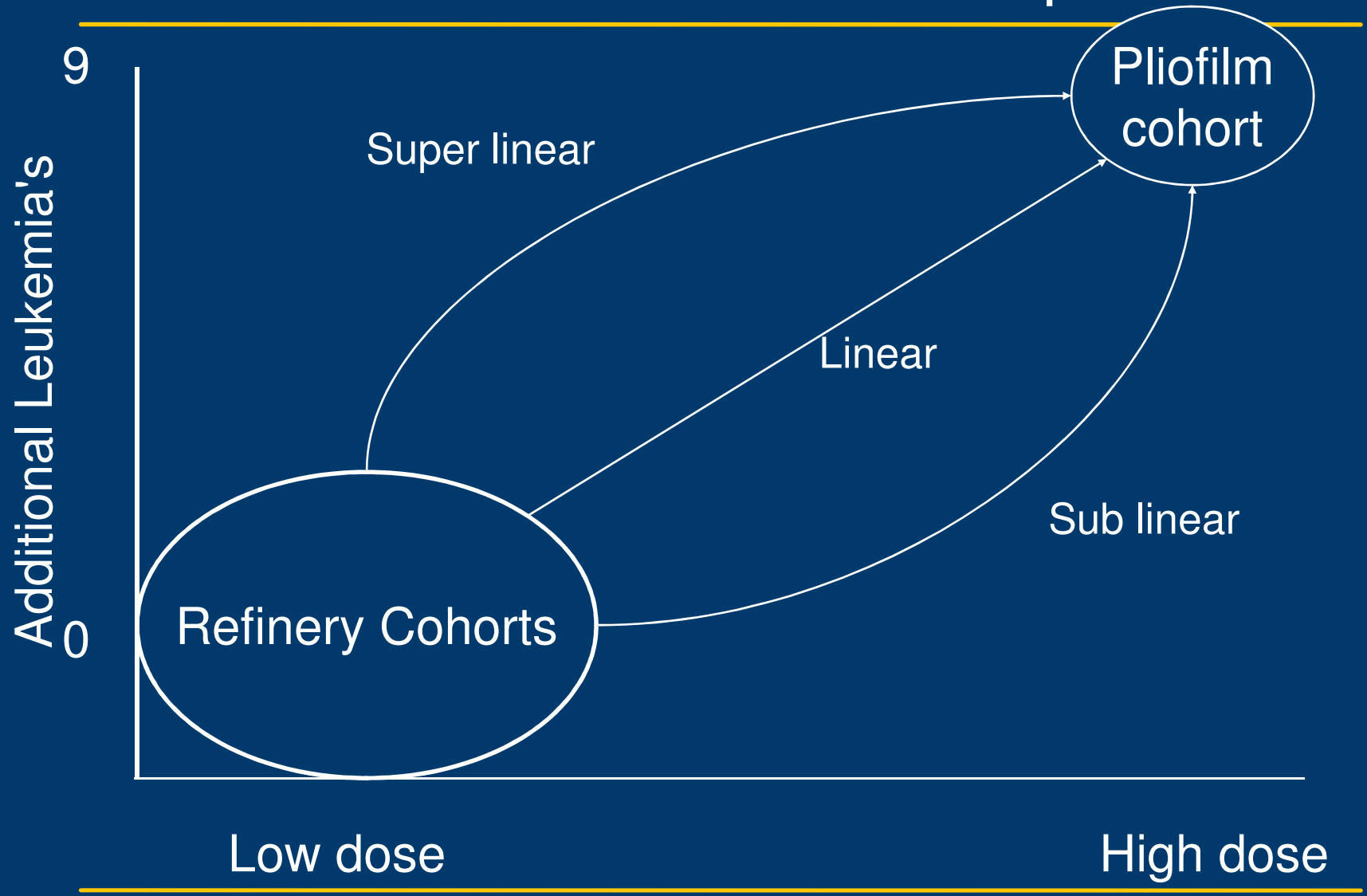
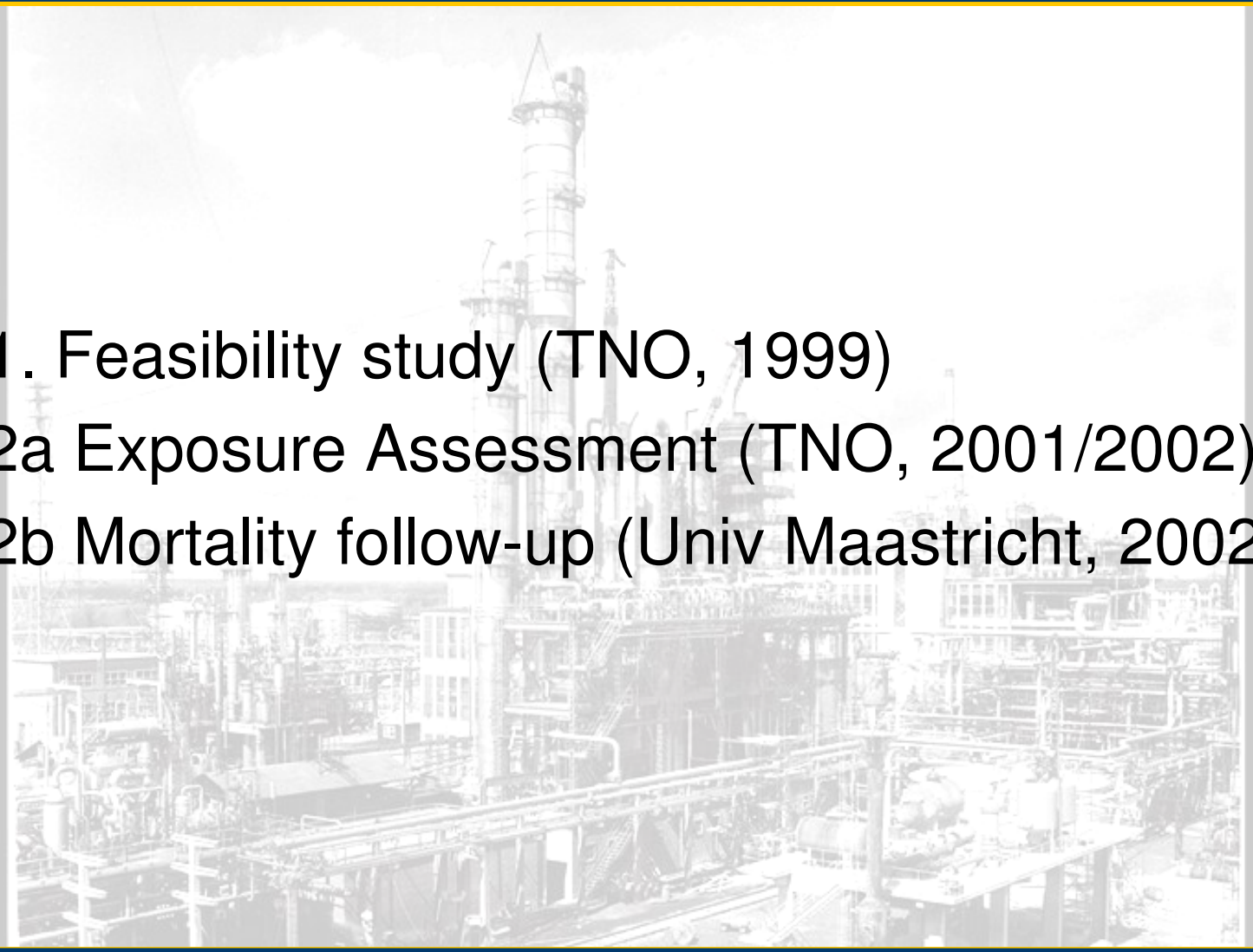
Leukemia benzene dose response ?



