# Observational studies in APL

## What have we learned and what can we still learn?

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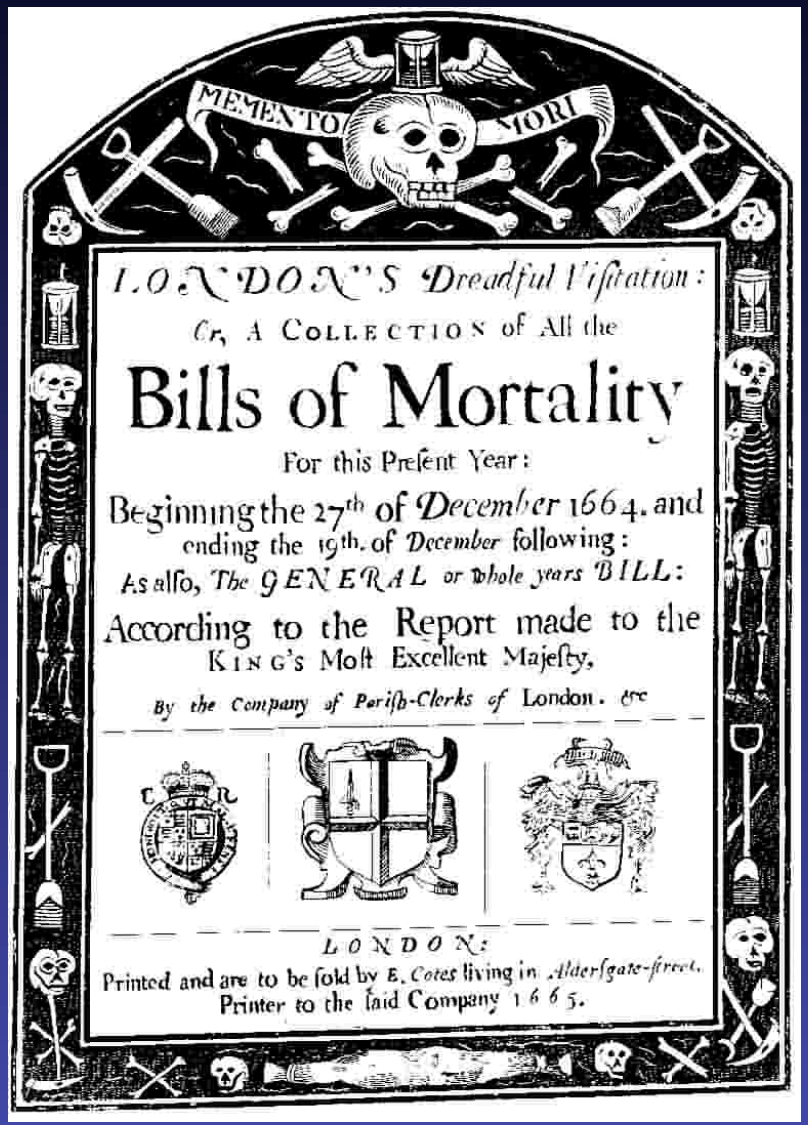
# Disclosures

| | |
|---|---|
| **Research support** | Lundbeck, BioCanRx |
| **Employee** | - |
| **Consultant** | Lundbeck, Janssen, Pfizer |
| **Stockholder** | - |
| **Speaker** | - |
| **Scientific advisory board** | Otsuka, Lundbeck, Amgen, Pfizer, Shire |

# The first observational study?



MEMENTO MORI

LONDON'S *Dreadful Visitation:*

*Or,* A COLLECTION of All the

# Bills of Mortality

For this Present Year:

Beginning the 27th of *December* 1664. and ending the 19th. of *December* following:

