Survivorship – a good problem?

John Kuruvilla

University of Toronto

Princess Margaret Hospital
University Health Network

Objectives - Survivorship

- Issues to discuss
  - Recurrence of disease – what to watch for
  - Late effects – complications of treatment
  - Vaccinations – what to do?

Recurrence

- Monitoring
  - No regular imaging
  - Bloodwork typically not helpful
    - Generally there is no blood test to diagnose recurrence of lymphoma
  - Relapse often identified in the clinic (or by you)

What to watch for...

- What symptoms did the lymphoma cause originally?
- Lumps and bumps
- Pain (or other symptoms) that are uncommon and unexplained for you (and that don’t resolve)
- Persisting unexplained fever, drenching night sweats and/or weight loss (10% of body weight)

Recurrence

- Varies with the disease and time from prior therapy
- May be curable
- May have very good outcome
- Very difficult to generalize

Late Effects

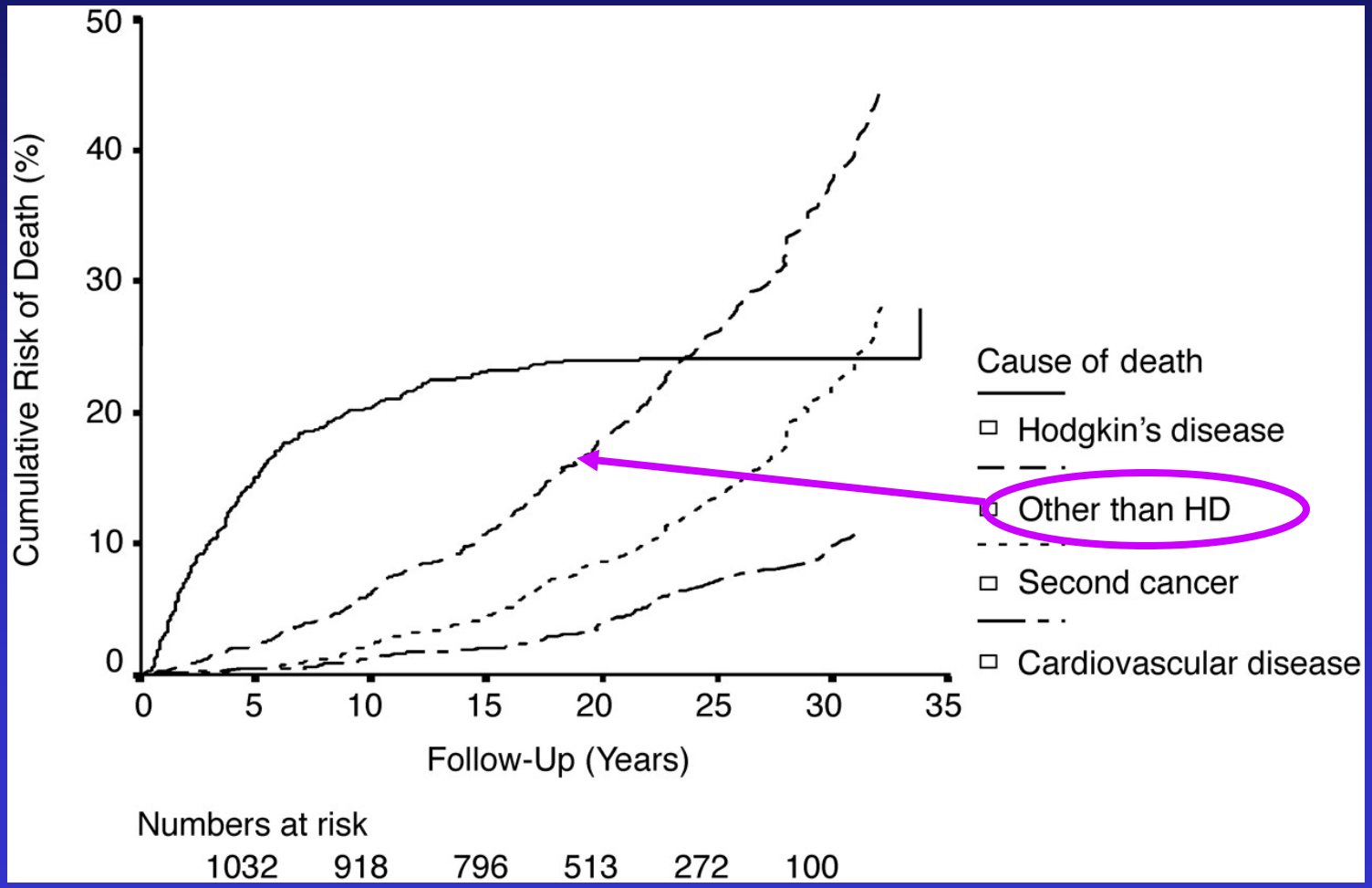
- Typically considered to be consequences of treatment seen in people that are cured
  - Beyond 3-5 years after completion
- Second cancers
- Cardiac disease
- Fertility