Why Caprolactam and benzene?

- Pure benzene (rare in Epi studies)
- Old technology and plants, long follow-up
- High/intermediate benzene exposure,
- Remarkable quality of archives in the fifties & sixties.
- No lymphopoetic modifiers

Approach



- 1. Feasibility study (TNO, 1999)
- 2a Exposure Assessment (TNO, 2001/2002)
- 2b Mortality follow-up (Univ Maastricht, 2002)

Feasibility study (TNO, 1999)

Availability, quality an completeness of key data on workers exposure (Pat Stewart 1991)

- **Plant layouts, process description,** √
- **organizational charts, SOP, etc.,** √
- **Work history, Job description, medical records** √
- **Industrial hygiene data,** √
- **Air and dermal exposure.** √

Caprolactam technology periods

PERIOD 1 (1952 - 57)

- Pilot plant and French extraction
- PERIOD 2 (1958 - 62)
- Comprimo extraction

PERIODE 3 (1962 - 68)

- Introduction of RDC and
- revamp to 100 ton

retrospective, occupational exposure assessment

Individual, benzene air exposure assessment
(Tom Armstrong 1991)

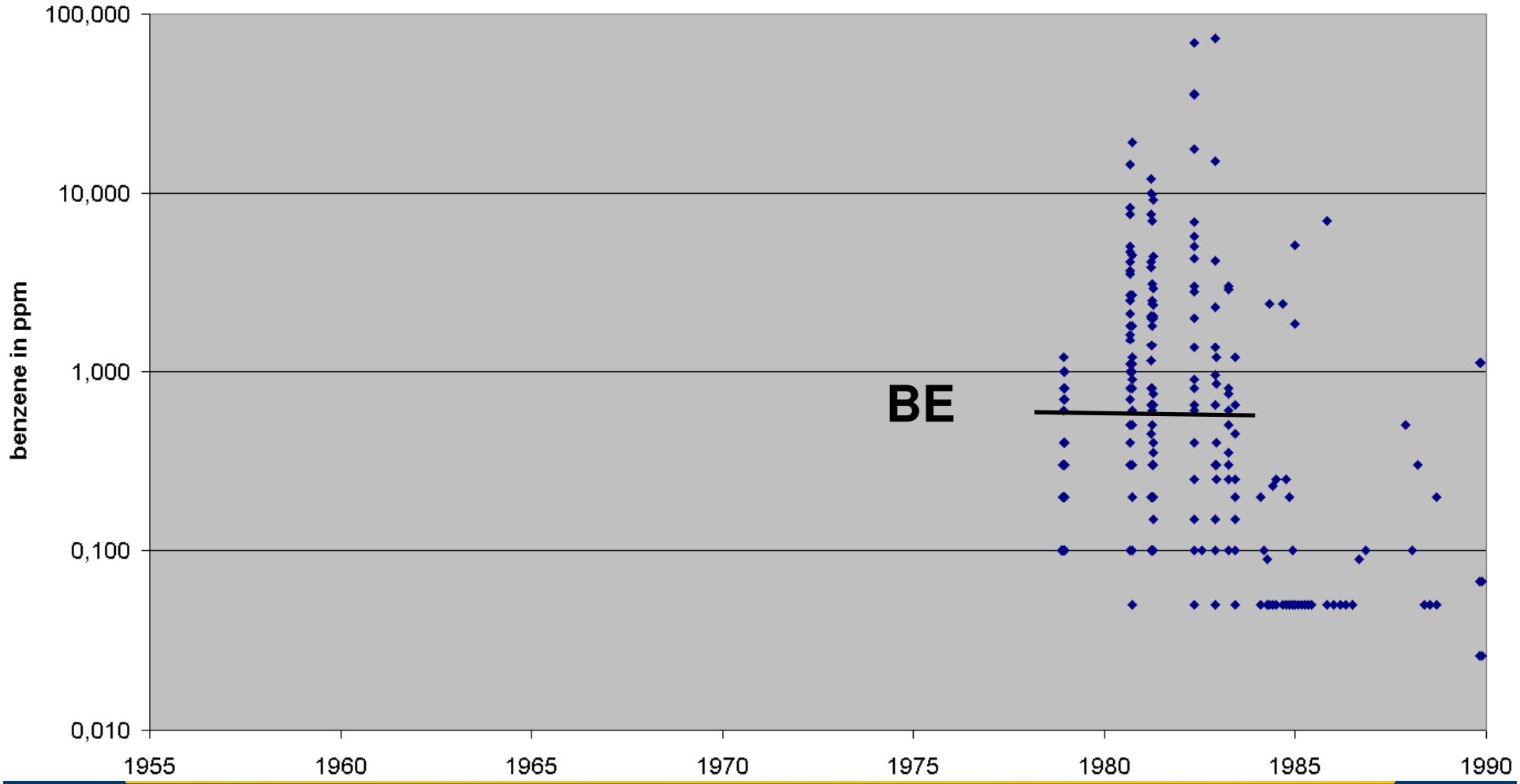
- SKINPERM dermal route
- Validation check with EASE, OEL trend, Backwards regression of PAS data >1978

