# The impact of pharmaceutical innovation on New Zealand cancer patients

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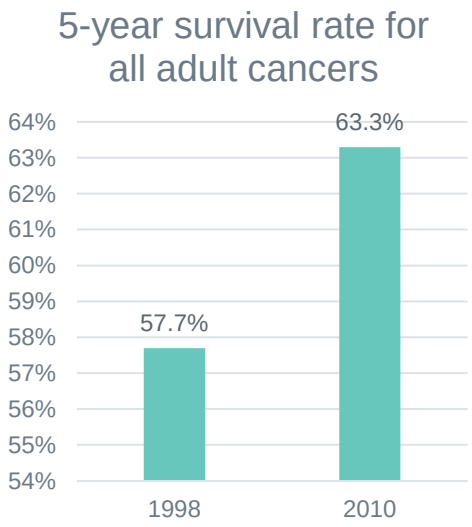
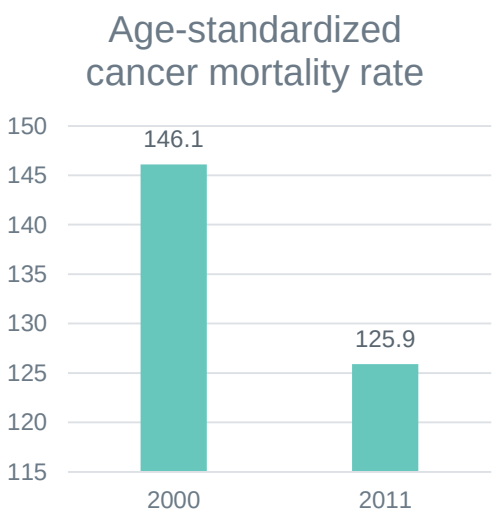
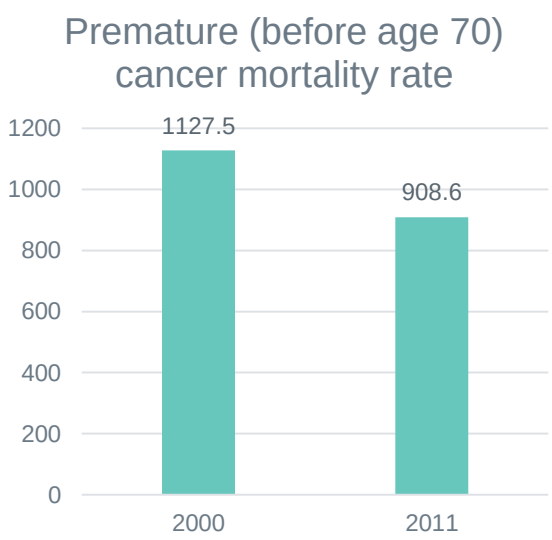
# The longevity of New Zealand cancer patients has increased




The age-standardised cancer incidence rate declined between 2000 and 2011, but by less than half as much (9.3%) as the premature mortality rate

