

# Survival of Patients with Hematological Malignancies in Sweden

Paul W Dickman

Department of Medical Epidemiology and Biostatistics,  
Karolinska Institutet, Stockholm, Sweden

NAACCR Annual Conference  
Portland, Oregon  
7 June 2012

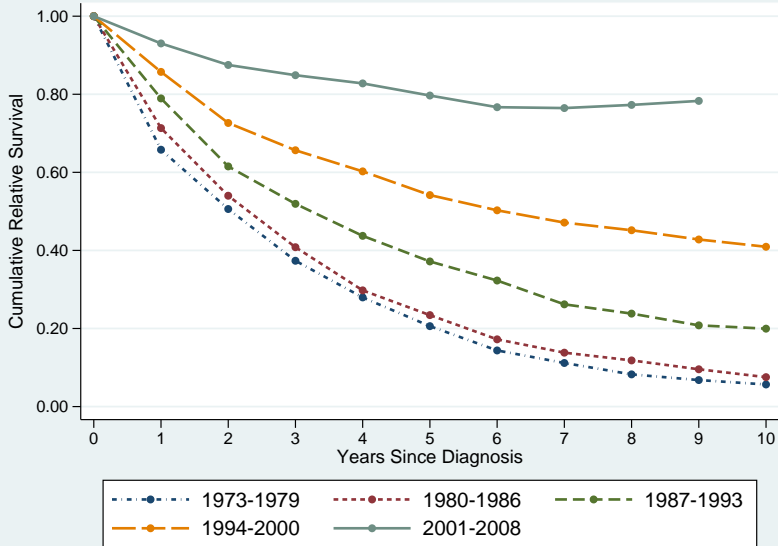


- Why should North Americans care?
- Chronic Myeloid Leukemia (CML)
- Hodgkin lymphoma (HL)
- HL (partitioning excess mortality)
- Acute Myeloid Leukemia (AML) cure models
- Myeloproliferative neoplasms (MPN)

# Why should North Americans care?

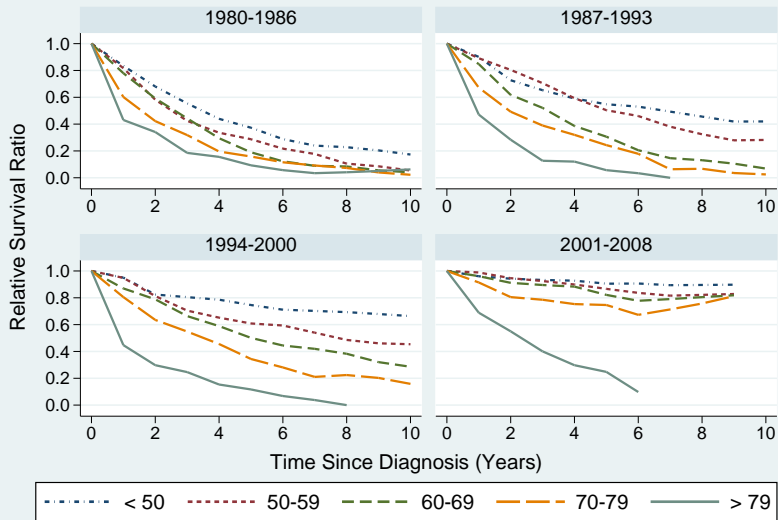
- High-quality population-based cancer registration.
  - Reporting mandatory by law; ID number.
  - Close to 100% ascertainment of incident cases and deaths.
  - Commenced 1958; these analyses are from 1973.
- Well-established government-funded public health-care system in which all residents are entitled to equal access.
- Patients are almost exclusively diagnosed and treated at non-private hospital-based hematology/oncology units.
- Treatment decisions based on patient- and disease-related factors, independent of financial considerations.