Retrospective air exposure assessment

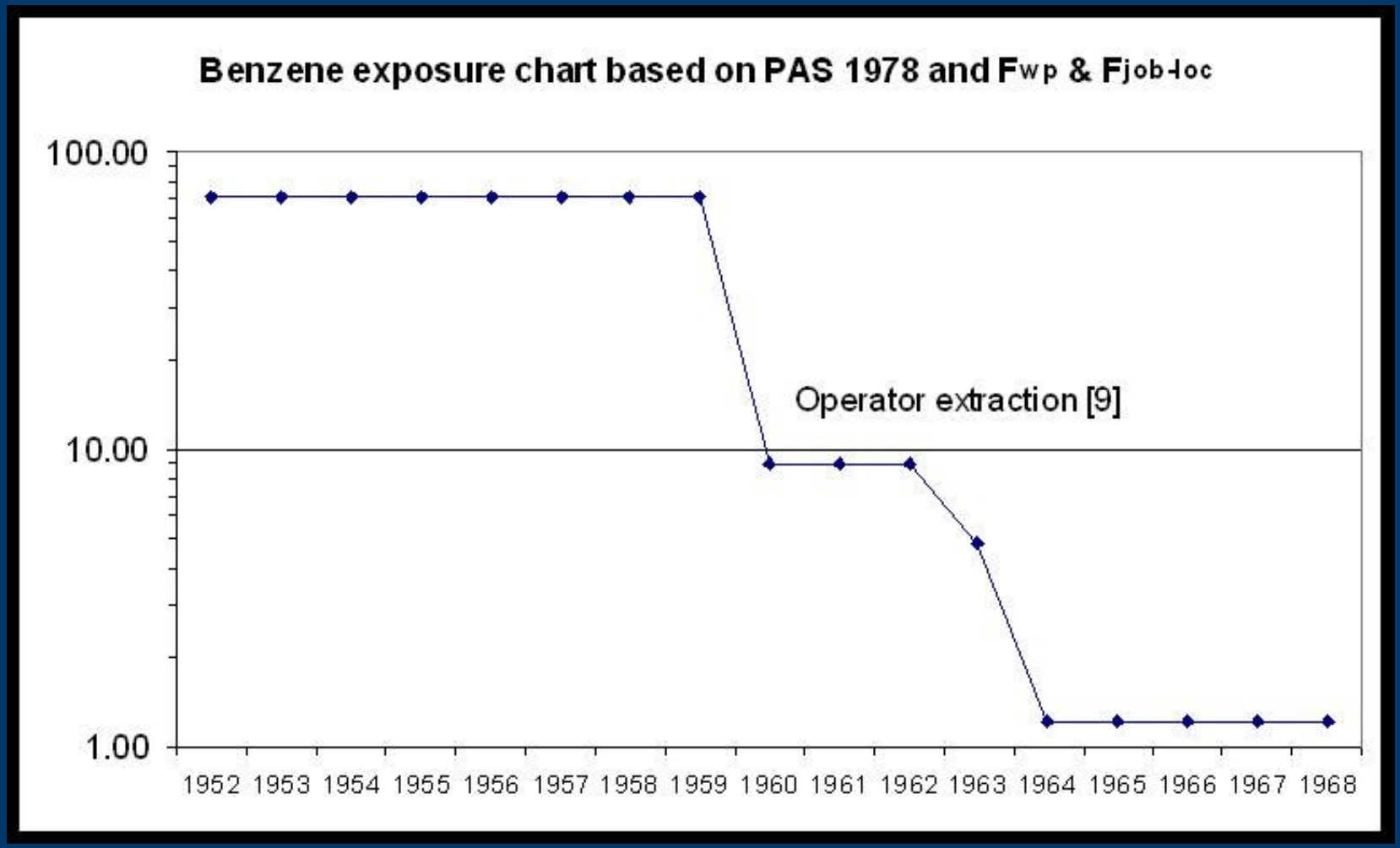
$$WE_i = BE * K_{job\text{-}location} * K_{workplace}$$

- WE_i =Worker exposure in year i;
- BE= Base estimate distribution of benzene exposure (ppm);
- $K_{job\text{-}location}$= Modifying factor for job-location combinations (1-6);
- $K_{workplace}$ = Modifying factor for the workplace (2,4,8)
- Factors on function (1-6) and workplace (2,4,8) based on expert judgement of a panel of (former) employees

