Accurate Staging of Prostate Cancer

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What imaging tools are available?

When do I use them?

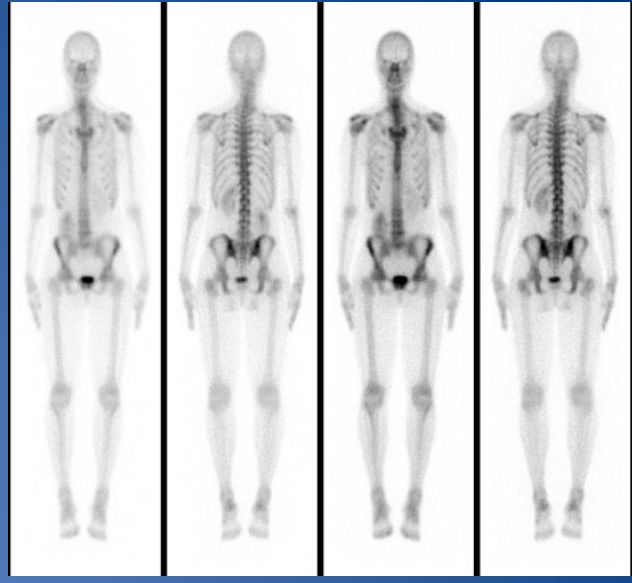
Table 1. Summary of recommendations for scanning metastatic disease in patients with prostate cancer

		Recommendation					
			Imaging for Bone Mets		Imaging for Soft Tissue Mets		Imaging Frequency
Organization	Y	Patient Type	Criteria	Modality	Criteria	Modality	
PCWG2[7]	2007	Trial eligibility for metastatic CRPC or baseline diagnosis	Progression = appearance of 2 or more new lesions	Bone scan; CT/MRI to confirm ambiguous lesions	Only report changes in lymph nodes ≥2 cm in diameter at baseline	CT	Every 12 wk in clinical trials
ACR[17]	2010	Diagnosis and staging	PSA ≥20 ng/mL or poorly differentiated primary tumors	Bone scan	NA	NA	NA
			Back pain and partially collapsed vertebra on radiography	MRI; Bone scan with SPECT spine; FDG-PET			
ESMO[18]	2010	Diagnosis and staging	PSA ≥15 ng/mL, Gleason ≥7, or ≥T3	Bone scan; pelvis CT/MRI	NA	NA	NA
AUA[19,20]	2007 Update	Diagnosis and staging	PSA >20 ng/mL or Gleason >7	Bone scan; CT	NA	NA	NA
	2011 Annual meeting	Diagnosis and staging	PSA >20 ng/mL, T2c, or Gleason ≥8	Bone scan; CT	NA	NA	NA
EAU[21]	2012	Diagnosis and staging	PSA >20 ng/mL	Bone scan; PET/CT or MRI for equivocal cases	Symptoms suggested the possibility of soft tissue mets	X-ray; ultrasound; CT/MRI	NA
		Follow-up after treatment with curative intent	PSA >20 ng/mL or patient has bone pain	Bone scan; pelvic CT/MRI			NA
		Follow-up after hormonal treatment	Symptomatic with unstable PSA	Bone scan			NA
		Diagnosis for PSA relapse after RP	PSA >20 ng/mL or PSA velocity >20 ng/mL/y	Bone scan; CT			NA
NCCN[22]	2013	Initial clinical assessment and staging	T1 with PSA >20 ng/mL; T2 with PSA >10; Gleason ≥8; T3, T4 or symptomatic	Bone scan	T3 or T4; T1 or T2 and nomogram indicated probability of lymph node involvement >20%	Pelvic CT/MRI	NA
		Postradical prostatectomy recurrence	Symptomatic or PSA increasing rapidly	Bone scan	NA	NA	NA
		Systemic therapy for metastatic CRPC	Should be monitored closely	Bone scan; CT	NA	NA	NA

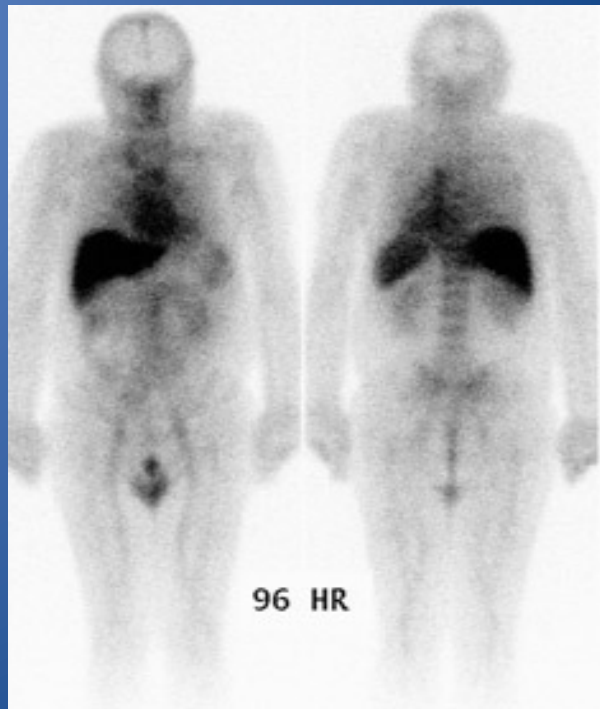
ACR, American College of Radiology; AUA, American Urological Association; CRPC, castration-resistant prostate cancer; CT, computed tomography; EAU, European Association of Urology; ESMO, European Society for Medical Oncology; FDG, fluorodeoxyglucose; MRI, magnetic resonance imaging; NA, not addressed; NCCN, National Comprehensive Cancer Network; PCWG2, Prostate Cancer Clinical Trials Working Group 2; PET, positron emission tomography; PSA, prostate-specific antigen; RP, radical prostatectomy; SPECT, single photon emission computed tomography.