# CML; Björkholm *et al.* JCO 2011 [1]

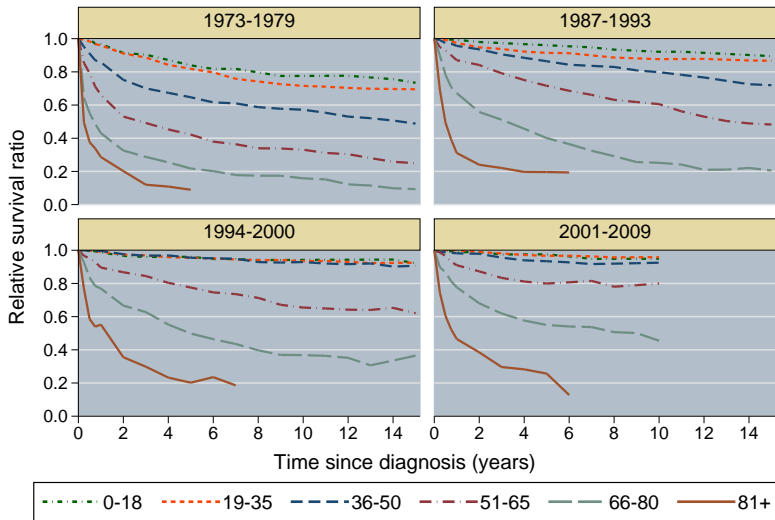


- Glivec (imatinib) approved for use in 2001 and was first line treatment for 80% of patients in 2006 (although only 18% for patients aged 80 years or older).
- Improvements for patients diagnosed 1994–2000 due to increasing use of allogeneic SCT, introduction of IFN- $\alpha$  and, for some patients, Glivec.

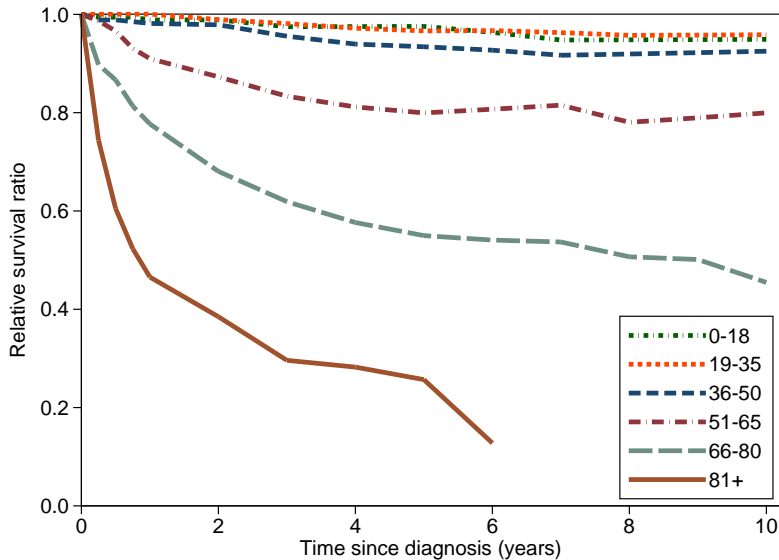
# CML survival by age and period



# Hodgkin Lymphoma; Sjöberg *et al. Blood* 2012 [2]

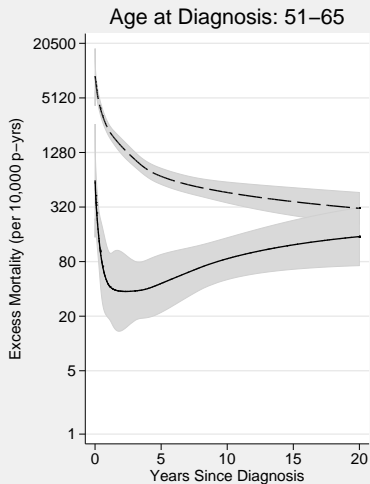
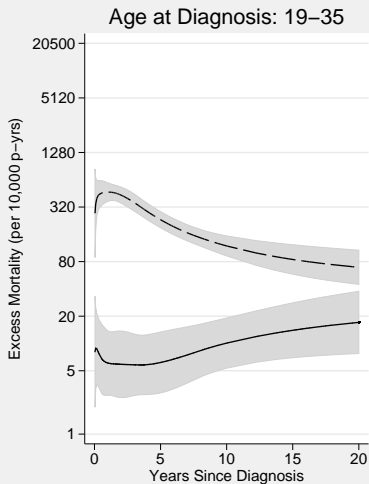