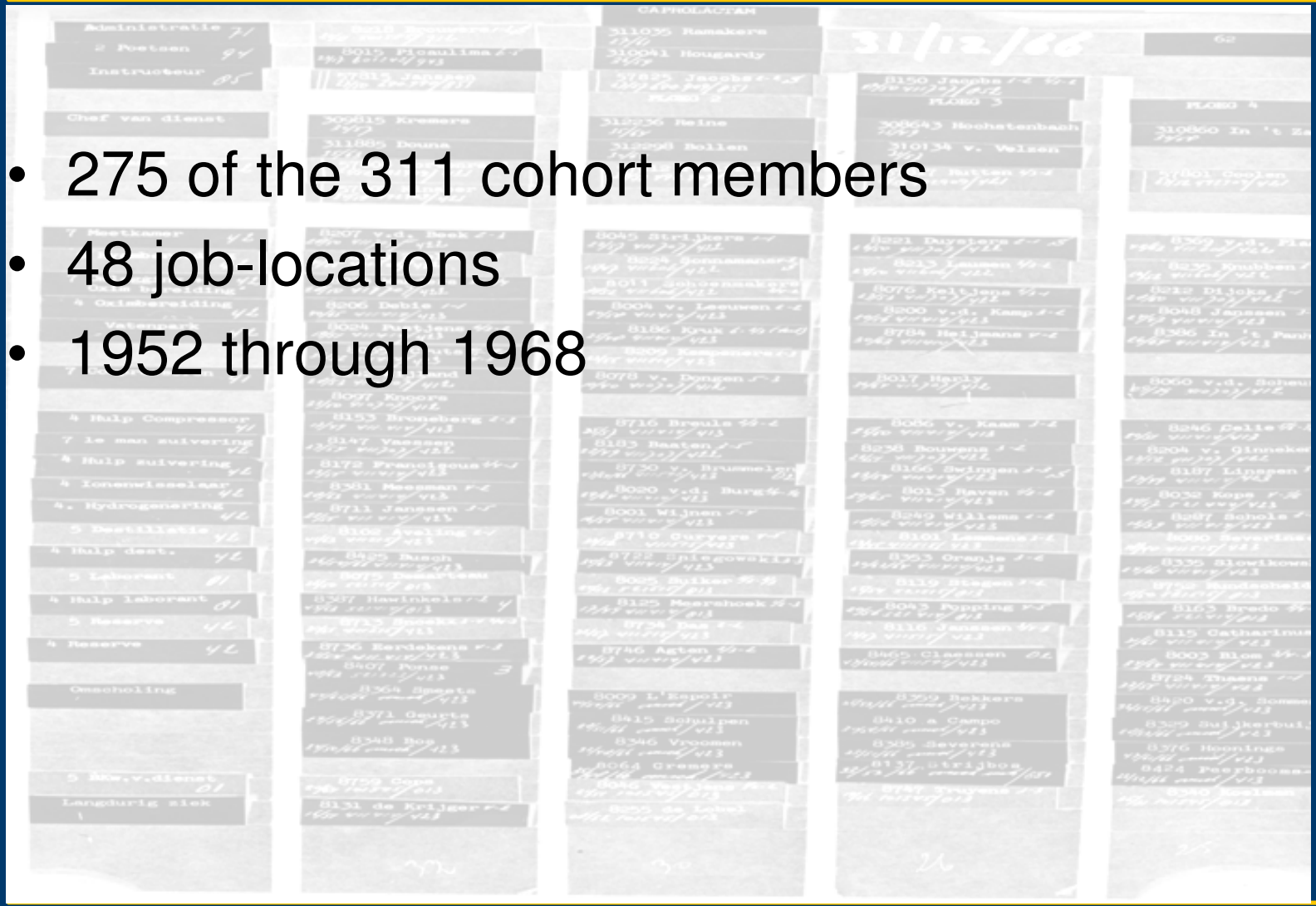
BE estimate on real exposure data



Calculated job exposure (1952-1968)

