NCCN Treatment Recommendations

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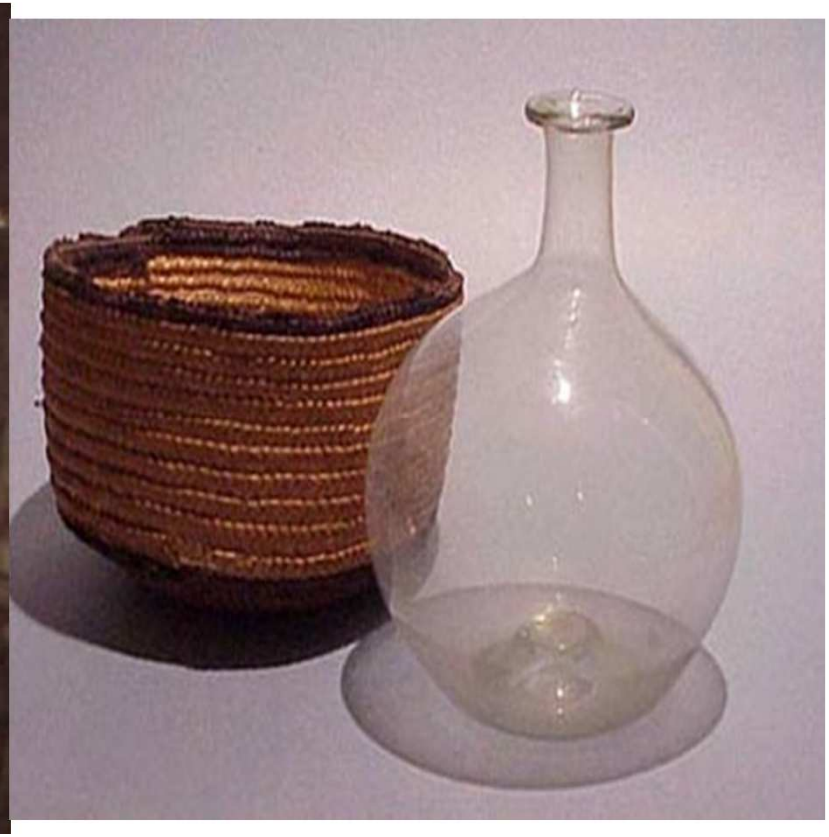
The Village Doctor