FUTURE
PAST
PRESENT

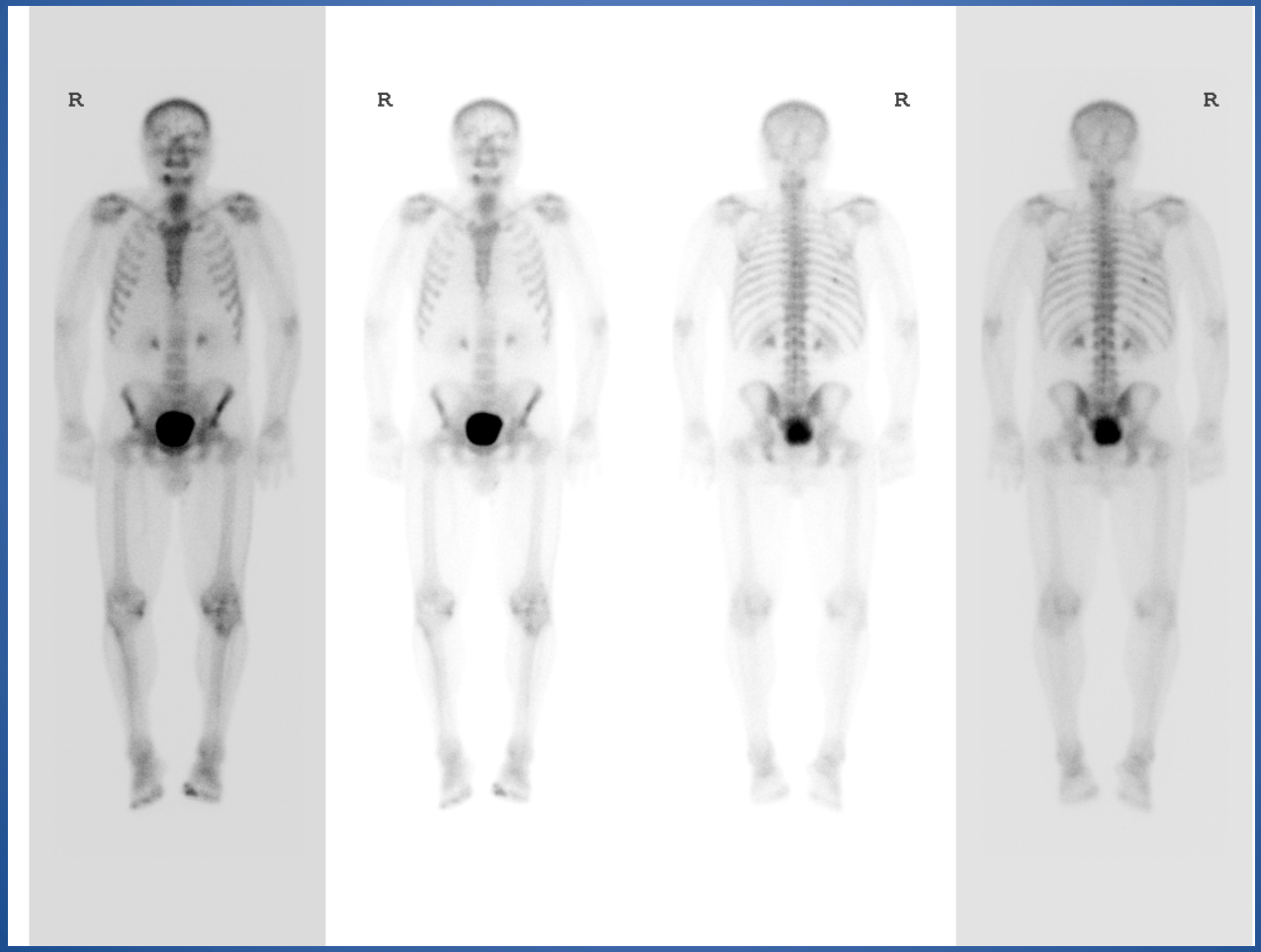
1st Generation



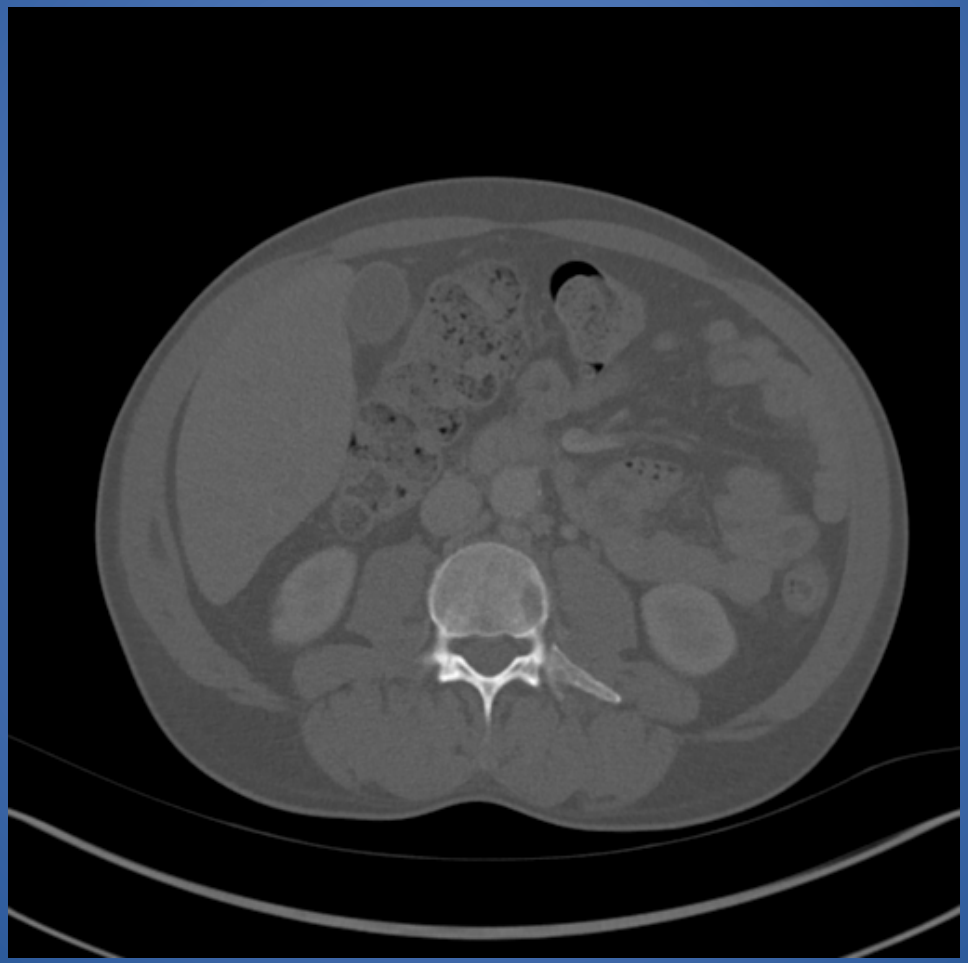
- Tc-99m diphosphonates
- Prostascint
- NaF