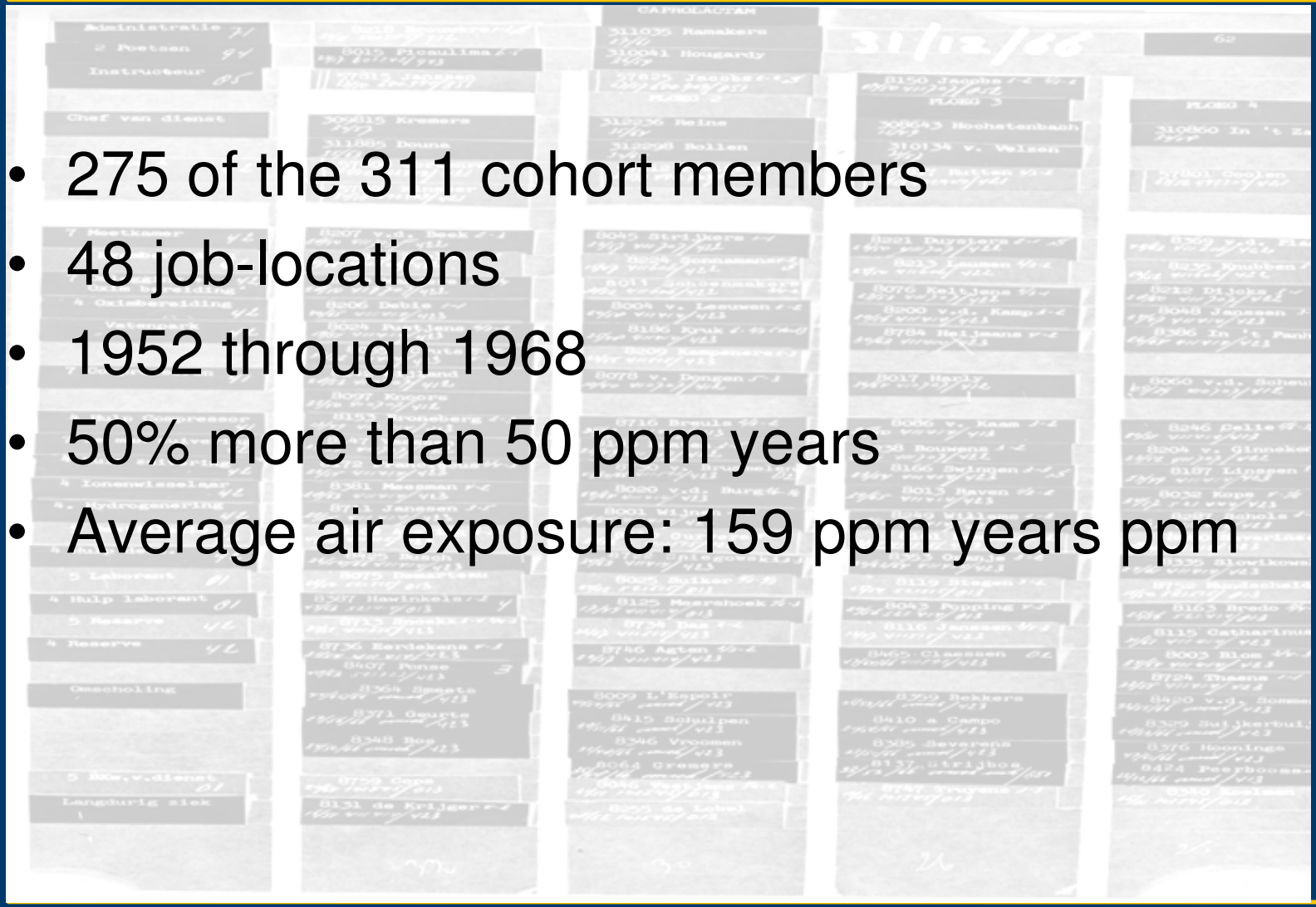


Exposure assessment



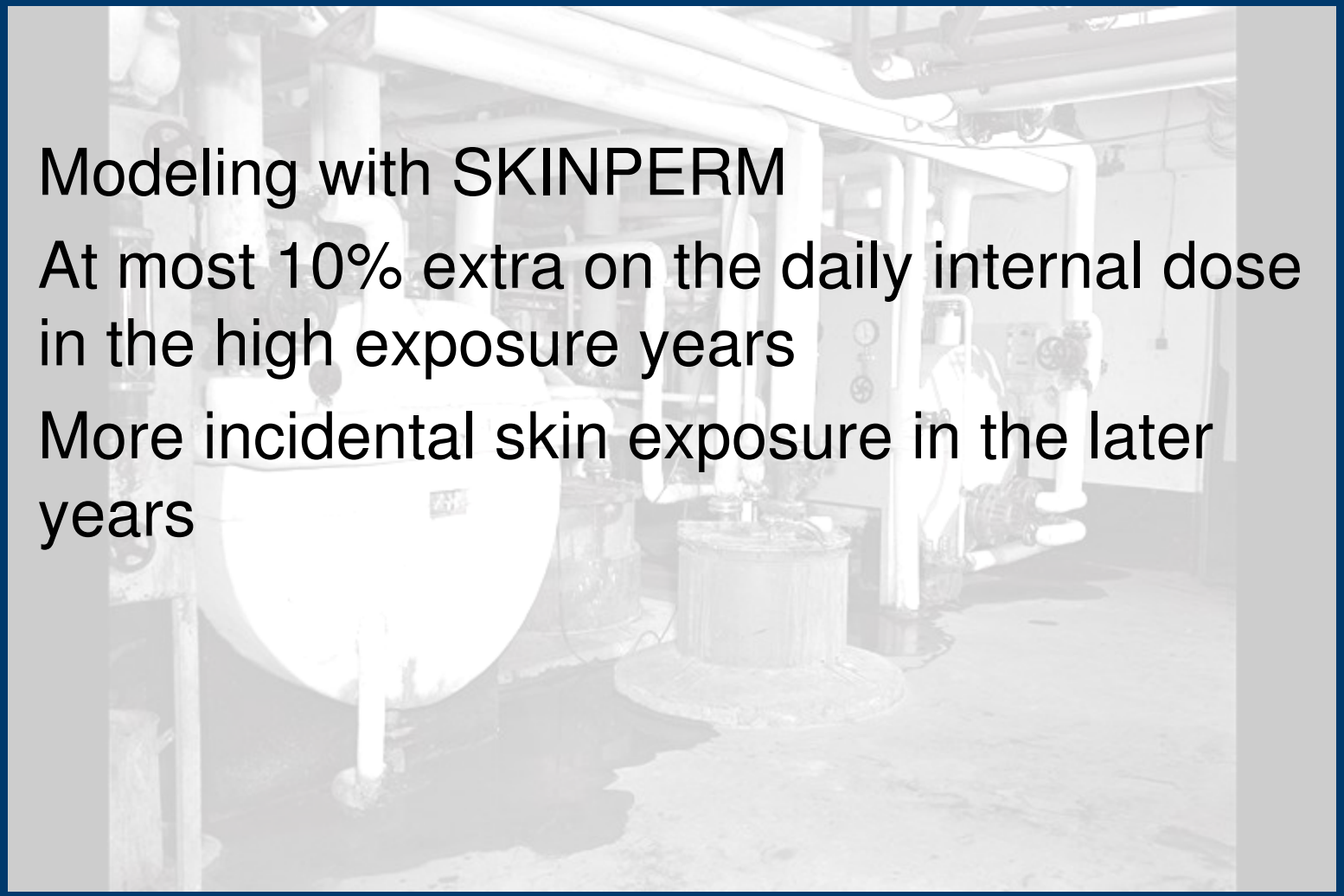
- 275 of the 311 cohort members
- 48 job-locations
- 1952 through 1968