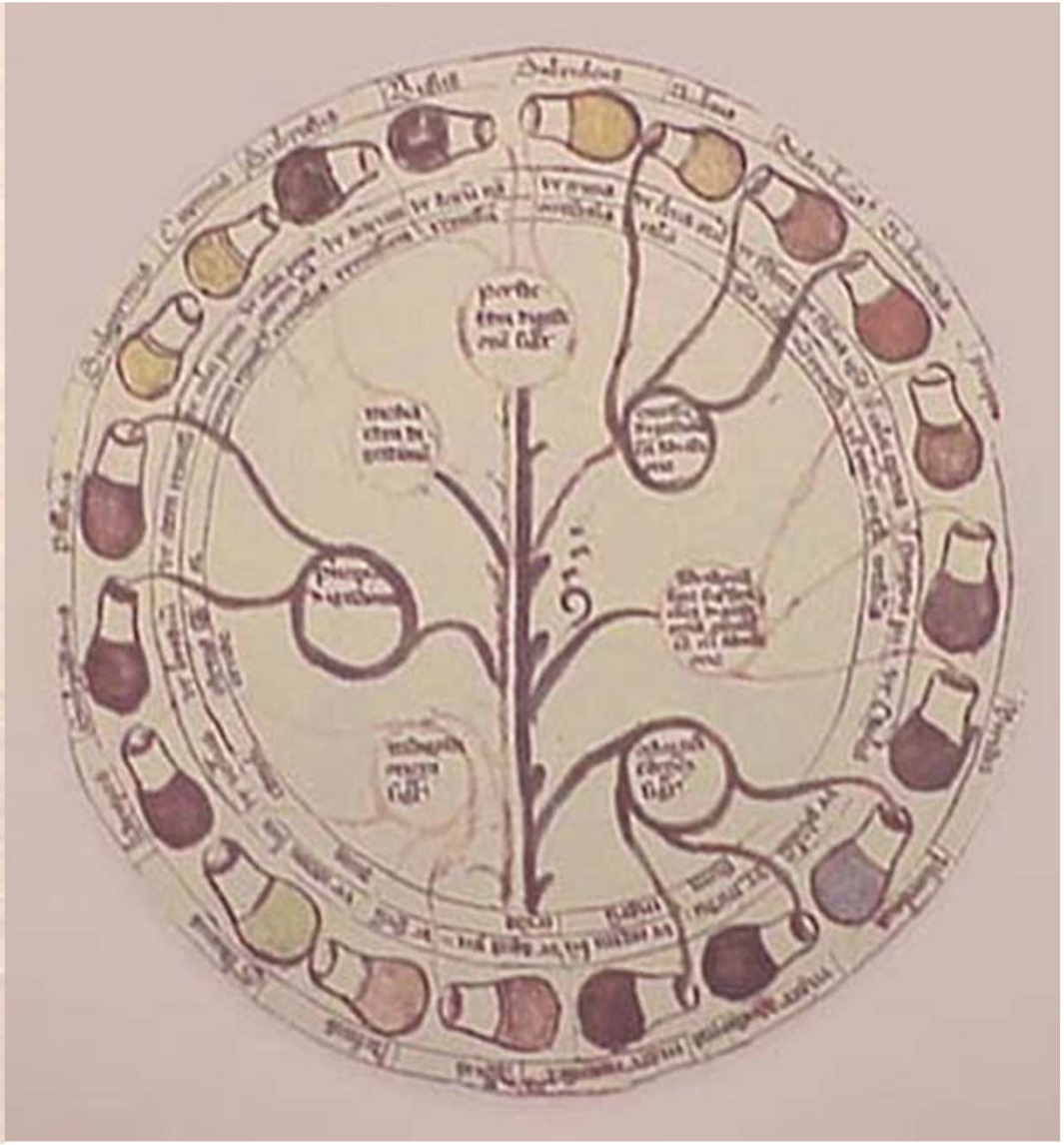
Uroscopy was the practice of diagnosing disease by examination of the urine

A painting illustrating the practice of uroscopy in the 17th century by David Teniers the Younger



Uroscopy Flask : free blown glass, pontiled with a woven basket, probably from the 17-18th century

Hold to light, angle. Color, consistency, smell, and sometimes taste to make a diagnosis



A diagram that linked the color of urine to a particular disease
The Fasciculus Medicinae by Johannes De Ketham, 1491

- In 1995, the National Comprehensive Cancer Network (NCCN) began a program to develop comprehensive guidelines (NCCN, 1996; 1997; 1998).
- These Guidelines encompass 97% of the tumors encountered.
- Each Guideline consists of an algorithm or decision pathway outlining care management, a manuscript discussing important issues related to the algorithm, and references providing data on which recommendations are based

- The NCCN Guidelines are developed and updated by 44 panels, comprising nearly 800 clinicians / researchers from 21 NCCN Member Institutions .
- The Guidelines are composed of recommendations based on the best evidence available at the time they are derived, but it is essential that they be continuously updated and revised.
- The aim of these guidelines is to assist oncologists in making the major clinical decisions encountered in managing their patients

- NCCN Clinical Practice Guidelines in Oncology™ are defined as “systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances” (Field and Lohr, 1990).
- The determination of what is appropriate care involves assessing the balance between the sum of the benefits compared with the sum of the risks (Park et al, 1986).
- The third important component of the definition of clinical practice guidelines is that they must be systematically developed.