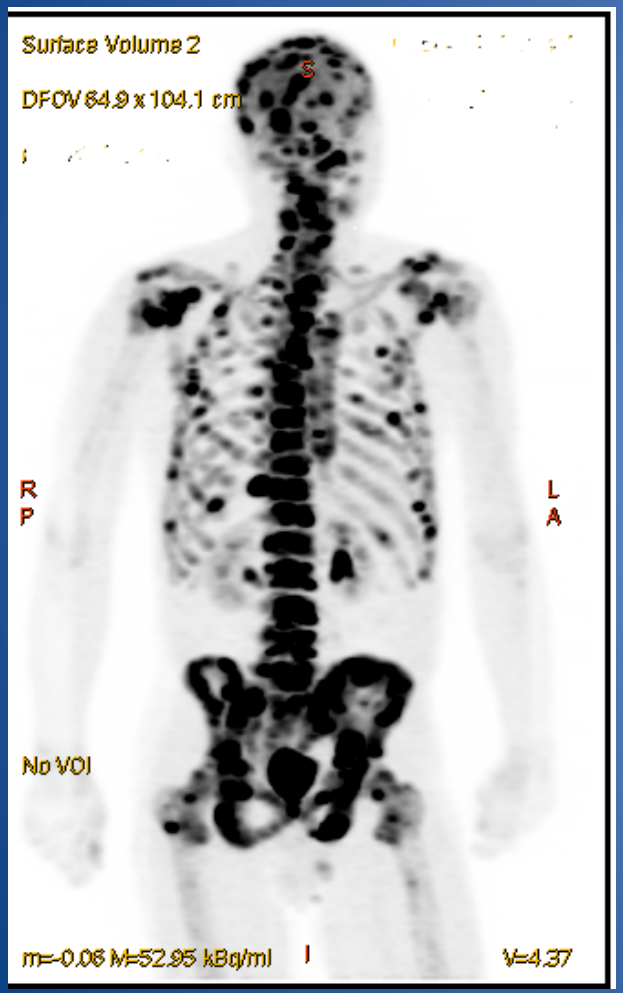
5/18/15
(GS 4 + 5; PSA on 4/9/15: 28.73)

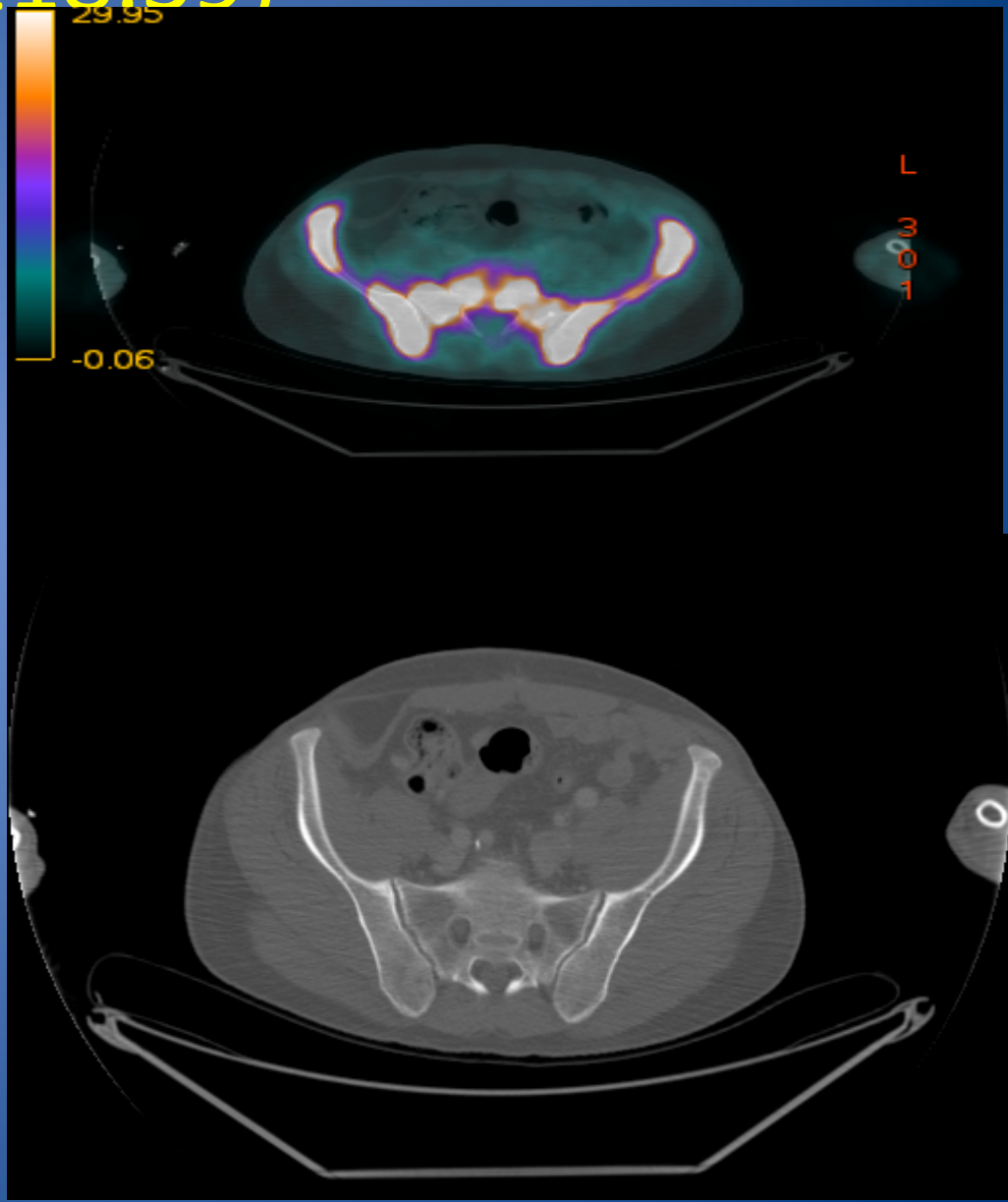


7/9/15



7/24/15
(PSA 118.39)