# Hodgkin Lymphoma diagnosed 2001-2009



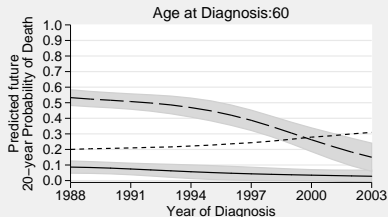
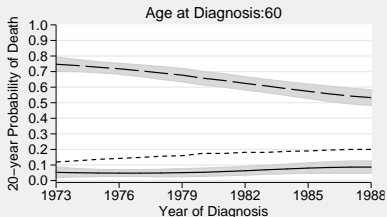
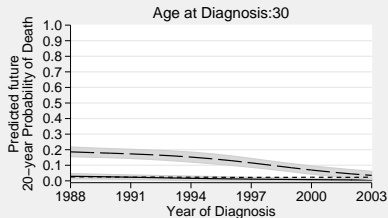
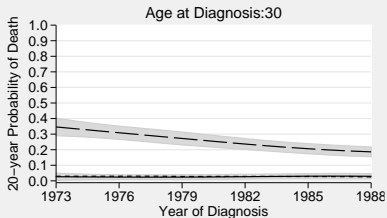


# Partitioning excess mortality (males HL); Eloranta

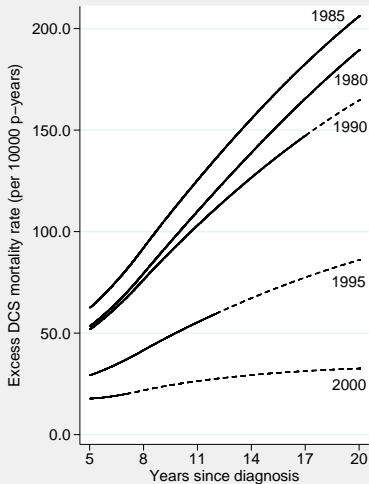
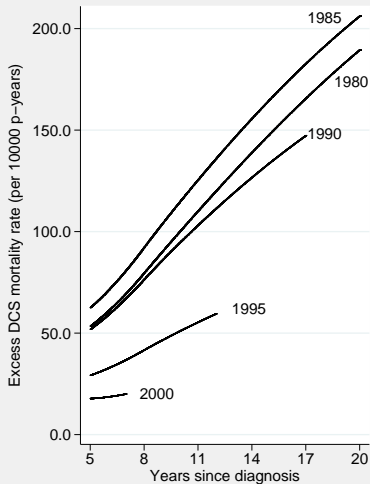


— Excess DCS Mortality    - - - Remaining Excess Mortality    95% C.I.

# Temporal trends in 20-year probability of death

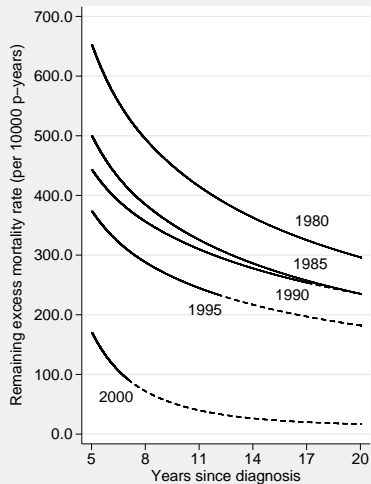
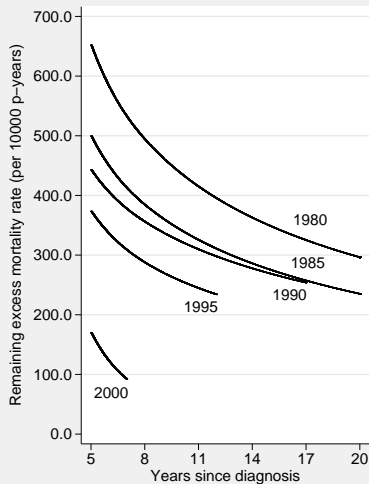