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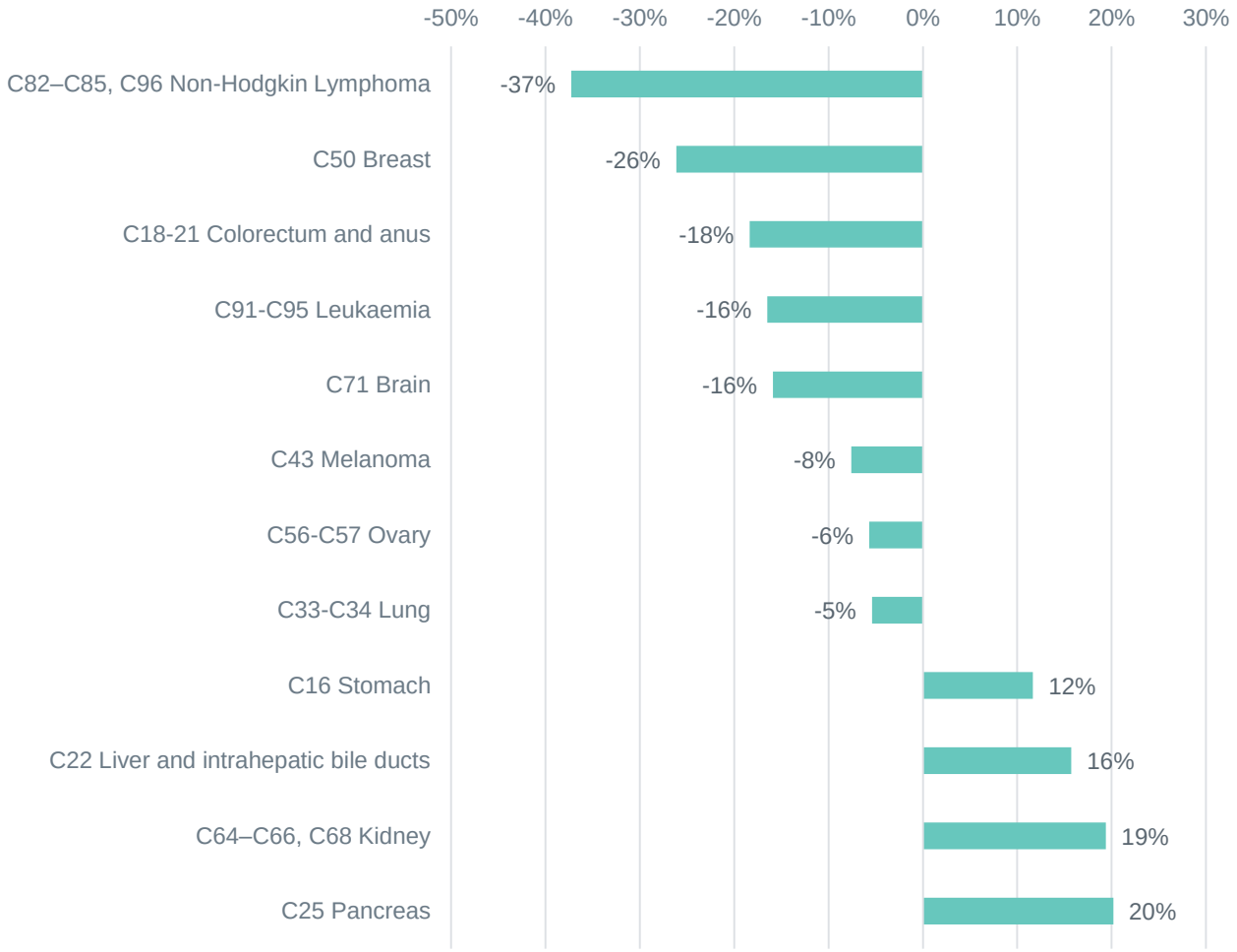
# Change in premature (before age 70) mortality rate, 2000-2011:12 cancers with largest average premature mortality rates

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# Research objective and approach

**Objective**

To analyse the effect that pharmaceutical innovation – the introduction and use of new drugs to treat cancer – had on the longevity and hospitalisation of New Zealand cancer patients during the period 1998-2012

**Research design**

We investigate whether the cancer sites (e.g. breast, prostate, colon) that experienced more pharmaceutical innovation had larger subsequent declines in premature (before age 70 or 65) mortality and hospitalisation rates and larger subsequent increases in 5-year survival rates, controlling for changes in incidence.

# Drugs for treating 3 different types of cancer approved in New Zealand

## C18-21 Colorectum and anus

| | |
|---|---|
| BETAMETHASONE | 1963 |
| DEXAMETHASONE | 1968 |
| CALCIUM FOLINATE | 1969 |
| METHYLPREDNISOLONE | 1969 |
| FLUOROURACIL | 1971 |
| DALTEPARIN | 1987 |
| ERYTHROPOIETIN | 1990 |
| FLUCONAZOLE | 1990 |
| IRINOTECAN | 1997 |
| DARBEPOETIN ALFA | 2001 |
| ZOLEDRONIC ACID | 2001 |
| CAPECITABINE | 2002 |
| OXALIPLATIN | 2004 |
| CETUXIMAB | 2006 |
| BEVACIZUMAB | 2009 |
| MITOMYCIN | 2010 |

## C43 Melanoma

| | |
|---|---|
| BETAMETHASONE | 1963 |
| DEXAMETHASONE | 1968 |
| CALCIUM FOLINATE | 1969 |
| METHYLPREDNISOLONE | 1969 |
| CARMUSTINE | 1975 |
| DACARBAZINE | 1976 |
| LOMUSTINE | 1980 |
| INTERFERON ALFA-2A | 1986 |
| INTERFERON ALFA-2B | 1986 |
| DALTEPARIN | 1987 |
| ERYTHROPOIETIN | 1990 |
| FLUCONAZOLE | 1990 |
| FOTEMUSTINE | 1991 |
| DARBEPOETIN ALFA | 2001 |
| ZOLEDRONIC ACID | 2001 |
| IPILIMUMAB | 2012 |