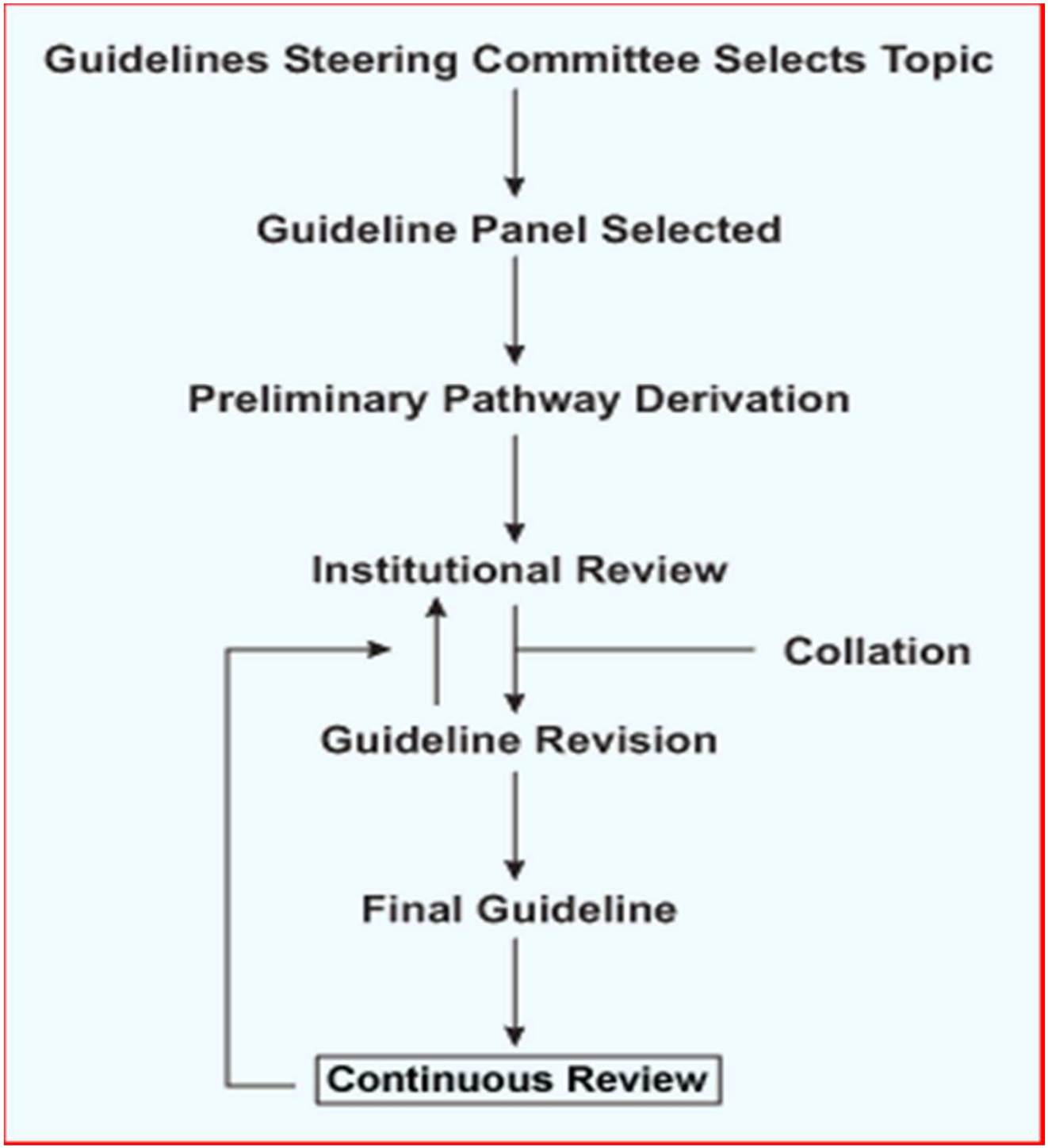
Critically Appraising Clinical Guidelines

