	0.83	27	51.8
6	Chin 1995 [355]	5	3	4	18	0.62	0.81	3.88	0.51	30	76.6
7	Valk 1995 [356]	15	14	9	38	0.51	0.8	2.32	0.51	76	69.7
8	Scott 1996 [357]	6	3	3	15	0.66	0.83	4	0.4	27	77.7
9	Sazon 1996 [358]	13	7	3	9	0.65	0.75	1.85	0.33	32	68.7
10	Sasaki 1996 359	11	7	6	47	0.61	0.88	4.99	0.4	71	81.6
11	Vansteenkiste 1997 [360]	10	13	5	22	0.43	0.81	1.79	0.53	50	64
12	Steinert 1997 [361]	16	5	12	79	0.76	0.86	9.6	0.45	112	84.8
13	Guhlmann 1997 [362]	8	3	7	14	0.76	0.86	9.6	0.45	112	19.6
14	Hagberg 1997 [363]	5	0	4	9	1	0.69	0	0.44	18	77.7
15	Bury 1997 [364]	11	8	3	44	0.57	0.93	5.1	0.25	66	83.3
16	Saunders 1999 [365]	3	7	12	62	0.3	8.83	1.97	0.89	84	77.3
17	Marom 1999 [366]	26	4	18	30	0.86	0.62	5.02	0.46	78	71.7
18	Pieterman 2000 [367]	24	24	8	46	0.5	0.85	2.18	0.38	102	68.6
19	Gupta 2000 [368]	36	36	17	79	0.5	0.82	2.16	0.46	168	68.4
20	Poncelet 2001 [369]	5	17	4	36	0.22	0.9	1.73	0.65	62	66.1
	Cummulative	**347**	**164**	**144**	**770**	**0.67**	**0.84**	**4.02**	**0.35**	**1425**	**78.3**

MRI- Lung cancer

	STUDY - MRI - Lung Cancer	TP	FP	FN	TN	PPV	NPV	LR+	LR-	Total	Over all accuracy
1	Tassia 2020 [318]	61	21	21	162	0.74	0.88	6.48	0.28	265	30.9
2	Yasuomi 2009 [370]	61	4	9	23	0.93	0.71	5.88	0.15	97	72.1
3	Yasuomi O 2009 [370]	8	1	18	0	0.88	0	0.3	0	27	96.2
4	Stuart 2019 [374]	26	9	26	126	0.74	0.82	7.5	0.53	187	81.2
5	Stuart A 2019 [374]	28	6	24	129	0.82	0.84	12.11	0.48	187	83.9
	Cummulative	**184**	**41**	**98**	**440**	**0.83**	**0.79**	**5.92**	**0.3**	**389**	**80.9**

Appendix VII

Queries in PubMed		
Search	**Query**	**Items found**
#1	Search ((cervical cancer [MeSH Terms]) OR lymph node) [MeSH Terms]) OR pelvic [MeSH Terms]	644598
#2	Search (((positron emission tomography computed tomography [MeSH Terms]) OR PET/CT[MeSH Terms]) AND positron emission tomography[MeSH Terms]) OR PET[MeSH Terms]	2018
#3	Search (((sensitivity[MeSH Terms]) OR sensitiveness[MeSH Terms]) AND specificity[MeSH Terms]) OR particularity[MeSH Terms]	93255
#4	Search (((positron emission tomography computed tomography[MeSH Terms]) OR PET/CT[MeSH Terms]) AND computed tomography) OR CT	794002
#5	Search (((positron emission tomography computed tomography[MeSH Terms]) OR PET/CT[MeSH Terms]) AND magnetic resonance imaging[MeSH Terms]) OR MRI[MeSH Terms]	84060
#6	Search (((Breast cancer[MeSH Terms]) OR Mammary glands[MeSH Terms]) OR malignant[MeSH Terms]) OR tumor[MeSH Terms]	458529
#7	Search ((((((((((((Breast cancer [MeSH Terms]) OR Mammary glands[MeSH Terms]) OR malignant[MeSH Terms]) OR tumor[MeSH Terms]) AND positron emission tomography computed tomography[MeSH Terms]) OR PET/CT[MeSH Terms]) OR computed tomography[MeSH Terms]) OR CT[MeSH Terms]) OR positron emission tomography[MeSH Terms]) OR PET[MeSH Terms]) OR magnetic resonance imaging[MeSH Terms]) OR MRI[MeSH Terms]) AND Sensitivity[MeSH Terms]) AND specificity[MeSH Terms]	15513
#8	Search (((Head and neck cancer) OR oropharyngeal cancer) OR Malignant) OR tumor	1693552
#9	Search ((((((((((((Head and neck cancer[MeSH Terms]) OR oropharyngeal cancer[MeSH Terms]) OR Malignant[MeSH	15513