Late effects – Second Cancers

- Why?
  - Chemo and Radiation damage DNA in normal cells
  - These may be become malignant
  - What about common cancers people are at risk for?
    - Difficult to know if these are related – but by definition we believe that they are

Long-Term Cause-Specific Mortality of Patients Treated for Hodgkin's Disease

J Clin Oncol 2003



Second Cancers Briefly

- leading cause of death for HL survivors
- majority are solid tumors/carcinomas
  - minimum latency 5-10 yrs
- related to treatment exposure (dose), age
- cancer risk reduction, screening, prevention must be explored

Second Cancers – Relative Risks

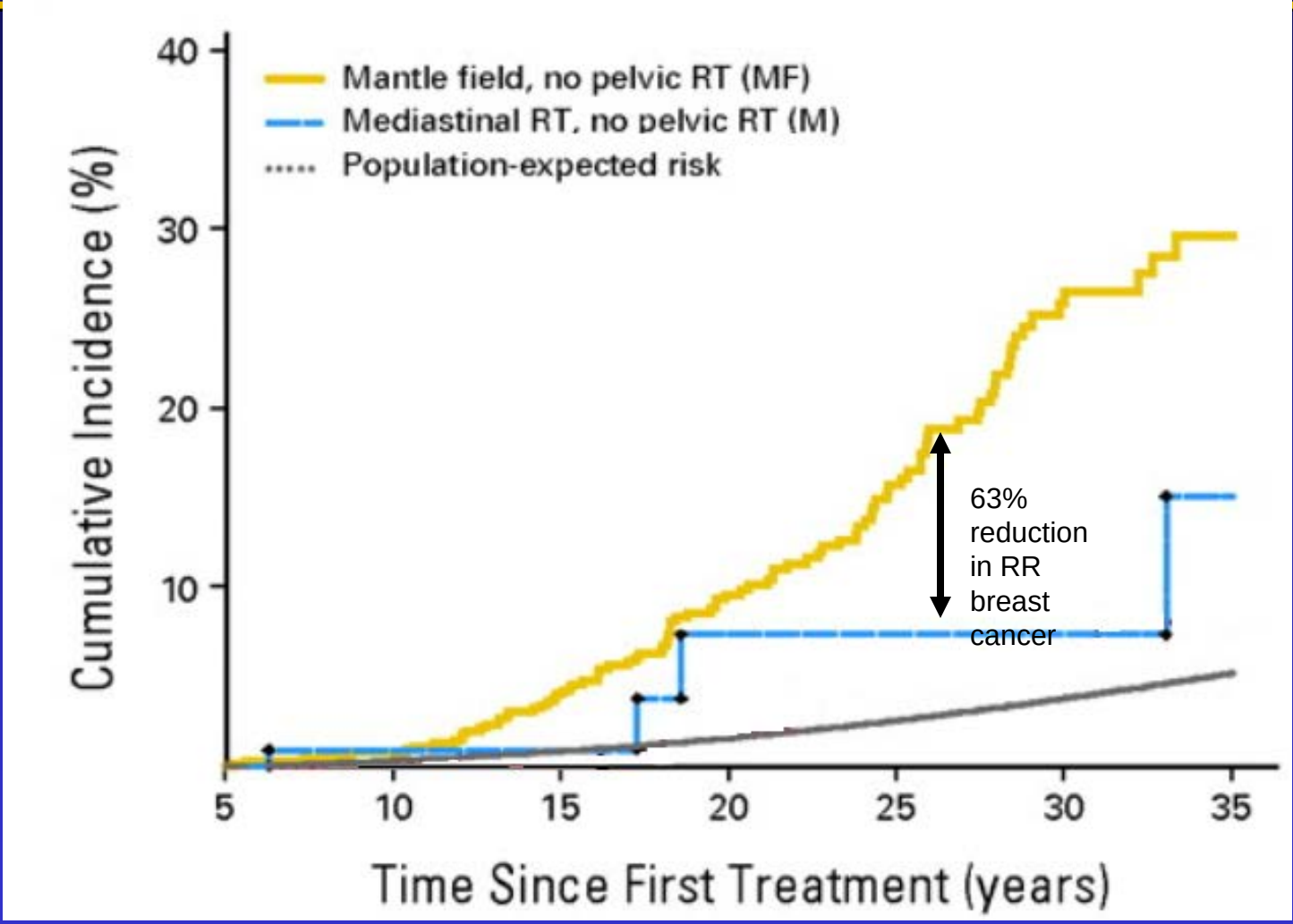
32,591 HL survivors

female breast	2.0	(1.8-2.3)
lung	2.9	(2.6-3.2)
colon	1.6	(1.4-1.9)
esophagus	2.8	(1.8-4.0)
stomach	1.9	(1.5-2.4)
leukemia	9.9	(8.7-11.2)

Dores, et al. JCO, 2002

Implications for Transition to IFRT

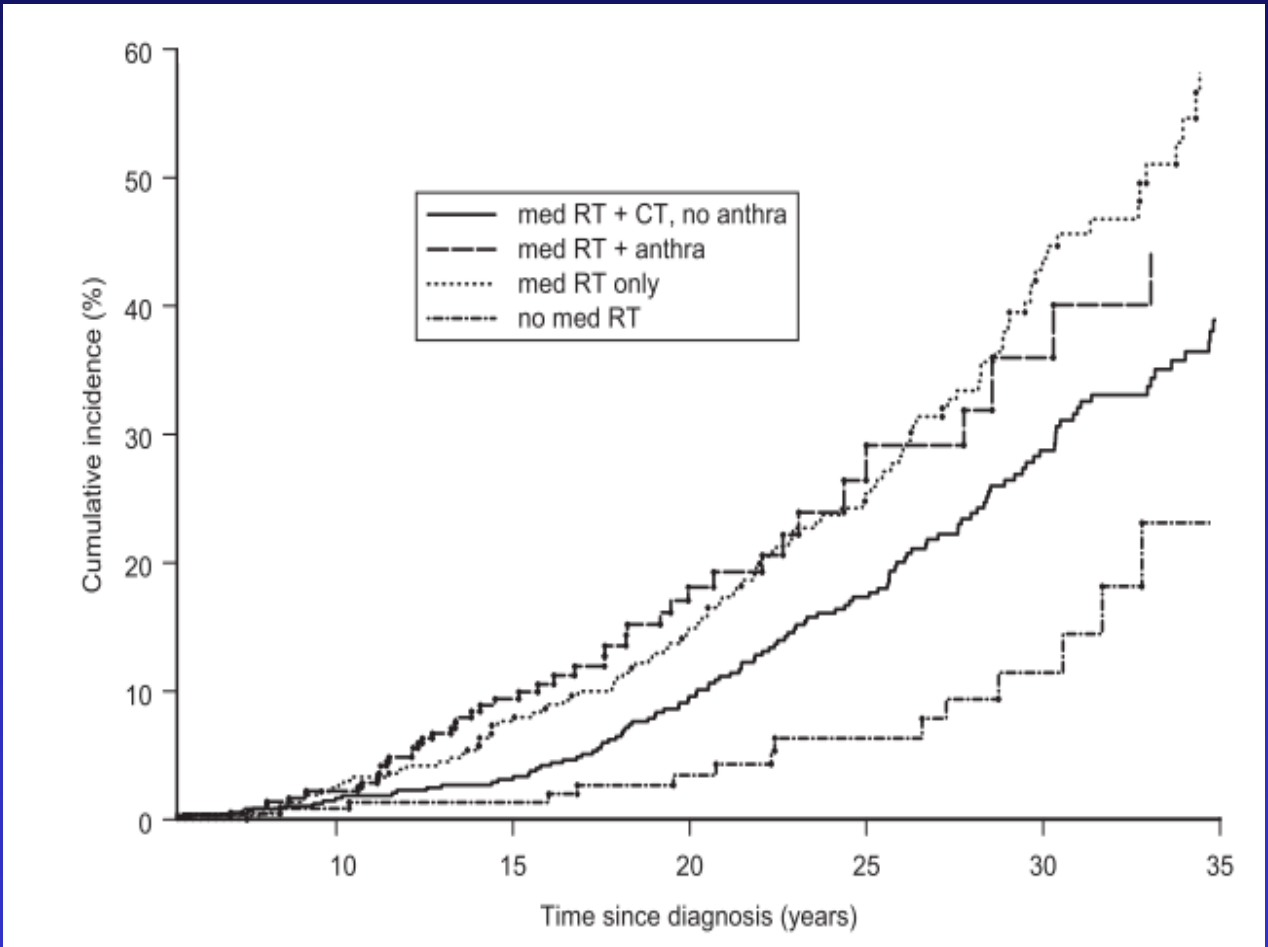
Clinical Evidence of Reduction in Breast Cancer Risk