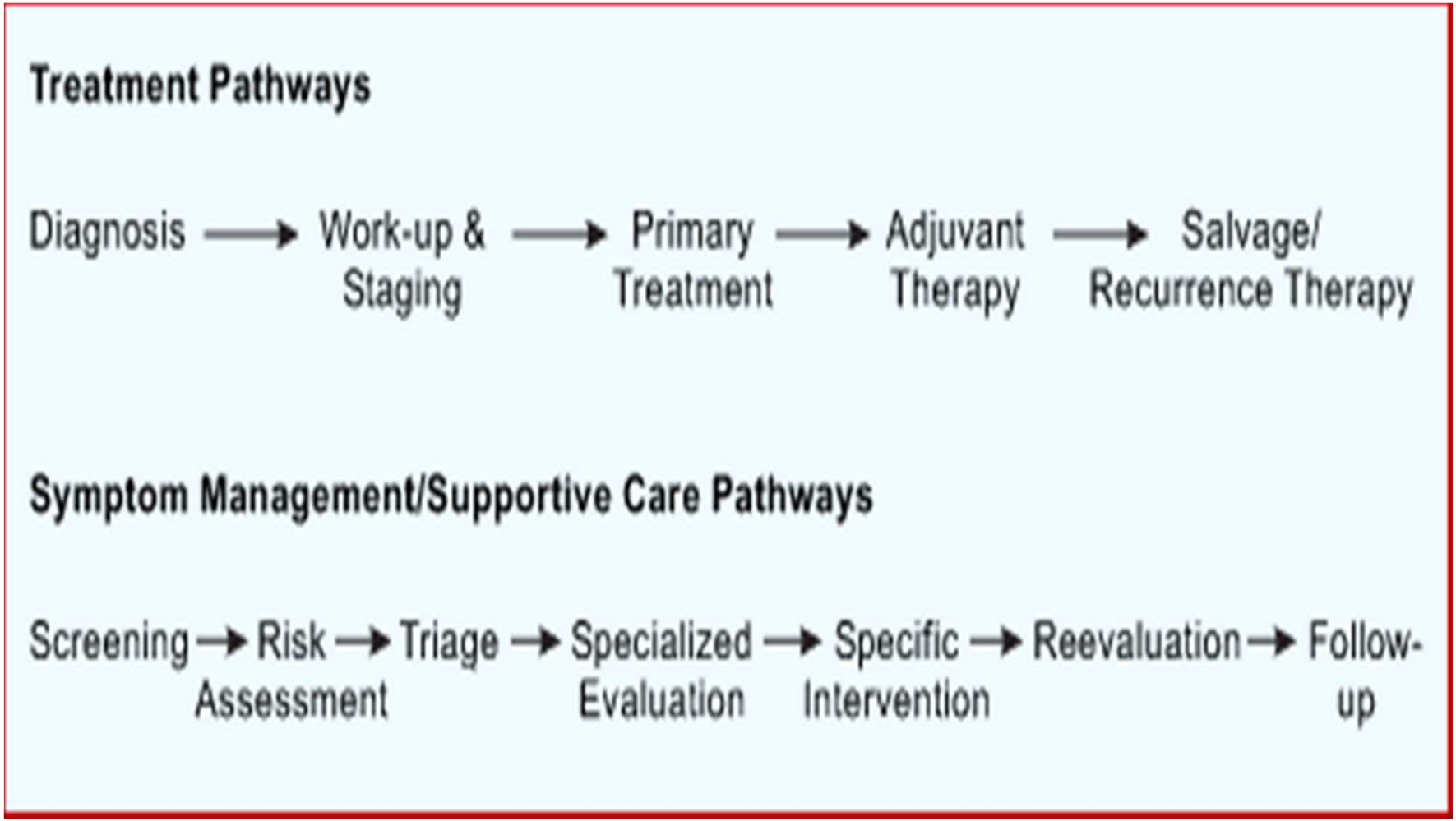
- What is the composition of the panel who developed the guideline?
- What entity provided financial sponsorship?
- What decision making process was used in developing the guideline?
- What clinical question was the guideline developed to address?
- How was the evidence used in the guideline gathered and evaluated?
- Were gaps in the evidence explicitly identified?

- How explicitly is the evidence linked to the recommendations in the guideline?
- If lower levels of evidence are incorporated how explicitly is this labeled, and are the reasons for the inclusion of expert opinion, the line of reasoning and the strength of extrapolation from other data clearly identified?
- How are patient preferences incorporated into the guideline?
- Is cost-effectiveness considered?
- What is the mechanism and interval for updating of the guideline?