	Terms]) OR tumor[MeSH Terms]) AND positron emission tomography computed tomography[MeSH Terms]) OR PET/CT[MeSH Terms]) OR computed tomography[MeSH Terms]) OR CT[MeSH Terms]) OR positron emission tomography[MeSH Terms]) OR PET[MeSH Terms]) OR magnetic resonance imaging[MeSH Terms]) OR MRI[MeSH Terms]) AND Sensitivity[MeSH Terms]) AND Specificity[MeSH Terms]	
#10	Search ((((Gastro intestinal cancer) OR gastric cancer) OR stomach cancer) OR malignant) OR tomor	727776
#11	Search ((((((((((((((Gastro intestinal cancer[MeSH Terms]) OR gastric cancer[MeSH Terms]) OR stomach cancer[MeSH Terms]) OR malignant[MeSH Terms]) OR tumor[MeSH Terms]) AND positron emission tomography computed tomography[MeSH Terms]) OR PET/CT[MeSH Terms]) OR computed tomography[MeSH Terms]) OR CT[MeSH Terms]) OR positron emission tomography[MeSH Terms]) OR PET[MeSH Terms]) OR magnetic resonance imaging[MeSH Terms]) OR MRI[MeSH Terms]) AND Sensitivity[MeSH Terms]) AND Specificity[MeSH Terms]	15513

Queries in Cochrane		
Search	**Query**	**Items found**
#1	Search (cervical cancer)):ti,ab,kw OR (lymph node)):ti,ab,kw OR (pelvic):ti,ab,kw	54321
#2	Search (positron emission tomography computed tomography):ti,ab,kw OR (PET/CT):ti,ab,kw AND (positron emission tomography):ti,ab,kw OR (PET):ti,ab,kw	24642
#3	Search (sensitivity) :ti,ab,kw OR (sensitiveness):ti,ab,kw AND specificity):ti,ab,kw	16617

#4	Search (positron emission tomography computed tomography):ti,ab,kw OR (PET/CT):ti,ab,kw AND (computed tomography):ti,ab,kw OR 9CT):ti,ab,kw	744256
#5	Search (positron emission tomography computed tomography):ti,ab,kw OR (PET/CT):ti,ab,kw AND magnetic resonance imaging):ti,ab,kw OR (MRI):ti,ab,kw	561469
#6	Search (Breast cancer):ti,ab,kw OR (Mammary glands):ti,ab,kw OR (malignant):ti,ab,kw OR (tumor):ti,ab,kw	37305
#7	Search (Breast cancer):ti,ab,kw OR (Mammary glands):ti,ab,kw OR (malignant))ti,ab,kw OR (tumor):ti,ab,kw AND (positron emission tomography computed tomography) :ti,ab,kw OR PET/CT):ti,ab,kw OR computed tomography):ti,ab,kw OR CT):ti,ab,kw OR positron emission tomography):ti,ab,kw OR PET):ti,ab,kw OR magnetic resonance imaging):ti,ab,kw OR MRI):ti,ab,kw AND Sensitivity):ti,ab,kw AND specificity):ti,ab,kw	116881
#8	Search (Head and neck cancer)):ti,ab,kw OR oropharyngeal cancer)):ti,ab,kw OR Malignant)):ti,ab,kw OR tumor):ti,ab,kw	1693552
#9	Search (Head and neck cancer):ti,ab,kw OR oropharyngeal cancer):ti,ab,kw OR Malignant):ti,ab,kw OR tumor):ti,ab,kw AND positron emission tomography computed tomography):ti,ab,kw OR PET/CT):ti,ab,kw OR computed tomography):ti,ab,kw OR CT):ti,ab,kw OR positron emission tomography):ti,ab,kw OR PET):ti,ab,kw OR magnetic resonance imaging):ti,ab,kw OR MRI):ti,ab,kw AND Sensitivity):ti,ab,kw AND Specificity):ti,ab,kw	561196
#10	Search (Gastro intestinal cancer)):ti,ab,kw OR gastric cancer)):ti,ab,kw OR stomach cancer) OR malignant)):ti,ab,kw OR tomor):ti,ab,kw	8087
#11	Search (Gastro intestinal cancer):ti,ab,kw OR gastric cancer):ti,ab,kw OR stomach cancer):ti,ab,kw OR malignant):ti,ab,kw OR tumor):ti,ab,kw AND positron emission tomography computed tomography):ti,ab,kw OR PET/CT):ti,ab,kw OR computed tomography):ti,ab,kw OR	491396

	CT):ti,ab,kw OR positron emission tomography):ti,ab,kw OR PET):ti,ab,kw OR magnetic resonance imaging):ti,ab,kw OR MRI):ti,ab,kw AND Sensitivity):ti,ab,kw AND Specificity):ti,ab,kw	

Google scholar: 1122

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