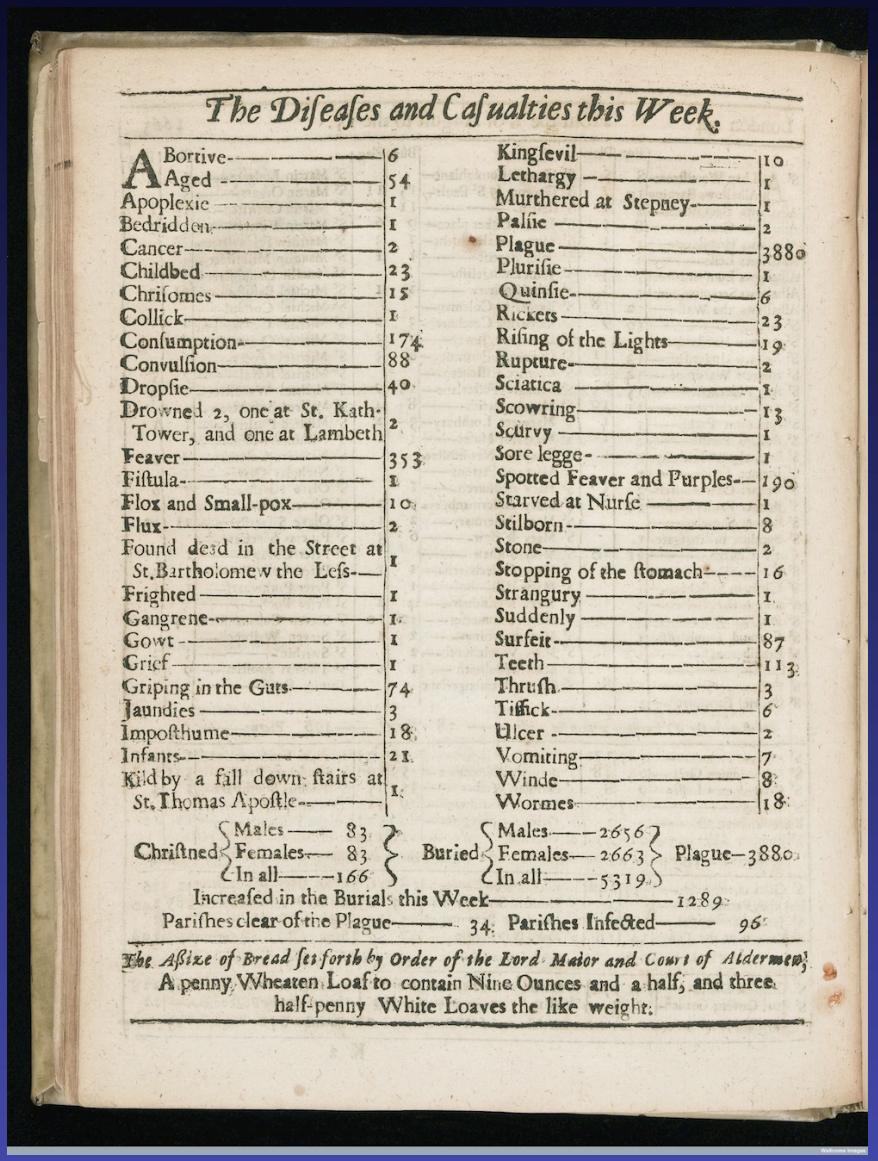
As also, *The* GENERAL *or Whole years* BILL:

According to the Report made to the KING's Most Excellent Majesty,

*By the Company of Parish-Clerks of* London. &c

LONDON:

Printed and are to be sold by E. *Cotes* living in *Aldersgate-street*. Printer to the said Company 1665.



## *The Diseases and Casualties this Week.*

| | | | |
|---|---|---|---|
| Abortive | 6 | Kingsevil | 10 |
| Aged | 54 | Lethargy | 1 |
| Apoplexie | 1 | Murthered at Stepney | 1 |
| Bedridden | 1 | Palsie | 2 |
| Cancer | 2 | Plague | 3880 |
| Childbed | 23 | Plurisie | 1 |
| Chrisomes | 15 | Quinsie | 6 |
| Collick | 1 | Rickets | 23 |
| Consumption | 174 | Rising of the Lights | 19 |
| Convulsion | 88 | Rupture | 2 |
| Dropsie | 40 | Sciatica | 1 |
| Drowned 2, one at St. Kath. Tower, and one at Lambeth | 2 | Scowring | 13 |
| | | Scurvy | 1 |
| Feaver | 353 | Sore legge | 1 |
| Fistula | 1 | Spotted Feaver and Purples | 190 |
| Flox and Small-pox | 10 | Starved at Nurse | 1 |
| Flux | 2 | Stilborn | 8 |
| Found dead in the Street at St. Bartholomew the Less | 1 | Stone | 2 |
| | | Stopping of the stomach | 16 |
| Frighted | 1 | Strangury | 1 |
| Gangrene | 1 | Suddenly | 1 |
| Gowt | 1 | Surfeit | 87 |
| Grief | 1 | Teeth | 113 |
| Griping in the Guts | 74 | Thrush | 3 |
| Jaundies | 3 | Tissick | 6 |
| Imposthume | 18 | Ulcer | 2 |
| Infants | 21 | Vomiting | 7 |
| Kild by a fall down stairs at St. Thomas Apostle | 1 | Winde | 8 |
| | | Wormes | 18 |

Christned { Males 83, Females 83, In all 166 } Buried { Males 2656, Females 2663, In all 5319 } Plague 3880

Increased in the Burials this Week 1289

Parishes clear of the Plague 34. Parishes Infected 96

*The Assize of Bread set forth by Order of the Lord Maior and Court of Aldermen:*

A penny Wheaten Loaf to contain Nine Ounces and a half, and three half-penny White Loaves the like weight.