Members who were part of the formulating team

- Radiotherapy/ radiation oncology
- Urology
- Medical Oncology
- Supportive care, including palliative, Pain Management, pastoral care & oncology social work
- Patient Advocacy
- Writing Committee member


Guidelines Steering Committee Selects Topic
Guideline Panel Selected
Preliminary Pathway Derivation
Institutional Review
Collation
Guideline Revision
Final Guideline
Continuous Review


Treatment Pathways
Diagnosis
Work-up & Staging
Primary Treatment
Adjuvant Therapy
Salvage/ Recurrence Therapy
Symptom Management/Supportive Care Pathways
Screening
Risk Assessment
Triage
Specialized Evaluation
Specific Intervention
Reevaluation
Follow-up

Category of Evidence and Consensus	Quality of Evidence	Level of Consensus
1	High	Uniform
2A	Lower	Uniform
2B	Lower	Non-uniform
3	Any	Major disagreement

DRE
PSA
Gleason Score

Initial Clinical Assessment

- Life Expectancy ≤ / > 5 years
- Symptomatic / Asymptomatic

Staging Work-Up

TNM Staging 2002

Risk Stratification

Low
Intermediate
High
Locally advanced
Metastatic

Life Expectancy

- http://www.ssa.gov/OACT/STATS/table4c6.html

40-41	0.002438	95,527	233	95,410	3,595,027	37.6
41-42	0.002632	95,294	251	95,168	3,499,617	36.7
42-43	0.002853	95,043	271	94,907	3,404,448	35.8
43-44	0.003113	94,772	295	94,624	3,309,541	34.9
44-45	0.003412	94,477	322	94,316	3,214,917	34.0
45-46	0.003735	94,154	352	93,979	3,120,601	33.1
46-47	0.004071	93,803	382	93,612	3,026,622	32.3
47-48	0.004428	93,421	414	93,214	2,933,010	31.4
48-49	0.004806	93,007	447	92,784	2,839,796	30.5
49-50	0.005206	92,560	482	92,319	2,747,012	29.7
50-51	0.005648	92,078	520	91,818	2,654,693	28.8
51-52	0.006121	91,558	560	91,278	2,562,875	28.0
52-53	0.006594	90,998	600	90,698	2,471,597	27.2
53-54	0.007045	90,398	637	90,079	2,380,899	26.3
54-55	0.007488	89,761	672	89,425	2,290,819	25.5
55-56	0.007946	89,089	708	88,735	2,201,394	24.7
56-57	0.008459	88,381	748	88,007	2,112,659	23.9
57-58	0.009064	87,633	794	87,236	2,024,652	23.1
58-59	0.009810	86,839	852	86,413	1,937,416	22.3
59-60	0.010706	85,987	921	85,527	1,851,002	21.5
60-61	0.011763	85,067	1,001	84,566	1,765,476	20.8
61-62	0.012934	84,066	1,087	83,522	1,680,909	20.0
62-63	0.014159	82,979	1,175	82,391	1,597,387	19.3
63-64	0.015362	81,804	1,257	81,175	1,514,996	18.5
64-65	0.016558	80,547	1,334	79,880	1,433,820	17.8
65-66	0.017847	79,213	1,414	78,507	1,353,940	17.1
66-67	0.019331	77,800	1,504	77,048	1,275,433	16.4
67-68	0.020992	76,296	1,602	75,495	1,198,386	15.7