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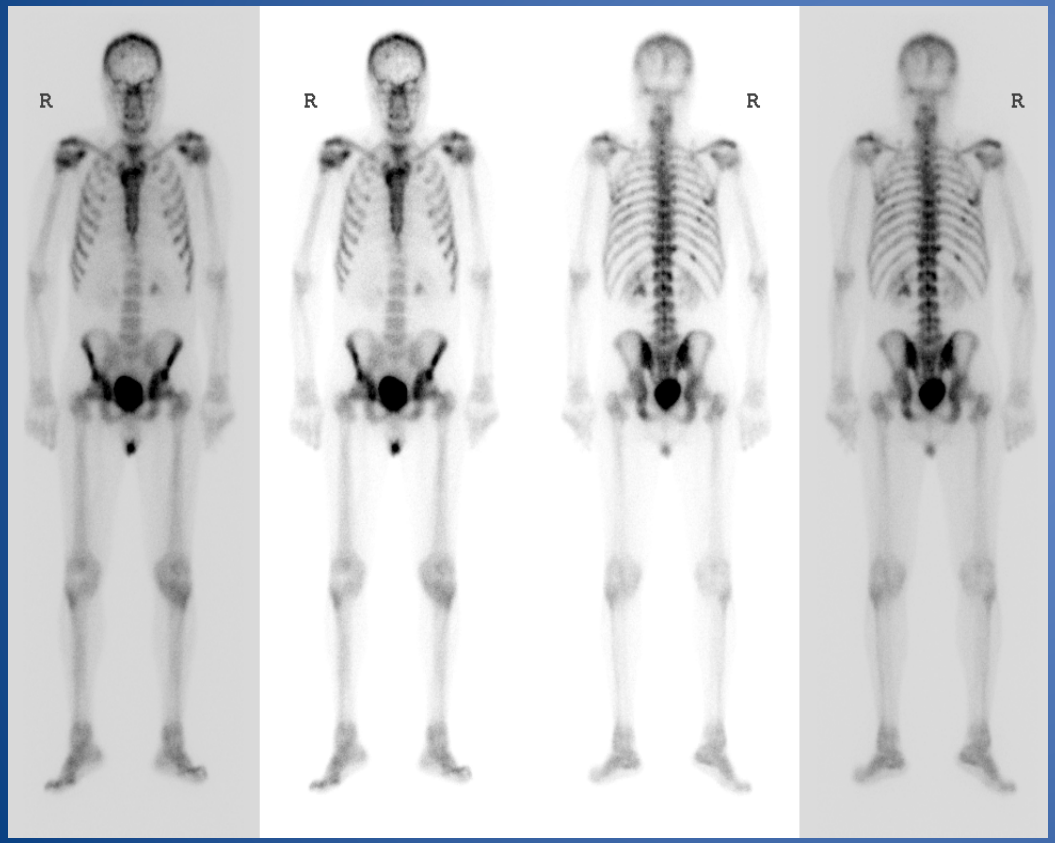

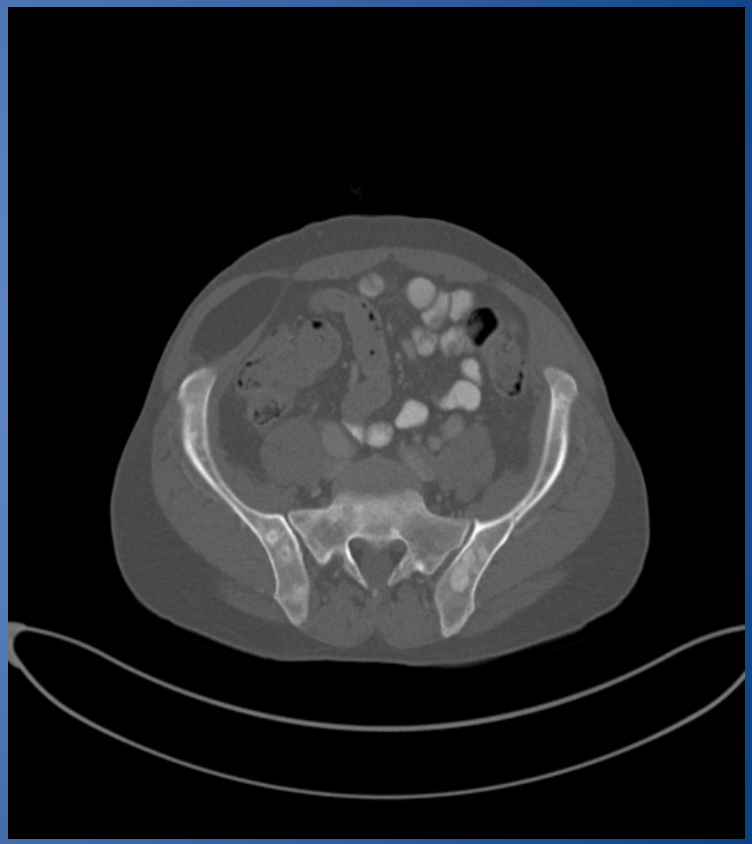

NOPR Update

Decision Summary

A. The Centers for Medicare & Medicaid Services (CMS) has determined that the evidence is sufficient to determine that use of a NaF-18 positron emission tomography (PET) scan to identify bone metastasis of cancer is not reasonable and necessary to diagnose or treat an illness or injury or to improve the functioning of a malformed body member and, therefore, is not covered under § 1862(a)(1)(A) of the Social Security Act.

B. CMS shall continue the requirement for coverage with evidence development (CED) under §1862(a)(1)(E) of the Social Security Act for NaF-18 PET to identify bone metastasis of cancer contained in section 220.6.19B of the Medicare National Coverage Determinations Manual for 24 months from the final date of this decision. This extension is to allow confirmatory analyses to be performed and resulting evidence to be published to definitely answer the following question:

Does the addition of NaF-18 PET imaging lead to:

- A change in patient management to more appropriate palliative care; or
- A change in patient management to more appropriate curative care; or
- Improved quality of life; or
- Improved survival?

All other uses and clinical indications for NaF-18 PET are nationally non-covered.

CMS will reconsider the NCD at such time when the evidence has been published in a peer-reviewed journal.