# Objectives

1. Summarize merits and limitations of observational data
2. Review the role of observational data in APL
3. Discuss future opportunities for observational data in APL

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Proposals for definition of MRD terms in ALL. Data from Gruggemann et al [] with permission.

# Goals of Observational Studies

**Hospital based**

Quality improvement
Professional education
Administrative information
Research hypotheses

**Population based**

Prevention
Early detection
Rates & Trends
Patterns of care and outcomes
Research hypotheses
Evaluation of control efforts

Proposals for definition of MRD terms in ALL. Data from Bruggemann et al [6 with permission.

# Goals of Observational Studies in APL

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# Objectives

1. Summarize merits and limitations of observational data
2. Review the importance of observational data in APL
3. Discuss future opportunities for observational data in APL

# Observational Studies in APL: Major findings

1. Incidence and distribution
2. Early Death
3. Long-term outcomes
4. Subgroups

    tAPL/APL variants

    Age extremes

    Geo-social determinants

    Pregnancy

# Observational Studies in APL: Major findings

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# APL incidence/distribution

Proposals for definition of MRD terms in ALL. Data from Brüggemann et al16 with permission.

# APL incidence
# Population-based registries

| Registry | Years | Age-standardized incidence (/100K) | Increasing? |
|---|---|---|---|
| US | 1992-2007 | 0.23 | Y (p=0.068) |
| US | 1975-2008 | 0.18 | Y (p<0.05) |
| Canada | 1993-2006 | 0.08 | N |
| EU | 2000-2007 | 0.12 (crude) | Not reported |

Park et al Blood 2011; Chen et al Cancer 2012;
Paulson et al Br J Haem 2014; Gatta et al Lancet Oncol 2017

# APL in ethnic/geographic subgroups

**High Frequency of Acute Promyelocytic Leukemia Among Latinos With Acute Myeloid Leukemia**

By Dan Douer, Susan Preston-Martin, Eric Chang, Peter W. Nichols, Kristy J. Watkins, and Alexandra M. Levine

Acute promyelocytic leukaemia in patients originating in Latin America is associated with an increased frequency of the bcr1 subtype of the *PML/RARα* fusion gene

Dan Douer,[1] Sergio Santillana,[2] Laleh Ramezani,[1] Cesar Samanez,[2] Marilyn L. Slovak,[3] Ming S. Lee,[4] Kristy Watkins,[1] Tony Williams[1] and Carlos Vallejos[2] [1]*Division of Haematology,*

**Acute promyelocytic leukaemia is highly frequent among acute myeloid leukaemias in Brazil: a hospital-based cancer registry study from 2001 to 2012**

Luiz Claudio Santos Thuler [1] · Maria S. Pombo-de-Oliveira [2,3]

Douer D et al. Blood 1996; Douer D et al. Br J Haem 2003;
Thuler LCS et al. Ann Hematol 2017

# *Acute Promyelocytic Leukemia*

## *A Childhood Cluster*

RODNEY D. GILBERT, MB, CHB, DCH(SA), C. D. KARABUS, MMED (PAED), DCH, FRCP (LOND, EDIN), AND A. E. MILLS, MA, MB, BCH, DCP, DPATH