70-71	0.027065	71,168	1,926	70,205	976,973	13.7
71-72	0.029363	69,242	2,033	68,225	906,768	13.1
72-73	0.032031	67,209	2,153	66,132	838,543	12.5
73-74	0.035178	65,056	2,289	63,912	772,411	11.9
74-75	0.038734	62,767	2,431	61,552	708,499	11.3
75-76	0.042414	60,336	2,559	59,057	646,947	10.7
76-77	0.046171	57,777	2,668	56,443	587,891	10.2
77-78	0.050325	55,109	2,773	53,723	531,448	9.6
78-79	0.055085	52,336	2,883	50,894	477,725	9.1
79-80	0.060498	49,453	2,992	47,957	426,831	8.6
80-81	0.066557	46,461	3,092	44,915	378,873	8.2
81-82	0.072986	43,369	3,165	41,786	333,958	7.7
82-83	0.079682	40,204	3,204	38,602	292,172	7.3
83-84	0.086593	37,000	3,204	35,398	253,570	6.9
84-85	0.094013	33,796	3,177	32,207	218,172	6.5
85-86	0.102498	30,619	3,138	29,050	185,965	6.1
86-87	0.111640	27,481	3,068	25,947	156,915	5.7
87-88	0.121472	24,413	2,965	22,930	130,968	5.4
88-89	0.132023	21,447	2,832	20,031	108,039	5.0
89-90	0.143319	18,616	2,668	17,282	88,007	4.7
90-91	0.155383	15,948	2,478	14,709	70,726	4.4
91-92	0.168232	13,470	2,266	12,337	56,017	4.2
92-93	0.181880	11,204	2,038	10,185	43,680	3.9
93-94	0.196334	9,166	1,800	8,266	33,496	3.7
94-95	0.211592	7,366	1,559	6,587	25,229	3.4
95-96	0.227645	5,808	1,322	5,147	18,642	3.2
96-97	0.244476	4,486	1,097	3,937	13,496	3.0
97-98	0.262057	3,389	888	2,945	9,559	2.8

Evaluation of the (primary) tumor ('T')

- **TX**: cannot evaluate the primary tumor
- **T0**: no evidence of tumor
- **T1**: tumor present, but not detectable clinically or with imaging
  - **T1a**: tumor was incidentally found in less than 5% of prostate tissue resected (for other reasons)
  - **T1b**: tumor was incidentally found in greater than 5% of prostate tissue resected
  - **T1c**: tumor was found in a needle biopsy performed due to an elevated serum PSA
- **T2**: the tumor can be felt (palpated) on examination, but has not spread outside the prostate
  - **T2a**: the tumor is in half or less than half of one of the prostate gland's two lobes
  - **T2b**: the tumor is in more than half of one lobe, but not both
  - **T2c**: the tumor is in both lobes
- **T3**: the tumor has spread through the prostatic capsule (if it is only part-way through, it is still **T2**)
  - **T3a**: the tumor has spread through the capsule on one or both sides
  - **T3b**: the tumor has invaded one or both seminal vesicles
- **T4**: the tumor has invaded other nearby structures
- It should be stressed that the designation "T2c" implies a tumor which is *palpable* in both lobes of the prostate. Tumors which are found to be bilateral on biopsy only but which are not palpable bilaterally should not be staged as T2c.

Evaluation of the regional lymph nodes ('N')

- **NX**: cannot evaluate the regional lymph nodes
- **N0**: there has been no spread to the regional lymph nodes
- **N1**: there has been spread to the regional lymph nodes

Evaluation of distant metastasis ('M')

- **MX**: cannot evaluate distant metastasis
- **M0**: there is no distant metastasis
- **M1**: there is distant metastasis

Risk Strata

Risk stratification schemes have been developed based on:

PSA level,

Biopsy Gleason score, and

2002 AJCC clinical T-category

that are associated with the risk of PSA failure and prostate cancer-specific mortality following radical prostatectomy, external beam radiotherapy, or interstitial prostate brachytherapy.

Risk Strata

Low risk: PSA ≤10 ng/mL and a Gleason score of 6 or less and clinical stage T1c or T2a

Intermediate risk: PSA >10 to 20 ng/mL or a Gleason score of 7 or clinical stage T2b but not qualifying for high risk

High risk: PSA >20 ng/mL or a Gleason score of 8 to 10 or clinical stage T2c

Treatment Options

- ***Watchful Waiting and Active Surveillance***
- ***Interstitial Prostate Brachytherapy***
- ***External Beam Radiotherapy***
- ***Radical Prostatectomy***
- ***Primary Hormonal Therapy***
- ***Other Treatments***

Watchful Waiting

- Based on the premise that some patients will not benefit from definitive treatment .
- Decision made at the outset
  - to forgo definitive treatment *and*
  - provide palliative treatment for local or metastatic progression if and when it occurs.
- Options for palliation include
  - TURP /other procedures for management of urinary tract obstruction,
  - hormonal therapy or
  - radiotherapy for palliation of metastatic lesions.