2nd Generation

- C-11 Choline
- F-ACBC
- Detects disease in bone and soft tissues

FACBC vs. Choline

- Prospective study with 50 patients
- C-11 Choline and FACBC PET/CT within 1 week

TABLE 2. Patient-Based Analysis

50 Patients	^{11}C-Choline (−)	^{11}C-Choline (+)
Fluciclovine (−)	33	0
Fluciclovine (+)	6	11

$P < 0.000001$

TABLE 3. Lesion-Based Analysis

	No. Positive Lesions	
17 Fluciclovine-Positive Patients	^{11}C-Choline (+)	Fluciclovine (+)
6	1	1
1	3	3
1	9	9
2	1	2
1	3	4
3	0	1
2	0	2
1	0	4

$P < 0.0001$

Nanni, et al. Clinical Nuclear Medicine. Aug 2015.

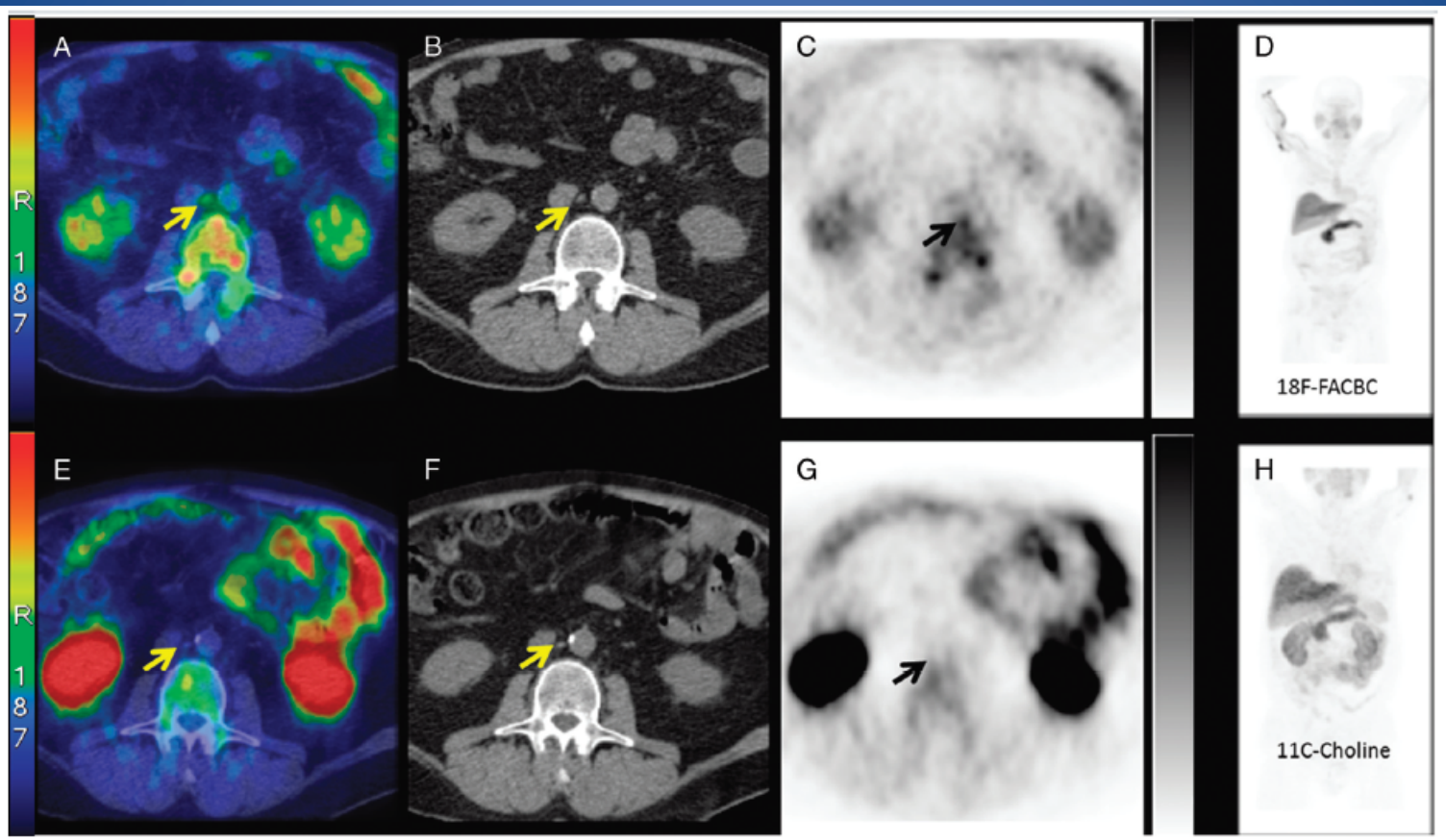

FIGURE 1. ^{18}F-fluciclovine axial cut (A, fusion; B, CT; C, PET; D, MIP) showing increased uptake in 1 small positive interaortocaval lymph node (arrow). Corresponding ^{11}C-choline axial cut (E, fusion; F, CT; G, PET; H, MIP) resulted completely negative.