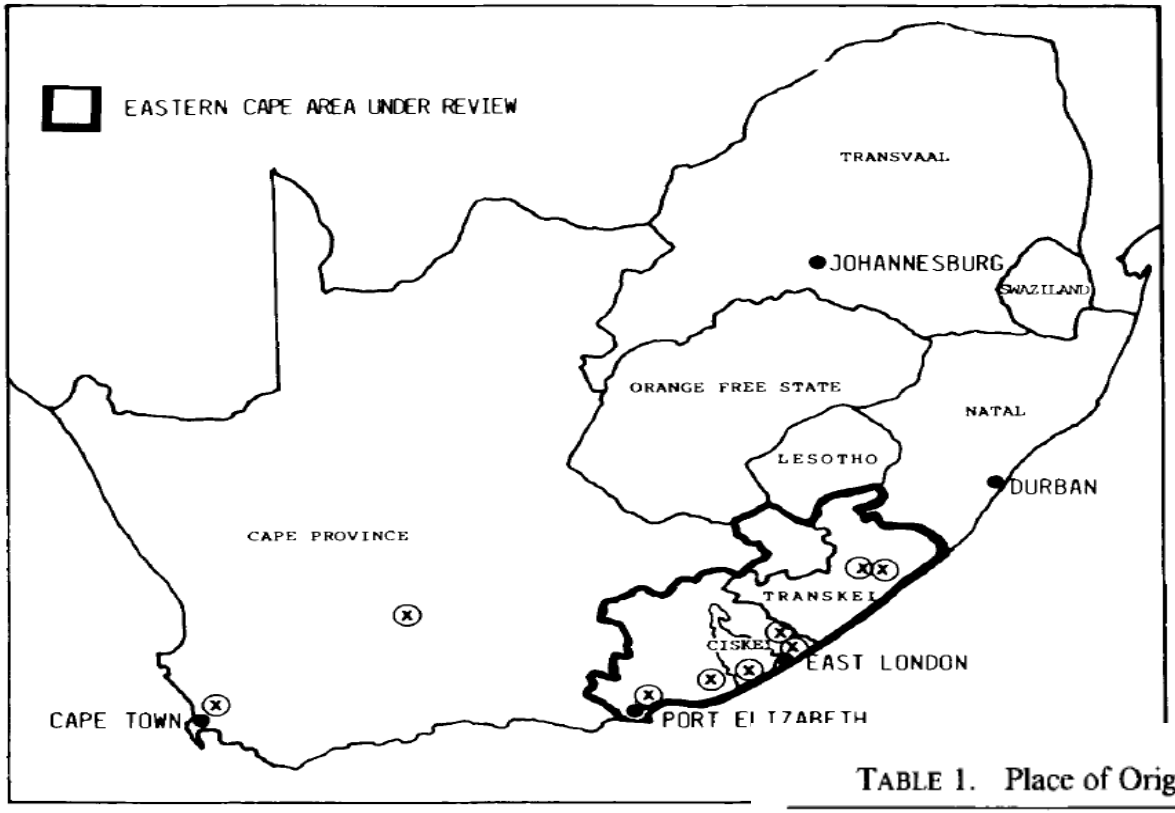


FIG. 1. Map of South Africa showing Eastern Cape area from which the majority of patients came. ⊗ indicates place of origin of each patient with APL.

TABLE 1. Place of Origin of Patients With Acute Leukemia

| Type of leukemia | Eastern Cape | Elsewhere | Total |
|---|---|---|---|
| ALL | 26 | 59 | 85 |
| ANLL (excluding APL) | 10 | 24 | 34 |
| APL | 7 | 2 | 9 |

**Gilbert R et al. Cancer 1987**

# Observational Studies in APL: Major findings

1. Incidence and distribution
2. Early Death
3. Long-term outcomes
4. Outcomes in subgroups

   tAPL/APL variants

   Age extremes

   Geo-social determinants

   Pregnancy

# Observational Studies in APL: Major findings

1. Incidence and distribution
2. Early Death — Zhu CO008; Park CO009
3. Long-term outcomes
4. Outcomes in subgroups

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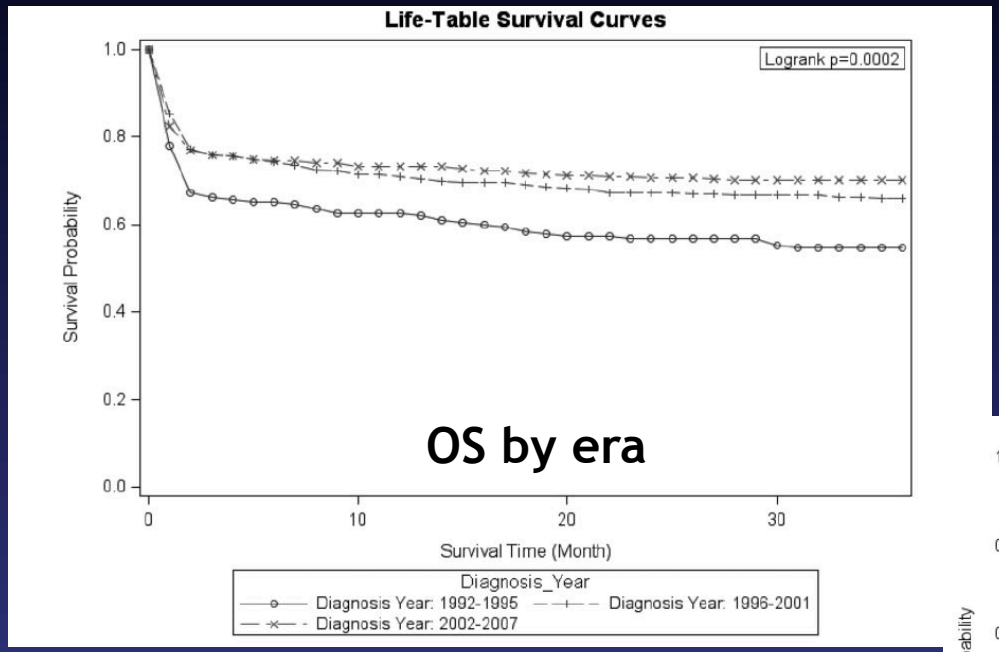
# Long-term Outcomes: SEER