## C64-C66, C68 Kidney

| | |
|---|---|
| CALCIUM FOLINATE | 1969 |
| DACTINOMYCIN | 1969 |
| METHYLPREDNISOLONE | 1969 |
| VINBLASTINE | 1969 |
| VINCRISTINE | 1969 |
| INTERFERON ALFA-2A | 1986 |
| DALTEPARIN | 1987 |
| ERYTHROPOIETIN | 1990 |
| FLUCONAZOLE | 1990 |
| DARBEPOETIN ALFA | 2001 |
| ZOLEDRONIC ACID | 2001 |
| BEVACIZUMAB | 2009 |
| PAZOPANIB | 2010 |

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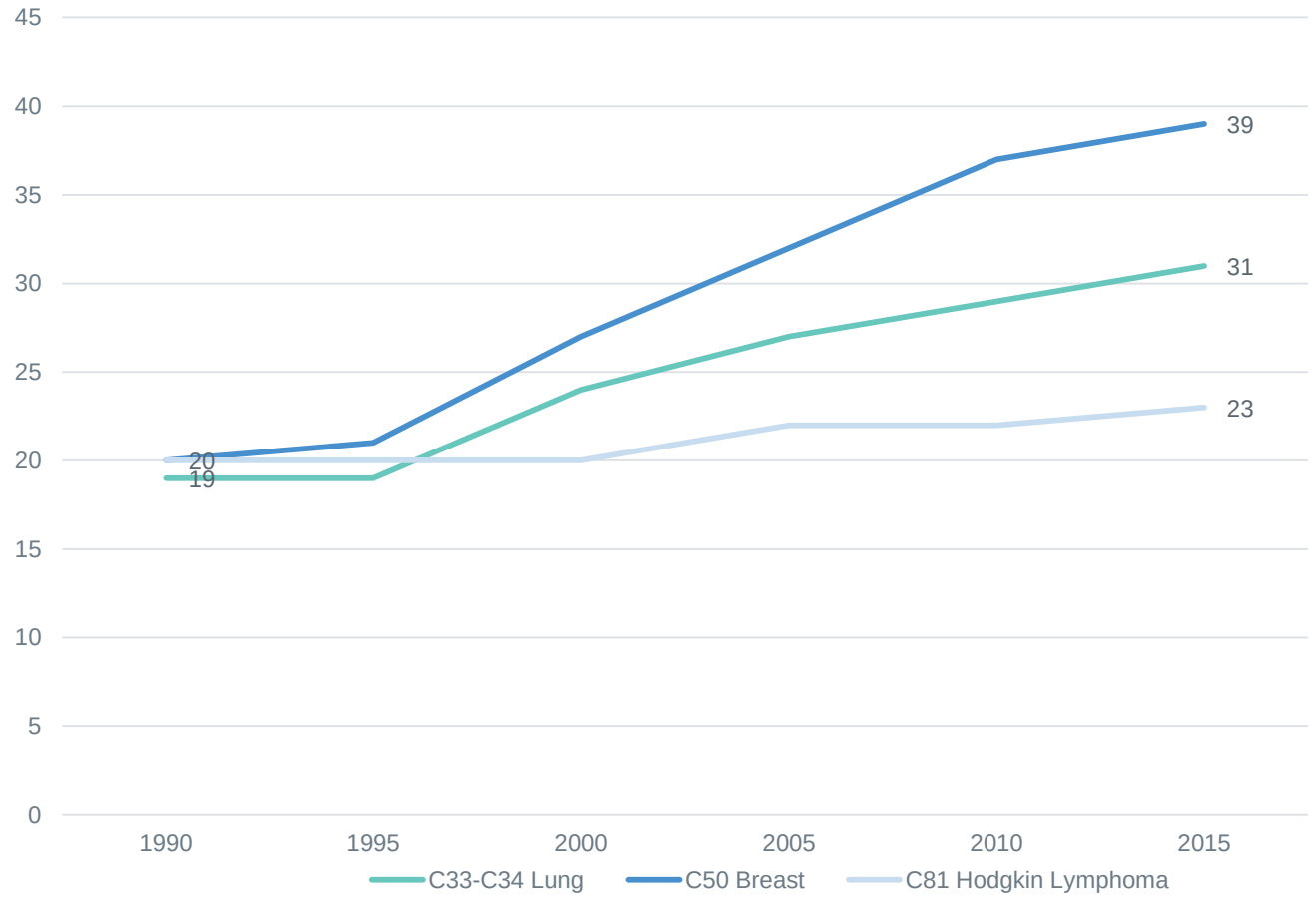
# Number of drugs approved in New Zealand for treating 3 types of cancer, 5-year intervals, 1990-2015