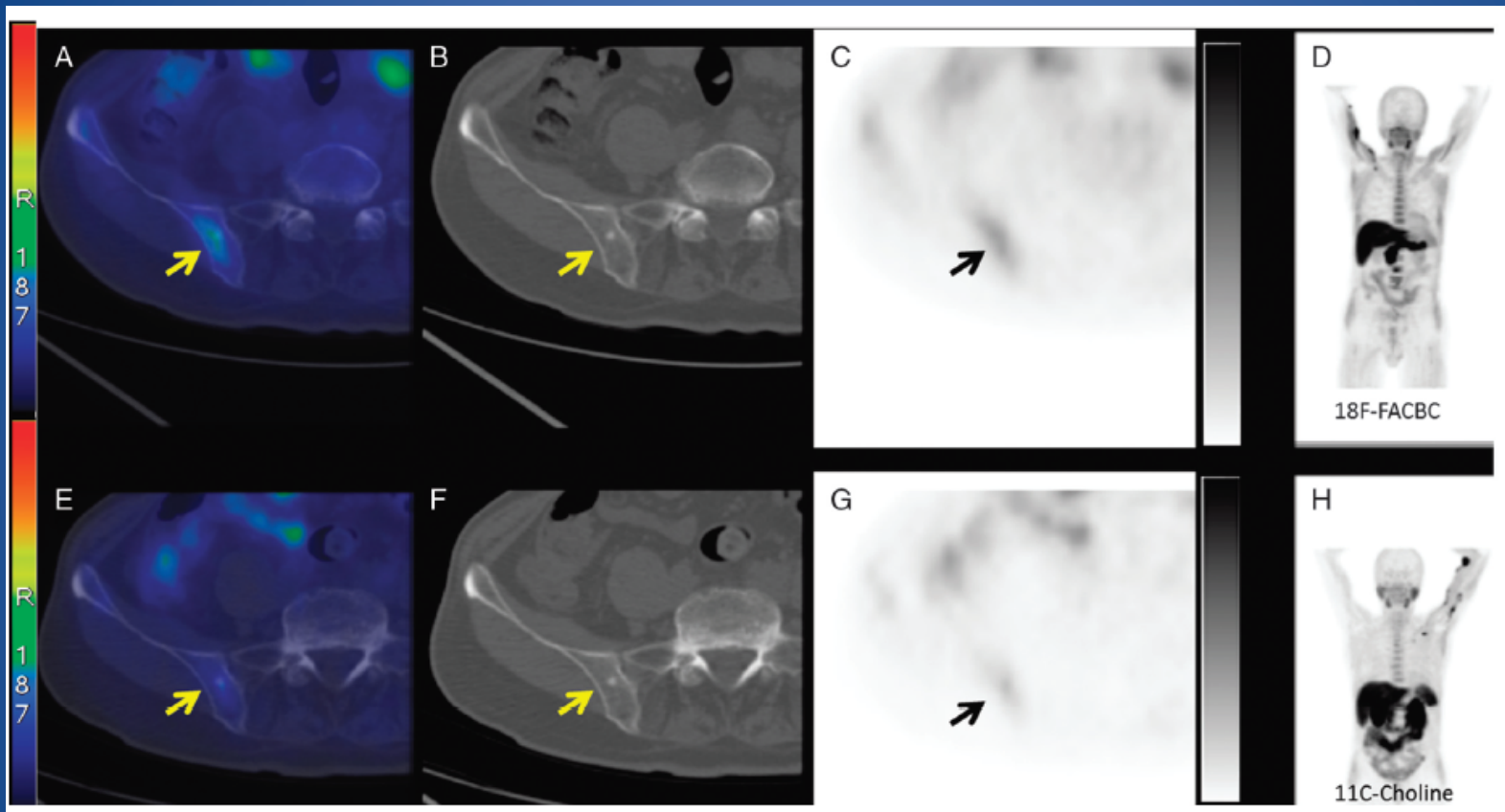

FIGURE 3. ^{18}F-fluciclovine axial cut (A, fusion; B, CT; C, PET; D, MIP) showing increased uptake in the right sacroiliac area, consistent with bone relapse (arrow). Corresponding ^{11}C-choline axial cut (E, fusion; F, CT; G, PET; H, MIP) demonstrated a very mild uptake, still consistent with normal bone marrow uptake.

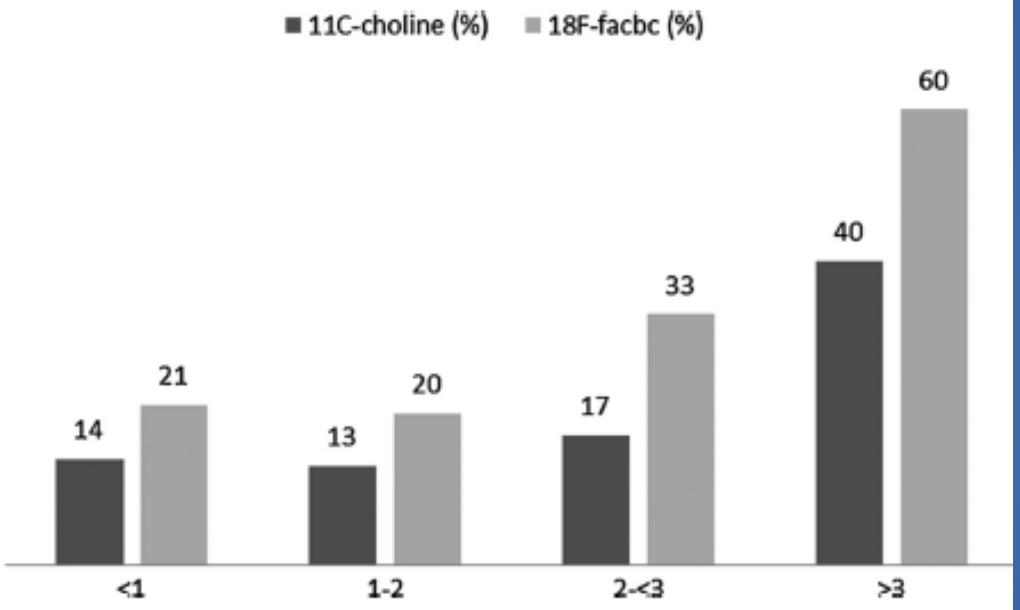

FIGURE 6. Detection rate (percent) of ^{18}F-fluciclovine and ^{11}C-choline in relation to different groups of PSA levels (nanogram/milliliter).

F-ACBC

- Blue Earth Diagnostics
- Manufactured and distributed in US by PETNET

FDA accepts Blue Earth's PET agent application
By AuntMinnie.com staff writers

December 2, 2015 -- Blue Earth Diagnostics announced that its new drug application (NDA) filing for the PET agent fluciclovine has been accepted by the U.S. Food and Drug Administration (FDA) for priority review.

The firm is seeking U.S. marketing approval of fluciclovine (F-18) for lesion detection and localization for prostate cancer patients experiencing biochemical recurrence. Fluciclovine is a synthetic amino acid investigational PET radiopharmaceutical being studied by Blue Earth in the imaging of various cancers, with its lead product being in prostate cancer. The NDA submission for fluciclovine is based on data from more than 700 prostate cancer patients, most with biochemical recurrence and some with high-risk primary disease, imaged in the U.S., Norway, and Italy.

If approved, Siemens Healthcare subsidiary PETNet Solutions will manufacture, distribute, and sell the radiopharmaceutical in the U.S.

3rd Generation

- PSMA
  - Ga-68 PSMA
    - PSA >=2: 97%
    - PSA <0.5: 58%
  - F-DCFBC
    - Not as sensitive compared to MRI
    - Higher specificity for high grade and larger tumors compared to MRI
    - PET/MRI
- Theranostics

Rowe, et al. J Nucl Med. July 2015.