Active Surveillance

- Based on the premise that some patients may benefit from definitive treatment :
  - provide definitive treatment for localized cancers that are likely to progress and
  - to reduce the risk of treatment-related complications for men with cancers that are not likely to progress.
- An ideal regimen for active surveillance has not been defined
  - could include periodic physical examination and PSA testing or
  - periodic repeat prostate biopsies to assess for sampling error of the initial biopsy as well as for subsequent progression of tumor grade and/or volume.

Wait & Watch :Pros And Cons

- Avoiding side effects
- QOL
- Indolent tumors
- Decreased costs

- Missed opportunity for cure
- May progress / metastasize
- Treatment later is more radical
- Nerve sparing is difficult
- Anxiety of living with disease
- Frequent checks
- Uncertain history
- No guidelines for surveillance

Interstitial Prostate Brachytherapy

- Permanent interstitial prostate brachytherapy as a treatment has been performed since the 1960s.
- Patients with clinically localized prostate cancer are considered candidates for interstitial prostate brachytherapy,
- Some practitioners will use this treatment option for low-risk disease only while others will treat both low and intermediate-risk patients.

External Beam Radiotherapy

- In use since the 1930s ;
- 1960s : linear accelerators allowed delivery high RT doses
- 1980s : CT based treatment planning improved the accuracy of treatment delivery, permitting more precise targeting of the prostate, seminal vesicles, and lymph nodes & better identification of adjacent dose limiting structures
- 1980s & 1990s : 3-D planning allowed for dose escalation & doses were increased safely from 65 Gy to 75 to 79 Gy.
- 1990s : the advent of IMRT and IGRT (either with transabdominal ultrasound or the intraprostatic placement of fiducial markers) further refined treatment delivery.

Radical Prostatectomy

- Radical prostatectomy involves removal of the entire prostate gland/ attached seminal vesicles plus the ampulla of the vas deferens . May be performed using a retropubic or perineal incision either laparoscopic ally or robotic assisted technique.
- Pelvic lymphadenectomy can be performed concurrently with radical prostatectomy and is generally reserved for patients with higher risk of nodal involvement
- Where the prostate cancer is of a high grade / when the tumor has spread outside of the prostate gland / when the tumor is not completely excised - adjuvant treatment

Primary Hormonal Therapy

- Primary androgen deprivation therapy (ADT) may be employed with the goal of providing symptomatic control of prostate cancer for patients in whom definitive treatment with surgery or radiation is not possible or acceptable.
- The concept of ADT should be distinguished from the use of neoadjuvant or adjuvant hormonal therapy.
- Because of the paucity of any data, primary ADT has not been considered a “standard” treatment option for localized disease.

Other Treatments

- These treatments include cryotherapy, high-intensity focused ultrasound, high-dose interstitial prostate brachytherapy, and combinations of treatments (e.g., external beam radiotherapy and interstitial prostate brachytherapy).

European Association of Urology

Stage	Treatment	Comment
T1a	Watchful waiting	Std Rx for Well/mod diff tumors & life expectancy<10yrs
	Radical Prostatectomy	Option in young pts with a . 10yrs life expectancy & poorly diff tumors
	RT	Option in young pts with a . 10yrs life expectancy & poorly diff tumors
	Hormones / Combination	Not an option
T1b– 2b	Watchful waiting	Asymptomatic pts with Well/mod diff tumors & life expectancy<10yrs;don't accept side effects
	Radical Prostatectomy	Pts with a > 10yrs life expectancy & accept Rx related side effects
	RT	Pts with a> 10yrs life expectancy, prefer RT & accept Rx related side effects Contraindications for surgery
	Hormones	Symptomatic – unfit for curative treatment
	Combination	NAHT + RP – no better NAHT + RT – better LC;no survival advantage