Exposure assessment



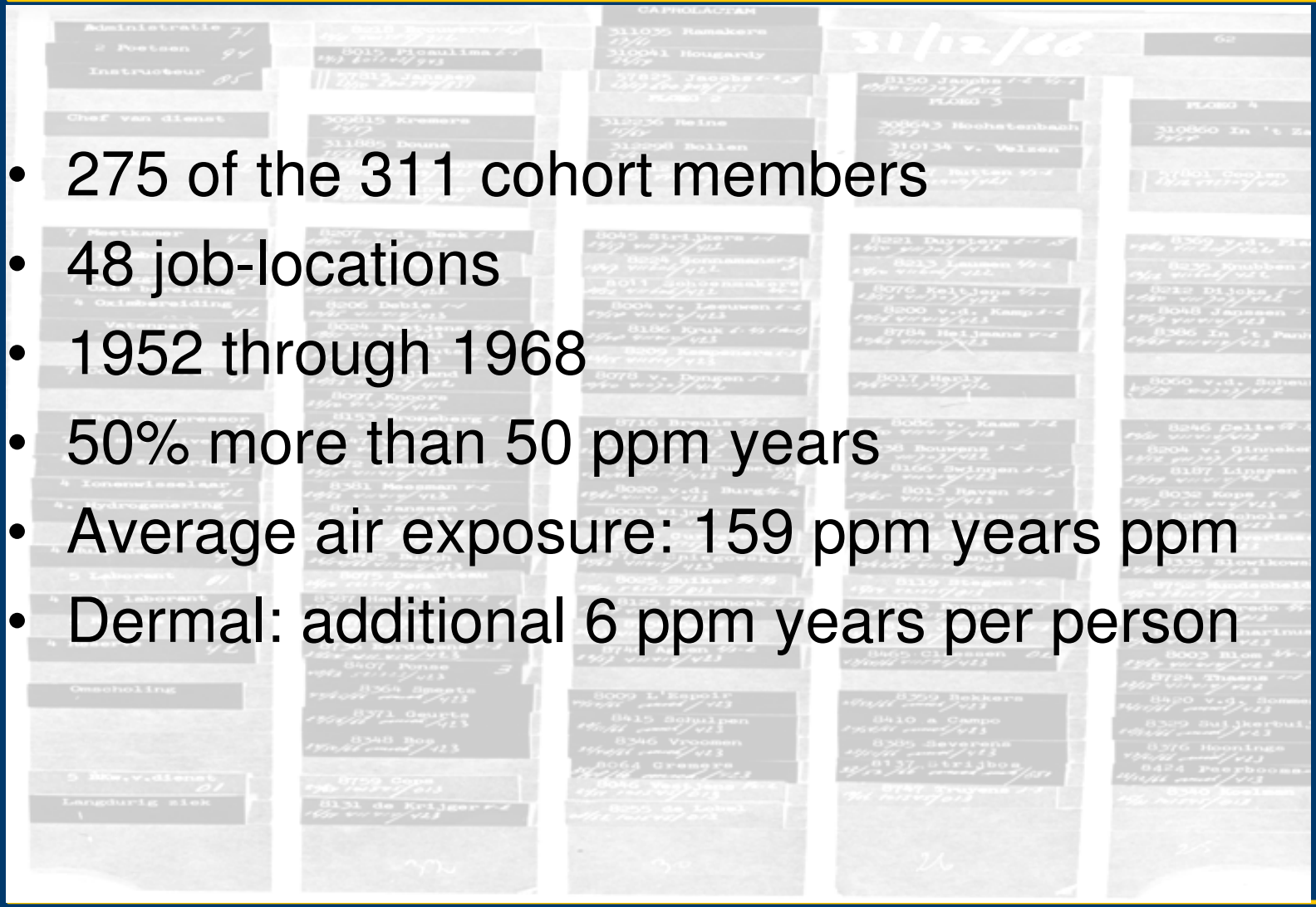
- 275 of the 311 cohort members
- 48 job-locations
- 1952 through 1968
- 50% more than 50 ppm years
- Average air exposure: 159 ppm years ppm

Additional skin exposure



- Modeling with SKINPERM
- At most 10% extra on the daily internal dose in the high exposure years
- More incidental skin exposure in the later years