# Assessing the appropriateness of predictions



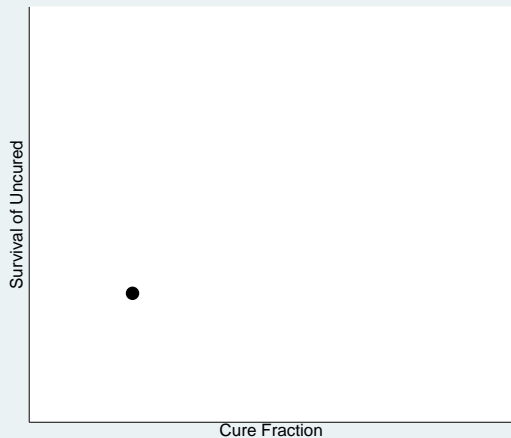
— Follow-up observable      - - - - - Extrapolated from the model

# Assessing the appropriateness of predictions



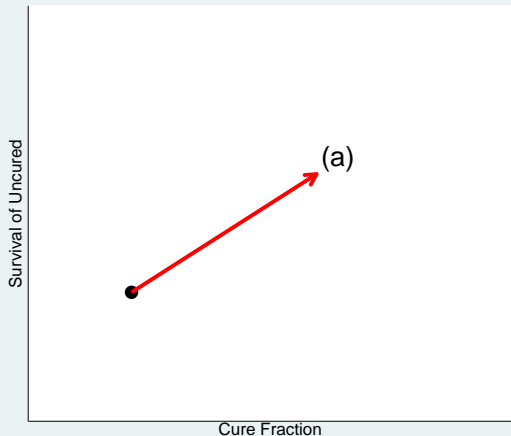
—— Follow-up observable      - - - - - Extrapolated from the model

# Cure models: Interpreting changes over time



Adapted from Verdecchia (1998)

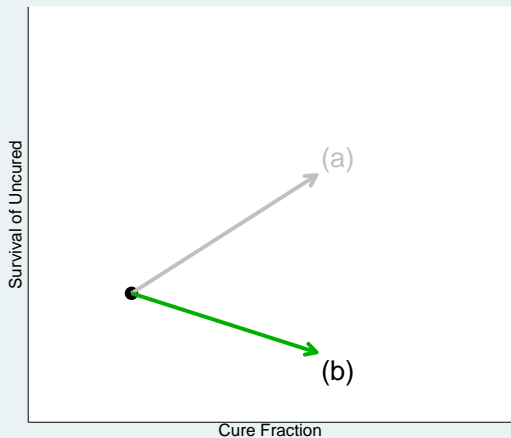
# Cure models: Interpreting changes over time



Adapted from Verdecchia (1998)

(a) General Improvement

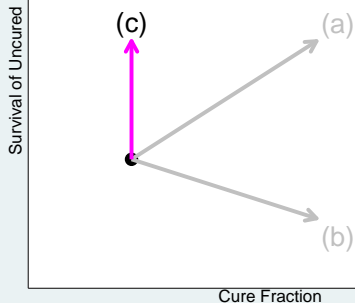
# Cure models: Interpreting changes over time



Adapted from Verdecchia (1998)

(b) Selective Improvement

# Cure models: Interpreting changes over time

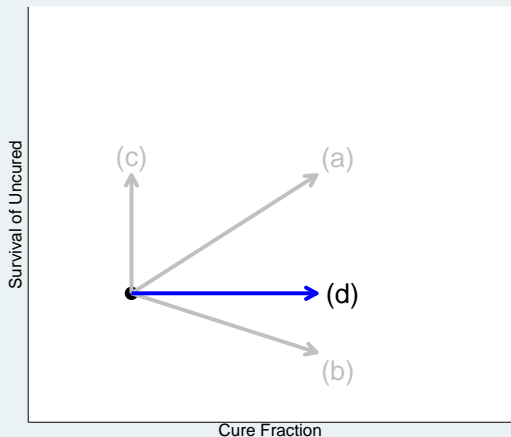


Adapted from Verdecchia (1998)