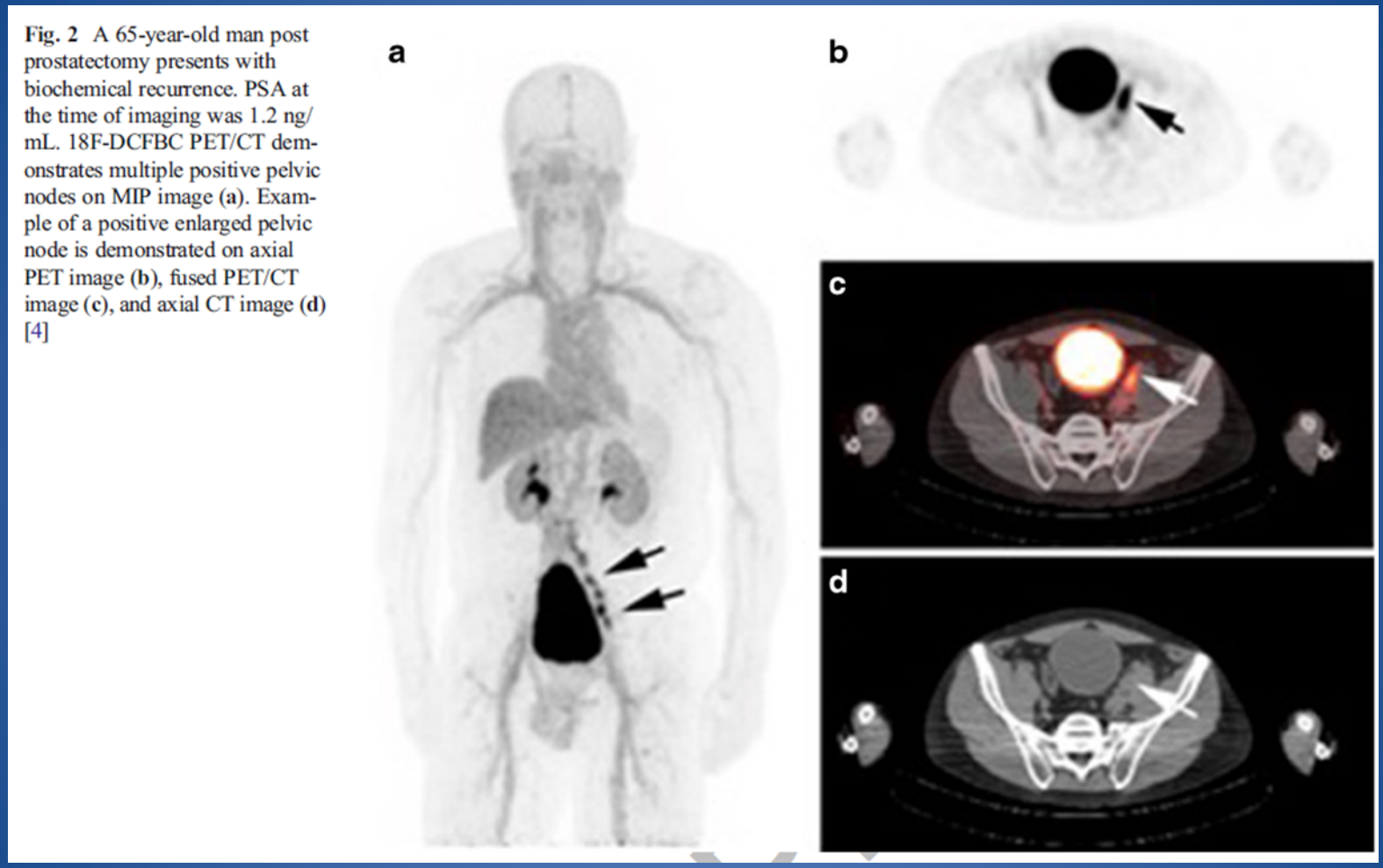

Fig. 2 A 65-year-old man post prostatectomy presents with biochemical recurrence. PSA at the time of imaging was 1.2 ng/mL. 18F-DCFBC PET/CT demonstrates multiple positive pelvic nodes on MIP image (**a**). Example of a positive enlarged pelvic node is demonstrated on axial PET image (**b**), fused PET/CT image (**c**), and axial CT image (**d**) [4]