OS by era

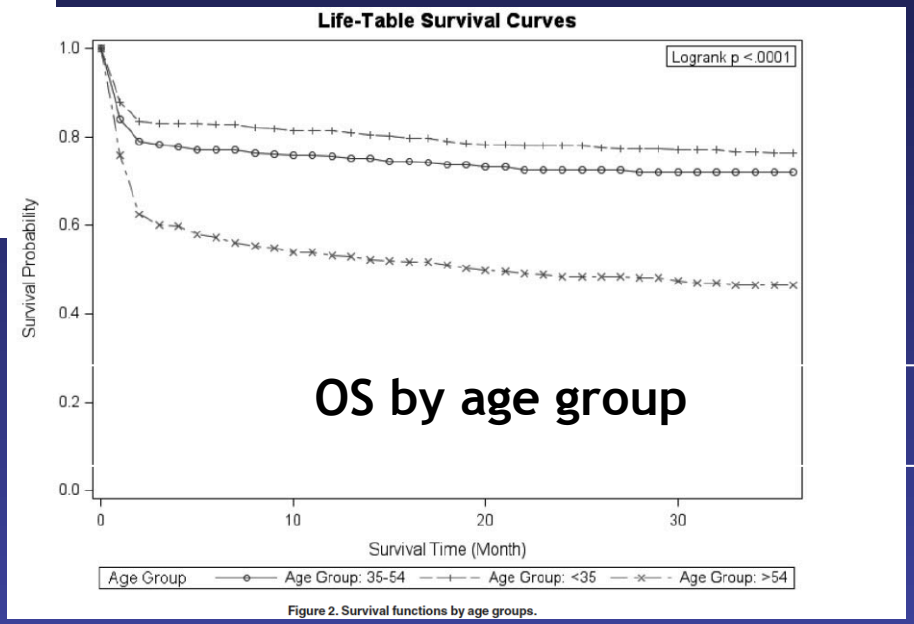



Figure 2. Survival functions by age groups.

OS by age group

Park J et al. Blood 2011

Proposals for definition of MRD terms in ALL. Data from Gruggemann et al [6] with permission.

# Long-term Outcomes: Canada

bjh research paper

## Acute promyelocytic leukaemia is characterized by stable incidence and improved survival that is restricted to patients managed in leukaemia referral centres: a pan-Canadian epidemiological study

Kristjan Paulson,[1,2] Anna Serebrin,[3] Pascal Lambert,[2] Julie Bergeron,[4,5] Janeve Everett,[6] Andrea Kew,[7,8] David Jones,[9] Salah Mahmud,[1,2] Catherine Meloche,[4,5] Mitchell Sabloff,[10,11] Ismail Sharif,[7] John Storring,[6] Donna Turner[1,2] and Matthew D. Seftel[1,2,12]

Br J Haem 2014

# Observational Studies in APL: Major findings

1. Incidence and distribution
2. Early Death
3. Long-term outcomes — Platzbecker PO027
4. Outcomes in subgroups

   tAPL/APL variants

   Age extremes

   Geo-social determinants

   Pregnancy

# Observational Studies in APL: Major findings

1. Incidence and distribution
2. Early Death
3. Long-term outcomes
4. Outcomes in subgroups

| | |
|---|---|
| tAPL/APL variants | Kayser C0003; Cicconi P0003 |
| Age extremes | Al Hada C0021; Salamero TO001 |
| Geo-social determinants | Farah CO038; Reddy CO039 |
| Pregnancy | Sole PO026 |

# Objectives

1. Summarize merits and limitations of observational data (registries, cross-sectional & cohort studies)
2. Review the role of observational data in APL
3. Discuss future opportunities for observational data in APL

# All tumours are rare, but some are rarer than others

"rare" tumours ~25% of all malignancies!

Gatta G et al Lancet Oncol 2017
Munro A. Lancet Oncol 2017

# Opportunities for observational data in APL

- Incidence rates
- Patterns of care & long term outcomes
- Cost of therapy
- Disparities
- Genomic & clinical subgroups

# Opportunities for observational data in APL


Canadian APL registry

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# Extra slides