(c) Improved palliative care or lead time



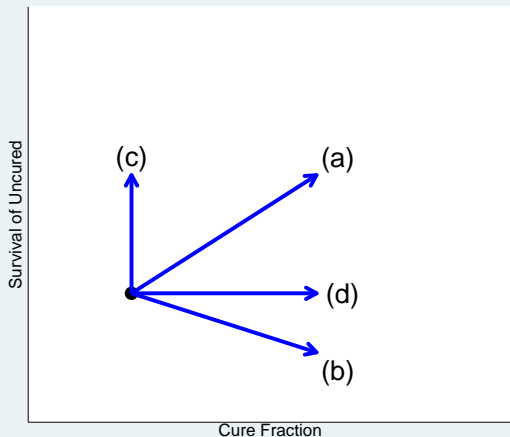
# Cure models: Interpreting changes over time



Adapted from Verdecchia (1998)

(d) Inclusion of subjects with no excess risk

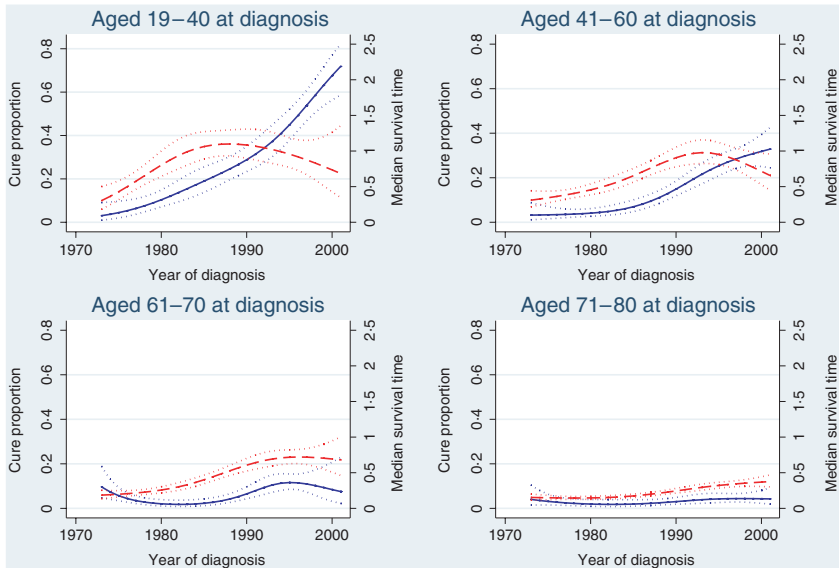
# Cure models: Interpreting changes over time



Adapted from Verdecchia (1998)

- (a) General Improvement
- (b) Selective Improvement
- (c) Improved palliative care or lead time
- (d) Inclusion of subjects with no excess risk

# Andersson 2010 [3]: trends in cure for AML



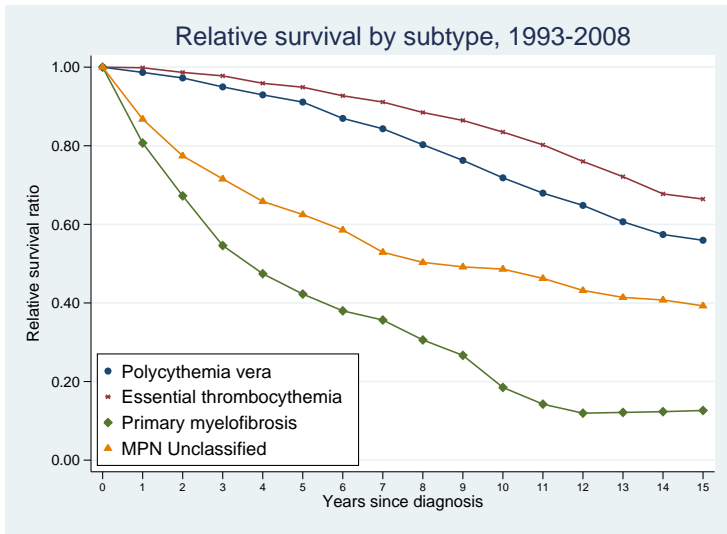
# AML treatment

- Allogeneic stem cell transplantation (allo-SCT) was introduced in the 1970s, initially associated with a considerable treatment-related mortality (TRM).
- Refinement of conditioning regimens, the use of larger amounts of stem cells, also from unrelated donors, and improvement in supportive care has reduced the TRM.
- The combination of intensive cytarabine post-remission treatment and better risk stratification lead to a continuous increase in the number of allo-SCT performed in Sweden during the study period.