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$$OUTCOME_{s,t} = \beta_k\ CUM\_NCE_{s,t-k} + \gamma\ \ln(INCIDENCE_{s,t}) + \alpha_s + \delta_t + \varepsilon_{s,t}$$

**where $OUTCOME_{s,t}$ is one of the following variables:**

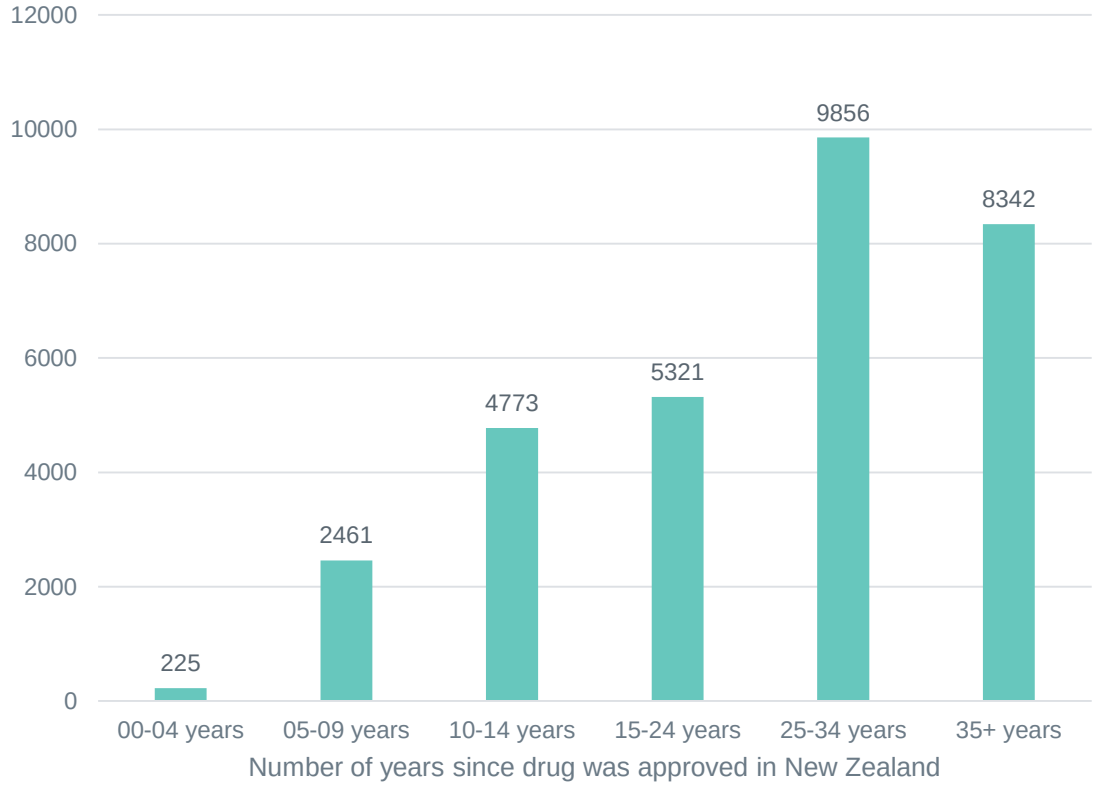
| | |
|---|---|
| $\ln(YPLL70_{s,t})$ | = the log of the number of years of potential life lost before age 70 due to cancer at site s in year t (t = 2000, 2011) |
| $\ln(YPLL65_{s,t})$ | = the log of the number of years of potential life lost before age 65 due to cancer at site s in year t (t = 2000, 2011) |
| $\ln(SURV5\%_{s,t}/(1 - SURV5\%_{s,t}))$ | = the log-odds of surviving at least 5 years after diagnosis with cancer at site s in year t (t = 1998, 2010) |
| $\ln(HOSP\_DAYS_{s,t})$ | = the log of the number of publicly-funded inpatient hospital days for cancer at site s in year t (t = 2004, 2012) |