Koo, et al. Curr Onc Reports. Dec 2015

RADAR Group Recommendations

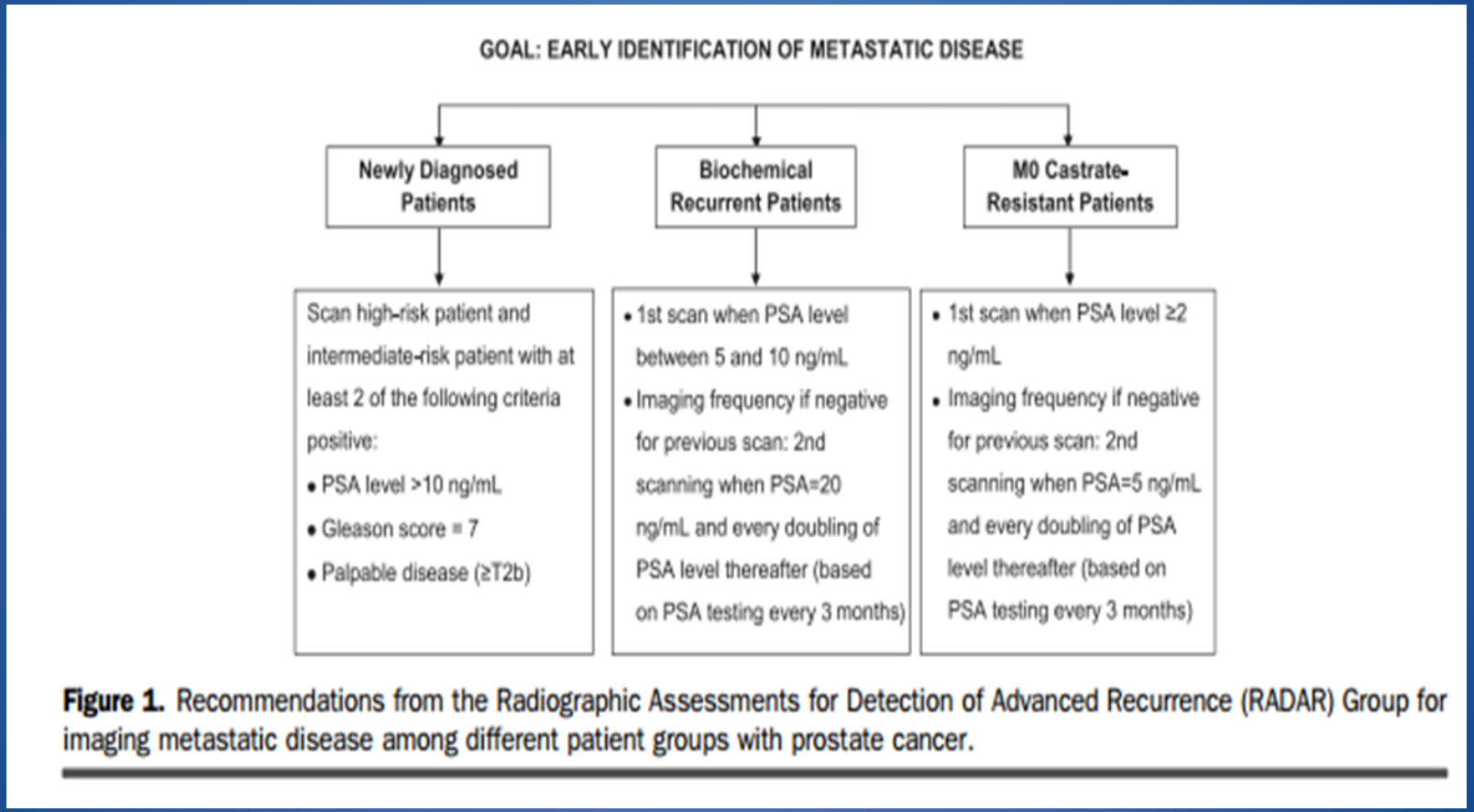

Figure 1. Recommendations from the Radiographic Assessments for Detection of Advanced Recurrence (RADAR) Group for imaging metastatic disease among different patient groups with prostate cancer.

Crawford, et al. Urology. March 2014.

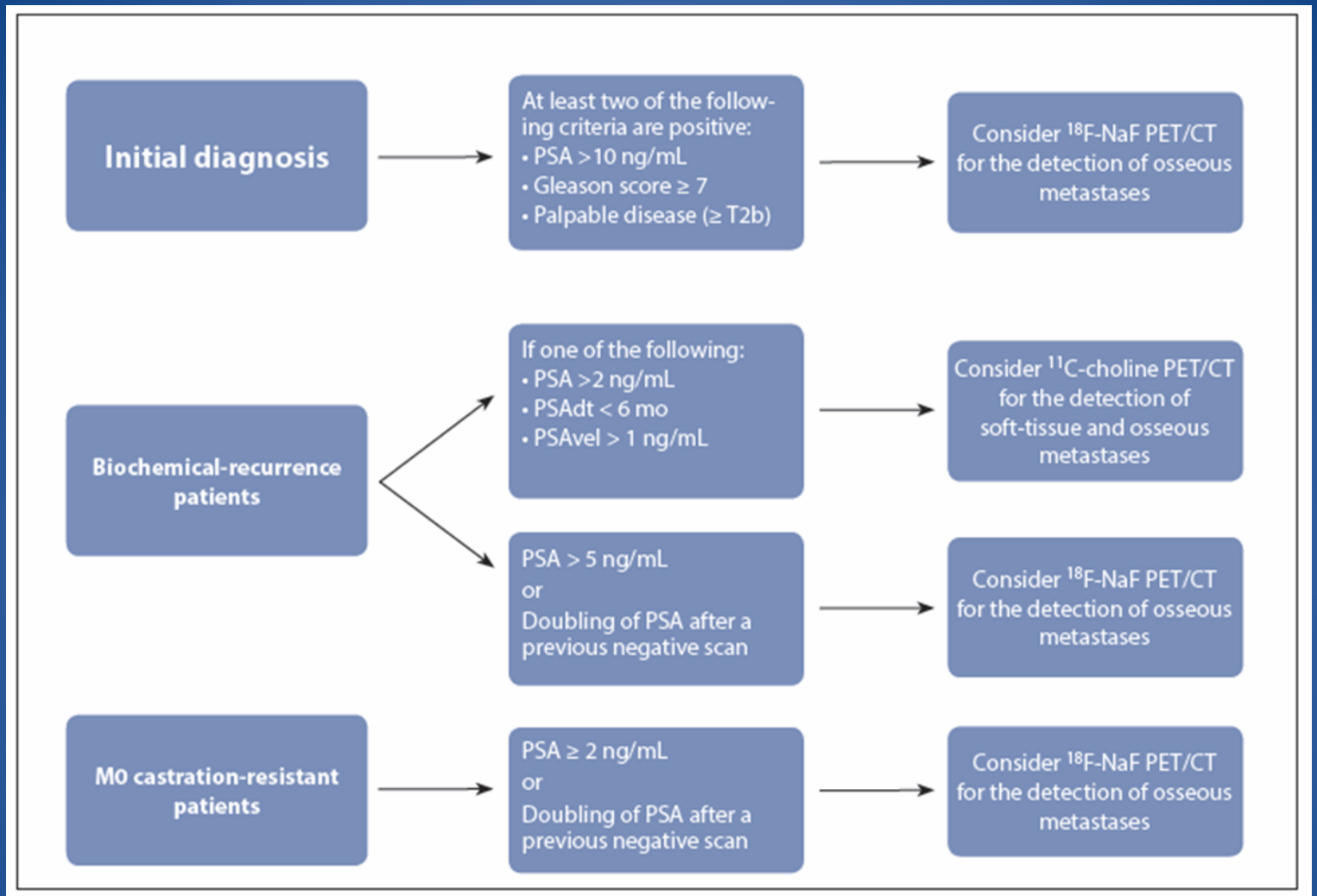

Figure 2: Potential Utilization Strategies for ^{18}F-NaF PET/CT and ^{11}C-choline PET/CT to Detect Advanced Disease in Different Patient Groups with Prostate Cancer—dt = doubling time; PSA = prostate-specific antigen; vel = velocity.

Koo, Crawford. Oncology (Williston Park).
Dec 2014.

Thank you!

When should a M0 CRPC patient initially be imaged?

1. Never
2. Annually
3. Symptomatic
4. PSA >= 2

Which of the following is most sensitive for the detection of metastatic disease?

1. Tc-99m bone scan
2. NaF PET/CT
3. C-11 Choline PET/CT
4. F-ACBC PET/CT