# Myeloproliferative neoplasms (MPNs)

- Diseases of the bone marrow in which excess cells are produced. Characterized by a relatively indolent course which can be complicated by thromboembolic events and transformation to acute myeloid leukemia.
- Patients with primary myelofibrosis (PMF) have a substantially reduced life expectancy while patients with polycythemia vera (PV) and essential thrombocythemia (ET) have a moderately reduced survival in most, but not all, studies.
- We used data from the Swedish cancer registry to establish patterns of survival in more than 9,000 MPN patients.
- Hultcrantz *et al.* *JCO* 2012 (in press).

# Myeloproliferative neoplasms, Hultcrantz *et al.* *JCO* in press



# HL treatment

The Stockholm Hodgkin lymphoma study group was established in 1973 and national Swedish treatment recommendations for HL were introduced in 1985 and have been up-dated over the years. In 1975, the successful use of the combination doxorubicin, bleomycin, vinblastine, and dacarbazine (ABVD) was reported<sup>26</sup> and since the early 1980's a variety of chemotherapy combinations other than conventional MOPP including ABVD, MOPP/ABDV, MOPP/ABV (younger patients) and ChLVPP (chlorambucil, vinblastine, procarbazine, prednisolone), LVPP/OEPA (chlorambucil, vinblastine, procarbazine, vincristine, etoposide, prednisone, doxorubicin), and CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) (mostly elderly patients) were used in previously untreated patients with stage IIB-IV disease.

## HL treatment 2

Since the 1980's patients with advanced disease reaching a complete remission after two cycles traditionally received in total 6 cycles of chemotherapy.

Very few HL patients with advanced disease and high-risk features received BEACOPP chemotherapy (bleomycin, etoposide, adriamycin, cyclophosphamide, vincristine, procarbazine, prednisone) during the study period.

Combined modality treatment for patients with limited stage disease became increasingly common during the 1980's.

Irradiation to previously bulky disease in patients with stage III-IV disease was also wide-spread during the 1980's and 1990's.

High-dose chemotherapy with autologous SCT for patients with refractory/relapsing disease was started in the mid-1980's with



# HL treatment 3

BEAM (carmustine, etoposide, cytarabine, melphalan) as the prevailing high-dose regimen.

Staging during the period 1972-1988 often included laparotomy and splenectomy. The management of frail elderly patients has been more varying.

During recent years, treatment of HL has been increasingly influenced by the goal of minimizing late therapy-related complications. Thus, a more tailored treatment has become an important concept to offer the best chance of cure with reduced risk of toxicity. As an example, a common Nordic protocol for patients with stage I-IIA disease based on risk-adjusted treatment was initiated in 1999.

# References

- [1] Björkholm M, Ohm L, Eloranta S, Derolf A, Hultcrantz M, Sjöberg J, *et al.*. Success story of targeted therapy in chronic myeloid leukemia: a population-based study of patients diagnosed in Sweden from 1973 to 2008. *J Clin Oncol* 2011;**29**:2514–2520.
- [2] Sjöberg J, Halthur C, Kristinsson SY, Landgren O, Nygell UA, Björkholm M, Dickman PW. Progress in Hodgkin lymphoma: a population-based study on patients diagnosed in Sweden from 1973-2009. *Blood* 2012;**119**:990–996.
- [3] Andersson TML, Lambert PC, Derolf AR, Kristinsson SY, Eloranta S, Landgren O, *et al.*. Temporal trends in the proportion cured among adults diagnosed with acute myeloid leukaemia in Sweden 1973-2001, a population-based study. *British Journal of Haematology* 2010;**148**:918–924.