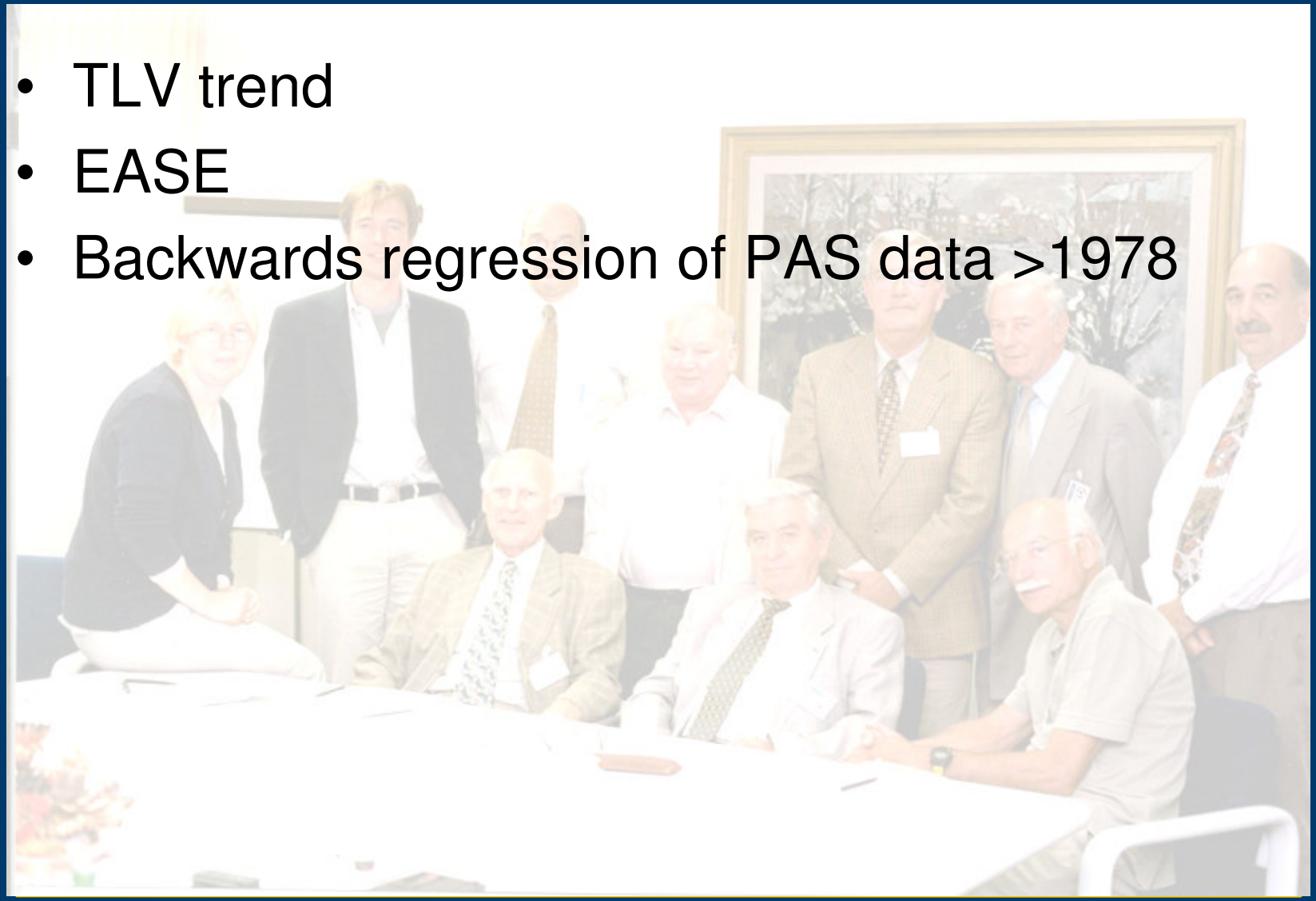
Exposure assessment



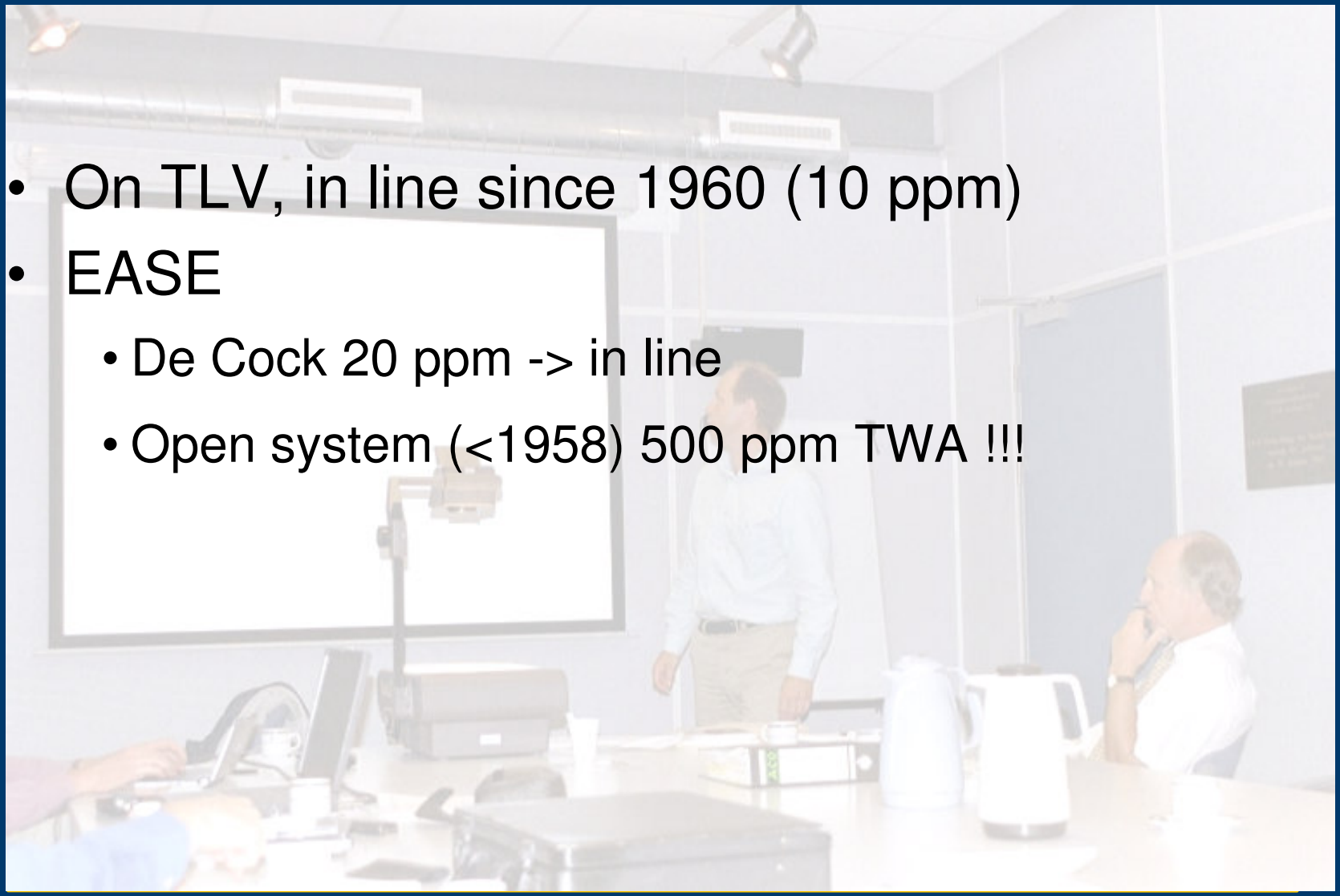
- 275 of the 311 cohort members
- 48 job-locations
- 1952 through 1968
- 50% more than 50 ppm years
- Average air exposure: 159 ppm years ppm
- Dermal: additional 6 ppm years per person