T3-T4	Watchful waiting	Asymptomatic pts with T3 Well/mod diff tumors & life expectancy<10yrs;
	Radical Prostatectomy	'Small'T3, PSA<20,. GS <8, LE >10yrs
	RT	T3(N0) > 5-10yrs LE; Dose > 70gy beneficial
	Hormones	Symptomatic, extensive T3-T4, PSA >25 ,unfit pts
	Combination	RT+HT – better than RT alone NAHT + RP – no benefit
N+ M0	Watchful waiting	Asymptomatic pts ; Pt driven
	Radical Prostatectomy	No standard option
	RT	No standard option
	Hormones	Standard therapy
	Combination	No standard option ; Pt driven

M0	Watchful waiting	No standard option
	Radical Prostatectomy	Not an option
	RT	Not an option
	Hormones	Standard therapy
	Combination	Not an option

Nomograms

- Nomograms are instruments that predict outcomes for the individual patient.
- Using algorithms that incorporate multiple variables, nomograms calculate the predicted probability that a patient will reach a clinical end point of interest.
- Nomograms tend to outperform both expert clinicians and predictive instruments based on risk grouping

The Kattan Nomograms

- *the probability of being progression-free* (after initial diagnosis)
- *predict probability of survival* for up to 10 years (post-prostatectomy)
- *predict the likelihood of success for salvage radiation therapy* at 6 years (post-prostatectomy).
- *predict 1- and 2-year survival (in Hormone refractory pts)*.

- The first evolution of these nomograms was published by Kattan, Wheeler & Scardino in 1999.
- By April 2008 Eastman, Scardino & Kattan had published what they are referring to as the “Trifecta” nomogram: a tool that may soon allow surgeons to predict the probability of freedom from cancer, recovery of continence, and recovery of sexual function for individual patients.
- This last nomogram is not yet integrated into the on-line nomograms, but we can probably look for it in the not too distant future.

NCCN :

- http://www.nccn.org/professionals/physician_gls/PDF/prostate.pdf

European Association of Urology

- http://www.urotoday.com/prod/pdf/eau/prostatecancer.pdf
- http://www.uroweb.org/fileadmin/user_upload/Guidelines/07_Prostate_Cancer_2007.pdf

American Urological Association

- http://www.auanet.org/guidelines/main_reports/proscan07/content.pdf

American Cancer Society Guidelines for the Early Detection of Cancer

- http://www.cancer.org/docroot/ped/content/ped_2_3x_acs_cancer_detection_guidelines_36.asp

Evidence-based Information and Recommendations for the Management of Localised Prostate Cancer - Australian Cancer network

- http://www.nhmrc.gov.au/publications/synopses/cp88syn.htm

UK – National Collaborative Centre for Cancer (NCC-C)

- http://www.nice.org.uk/nicemedia/pdf/CG58FullGuideline.pdf
- http://www.rcr.ac.uk/docs/oncology/other/prostate.htm

UK treatment guidelines - Prostate cancer

Advice on the development of low dose rate (permanent seed implant) brachytherapy services for localised prostate cancer in England - November 2006

- Guidance on Laparoscopic radical prostatectomy - NICE November 2006
- Docetaxel for the treatment of hormone-refractory metastatic prostate cancer - NICE June 2006
- High dose rate brachytherapy for prostate cancer - NICE May 2006
- Cryotherapy as a primary treatment for prostate cancer - NICE November 2005
- Low dose rate brachytherapy for localised prostate cancer: Guidance - July 2005
- Cryotherapy for recurrent prostate cancer: Guidance - May 2005
- High-intensity focused ultrasound for prostate cancer: Guidance - March 2005
- Guidance on Cancer Services: Improving Outcomes in Urological Cancers, The Manual - NICE 2002

- PROSTATE CANCER treatment decisions are complicated by the biologic heterogeneity of the disease
- For many patients with potentially curable prostate cancer, the benefits of treatment must be weighed against the risks of therapy and competing causes of mortality
- Patient Preference is of Paramount interest – almost as important as the physician's bias

- Thank you for allowing me to share my view point!