De Bruin M L et al. JCO 2009;27:4239-4246

Cardiac Disease in Adult HL Survivors

Median Age = 25.7 at HL Diagnosis



Any cardiac Dx
≈25% @ 25 yrs
≈35% @ 30 yrs

No mediastinal RT
≈ 5% @ 25 yrs
≈ 10% @ 30 yrs

Aleman et al. Blood, 2007

Increase Above Expected Rate in 30-year Late Toxicity with ABVD + IFRT

25-30 years old at HL Diagnosis

	All Second Cancer		Female Breast Cancer	Cardiac Morbidity	
	M	F	F	M	F
36-40Gy Mantle	20%	35%	22%	25%	17%
30Gy IFRT	↓↓	↓↓	<10%	↑↓	↑ ↓
20Gy IFRT	↓↓	↓↓	<10%	↑ ↓	↑ ↓

Breast Cancer After HL

Screening

- radiation to chest (age 10-30) - start 8 yrs after RT
  mammography + MRI annual (together ? or
  in sequence q 6 mos?)

Clin Radiology, 2004
Ca: Cancer J Clin, 2007

Prevention

•No clear data at this time to suggest hormones etc to reduce likelihood of developing breast cancer

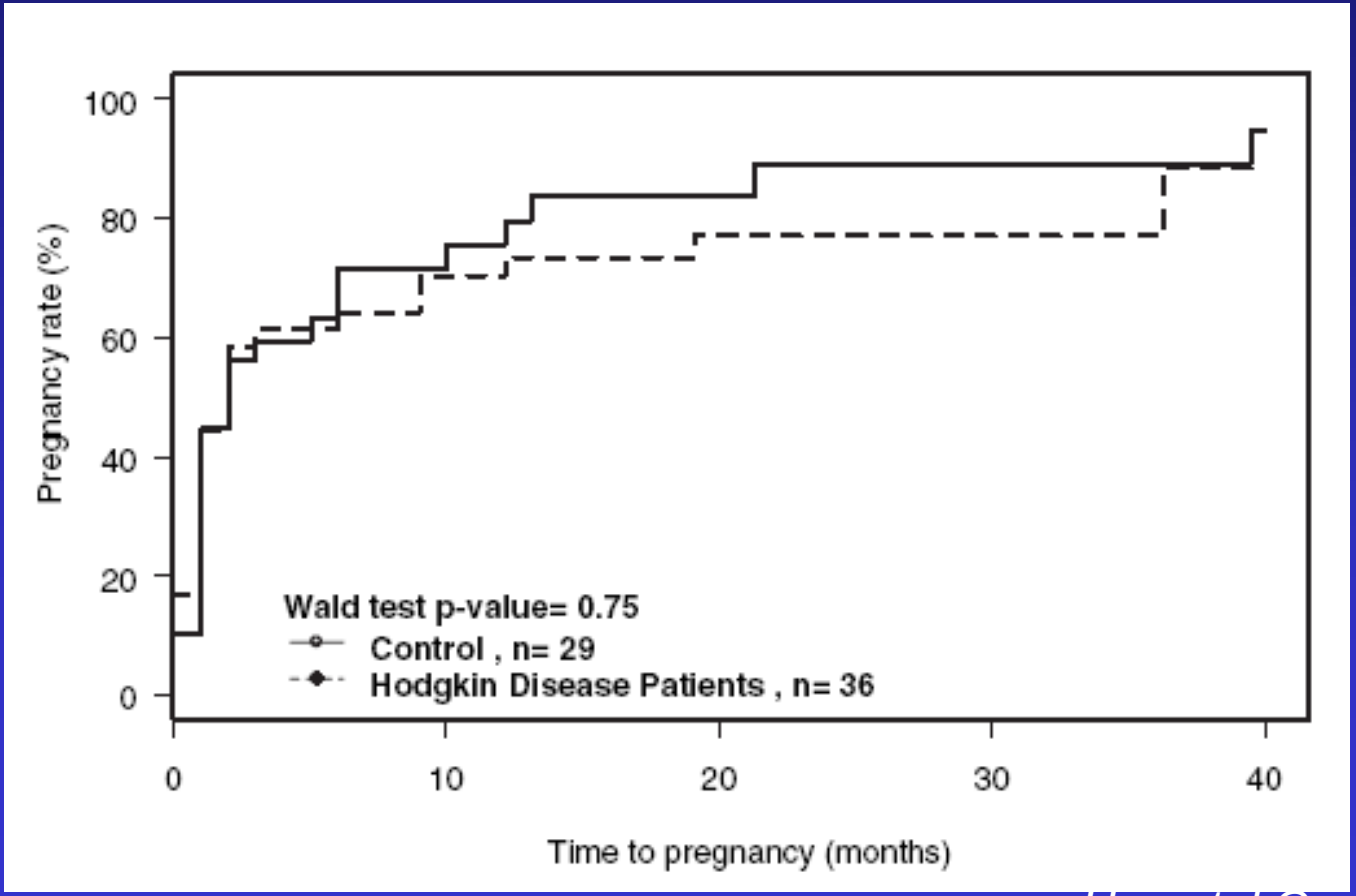
Fertility

- most literature describes surrogate measures of fertility
  - FSH levels, azospermia
  - amenorrhea

Males:	azospermic incidence	
	ABVD/non-alkylator:	10%
	BEACOPP	90%
Females:	amenorrhea	
	ABVD/non-alkylator	<5%
	BEACOPP	50%

Time to pregnancy following ABVD

- median age at dx 25 y; age at pregnancy: 32y
- 2-6 cycles (med 4); 50% abd XRT



Hematol Oncol 2007

Preservation is likely the best strategy

Males: sperm cryopreservation
- even if “suboptimal”

Females: ovarian suppression
- tissue/ovum cryopreservation
* data are poor

- IVF – expensive, need donor and takes time to perform

What we can learn from HL treatment

- Since cure rates and survival in other lymphomas are improving – we may expect similar late effects
  - Treatment paradigms are similar
  - Less reliance on radiation in NHL
  - Toxicity from treatment is improving
- Very important to have a gameplan
- Follow regular cancer screening advice as well

Vaccines in lymphoma and after lymphoma treatment

- Lymphoma increases risk of infection
- Vaccines affected by i. lymphoma, ii. chemotherapy and iii. GVH reaction
- Impact of immunosuppression:

  - decreased immune response

  -decreased duration of immunity

  -potential adverse events (live vaccines)

Courtesy J Keystone

Adult immunizations *key vaccines

vaccine	diseases
Td q10 yrs ; 1 Tdap	Tetanus , diphtheria, pertussis
Varicella (L)	chickenpox
MMR (L)	Measles , mumps, rubella
Polio	
Influenza (annual)	
Pneumococcal 2 doses 5 yrs apart	Pneumococcal pneumonia

Courtesy J Keystone

Adult immunizations *key vaccines

vaccine	diseases
Pneumococcal 2 doses 5 yrs apart	Pneumococcal pneumonia
Haemophilus Influenza	
meningococcal	Bacterial meningitis
Herpes zoster (L)	Shingles (chickenpox)
HPV	Human papilloma virus

Courtesy J Keystone

Principles of immunization in lymphoma

- Update routine immunizations before treatment (if possible)
- Inactivated vaccines only
- Vaccines given during chemotherapy; re-administer after treatment > 3 months
- Live vaccines can be given 3 mo. post chemotherapy if in remission (except HSCT)
- Re-administer *all* vaccines after either autologous & allogeneic stem cell transplants

Courtesy J Keystone

Immunizations after HSCT

Vaccine	Time post HSCT (mo)	Doses
Tdap	6-12	3
Varicella (L)	24	2
MMR (L)	24	1-2
polio	6-12	3
influenza	4-6	1

Courtesy J Keystone

Immunizations after HSCT

Vaccine	Time post HSCT (mo)	Doses
pneumococcal	3-6	2
Haemophilus influenza	6-12	3
meningococcal	6-12	1
Herpes zoster (L)	24	1
HPV	6-12	3

Courtesy J Keystone

Special vaccine issues

- **Tdap: give no matter when your last Td**
- **Pneumococcal vaccine: new approach**
  - **(2 vaccines prevnar 13 & pneumovax)**
- **If no previous pneumovax give Prevnar 13 (not covered) followed by pneumovax 2+ months later**
- **If pneumovax previously wait >1 year to give prevnar 13**

Courtesy J Keystone

Summary – The Fundamentals of Survivorship

- Hopefully, we all get to get old
  - We may get sick
- These things may or may not be related to treatment
- Need to take care
- Primary Care Physicians are important
- Contact with an expert center