Validation check

- TLV trend
- EASE
- Backwards regression of PAS data >1978

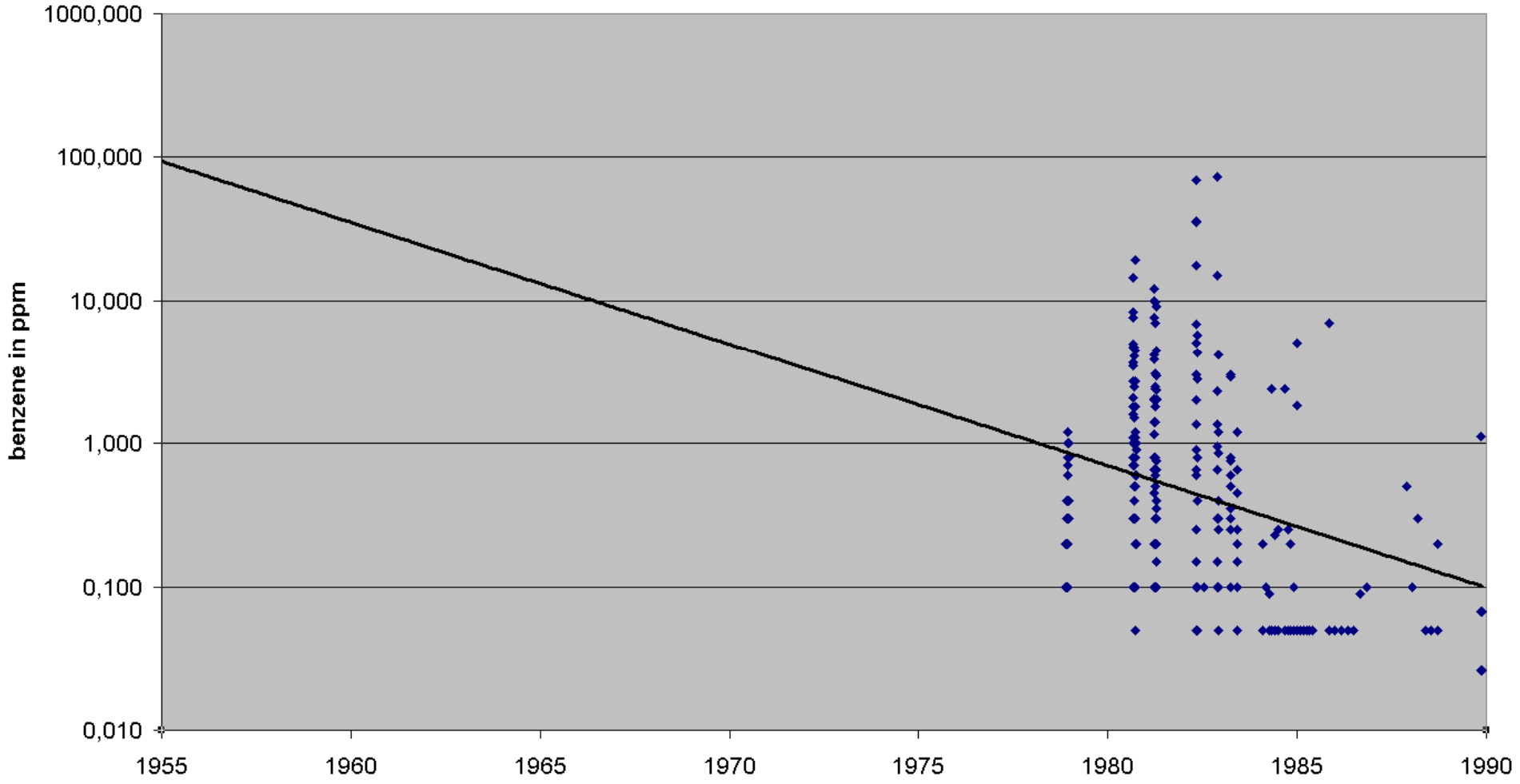


Validation check (1)



- On TLV, in line since 1960 (10 ppm)
- EASE
  - De Cock 20 ppm -> in line
  - Open system (<1958) 500 ppm TWA !!!

Validation check (2) backwards regression



Results

- Exposure assessed for 275 employees
- Cumulative dose 43.735 ppm-years
  - mean 159 ppm-year per person
  - Mean duration 9,6 year (sd 6 & max 18 jaar)
- Impressive reduction over the years
  - 26 ppm (1951) to 0,6 ppm (1968)
  - 47% below 50 ppm-years
  - 28% above 200 ppm-years

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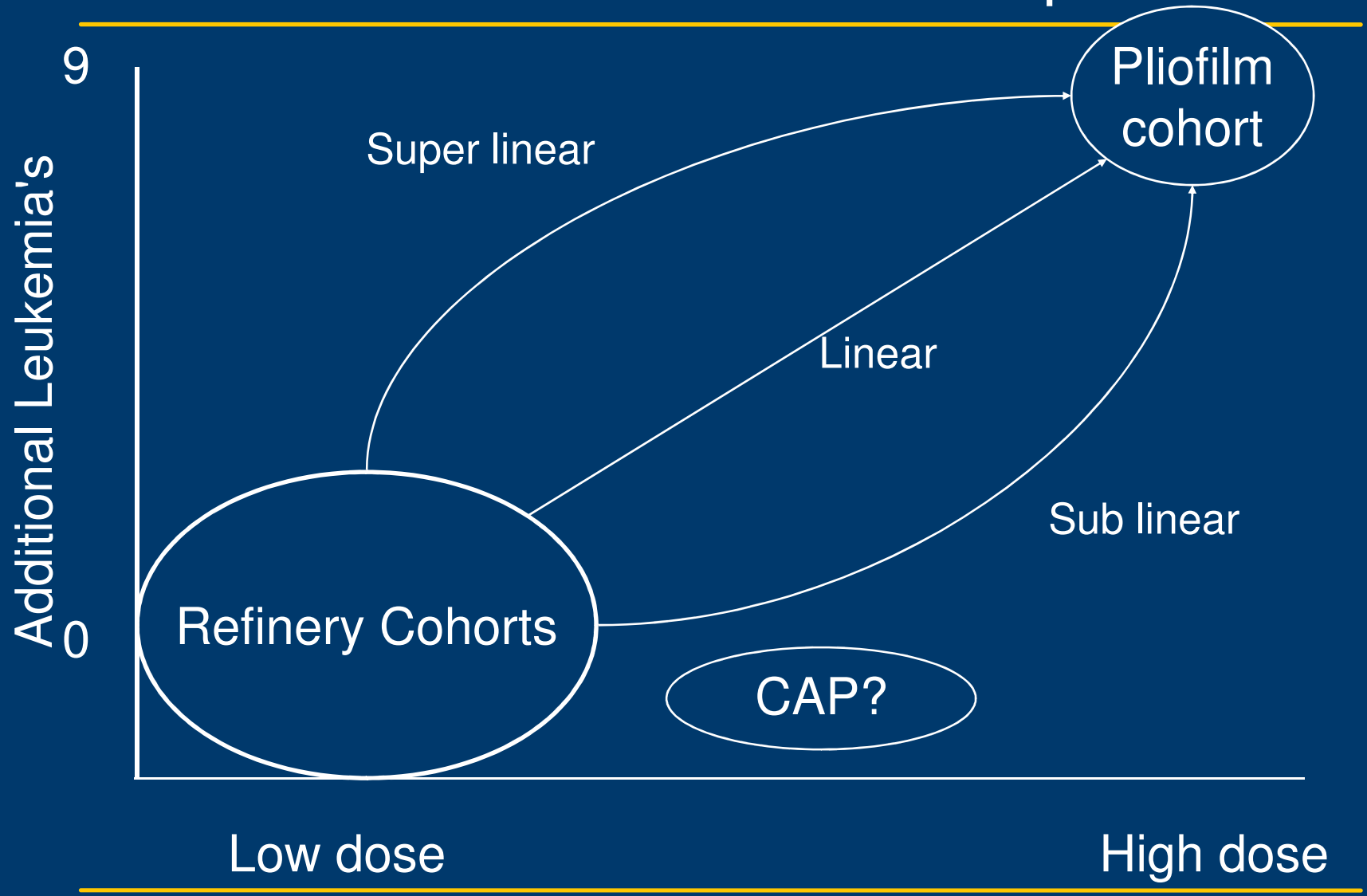

Thank you !

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