$$OUTCOME_{s,t} = \beta_k\ CUM\_NCE_{s,t-k} + \gamma\ ln(INCIDENCE_{s,t}) + \alpha_s + \delta_t + \varepsilon_{s,t}$$

| | |
|---|---|
| $CUM\_NCE_{s,t-k}$ | $= \sum_d IND_{ds}\ APPROVED_{d,t-k}$ = the number of new chemical entities (drugs) to treat cancer at site s that had been approved in New Zealand by the end of year t-k |
| $IND_{ds}$ | = 1 if drug d is used to treat (indicated for) cancer at site s<br>= 0 if drug d is not used to treat (indicated for) cancer at site s |
| $APPROVED_{d,t-k}$ | = 1 if drug d was approved in New Zealand by the end of year t-k<br>= 0 if drug d was not approved in New Zealand by the end of year t-k |
| $INCIDENCE_{s,t}$ | = the average annual number of patients diagnosed with cancer at site s in years t-10 to year t |
| $\alpha_s$ | = a fixed effect for cancer at site s |
| $\delta_t$ | = a fixed effect for year t |

# Average utilization of new drugs is much lower than average utilization of older drugs

## The entire cost of very new drugs is borne entirely by patients




## 23.7 months

The mean lag between regulatory approval of a drug in New Zealand and its inclusion in the New Zealand Pharmaceutical Schedule (a list of the prescription medicines and therapeutic products subsidised by the Government) is **23.7 months**

Barber and Sheehy 2015

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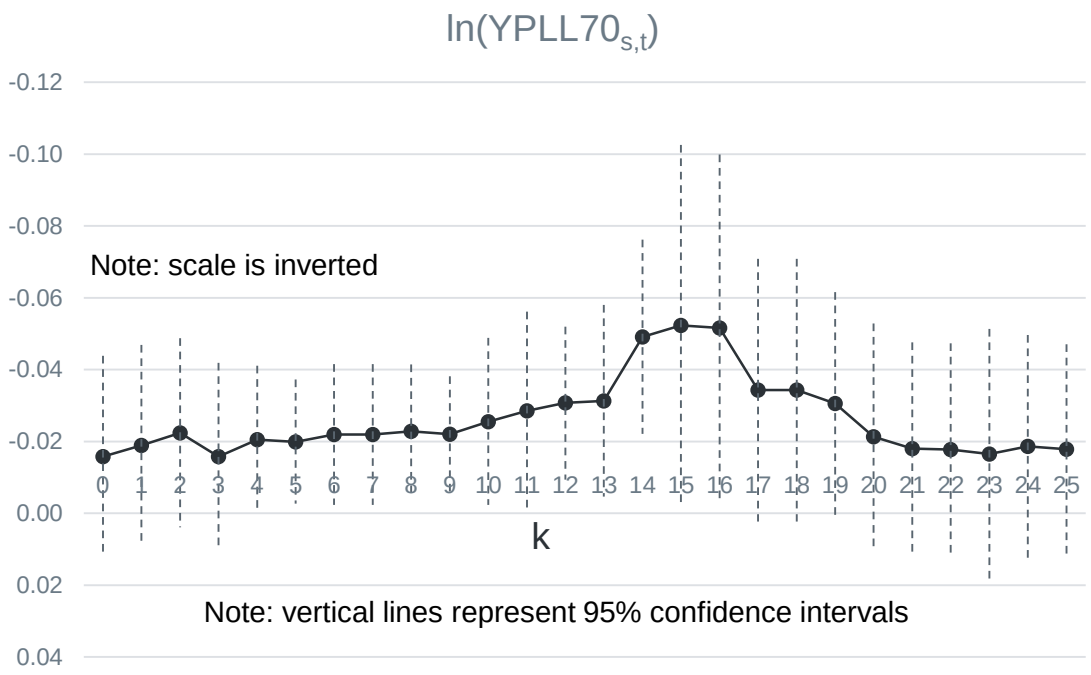
# Effect of number of drugs approved by the end of year t-k on potential years of life lost before age 70 in year 7




Premature (before age 70) mortality is inversely related to the number of drugs approved 5 to 16 years earlier

Premature mortality is most strongly inversely related to the number of drugs approved 14 years earlier

Approval of one additional drug for a cancer site reduces premature mortality from cancer at that site by about 5% 14 years later

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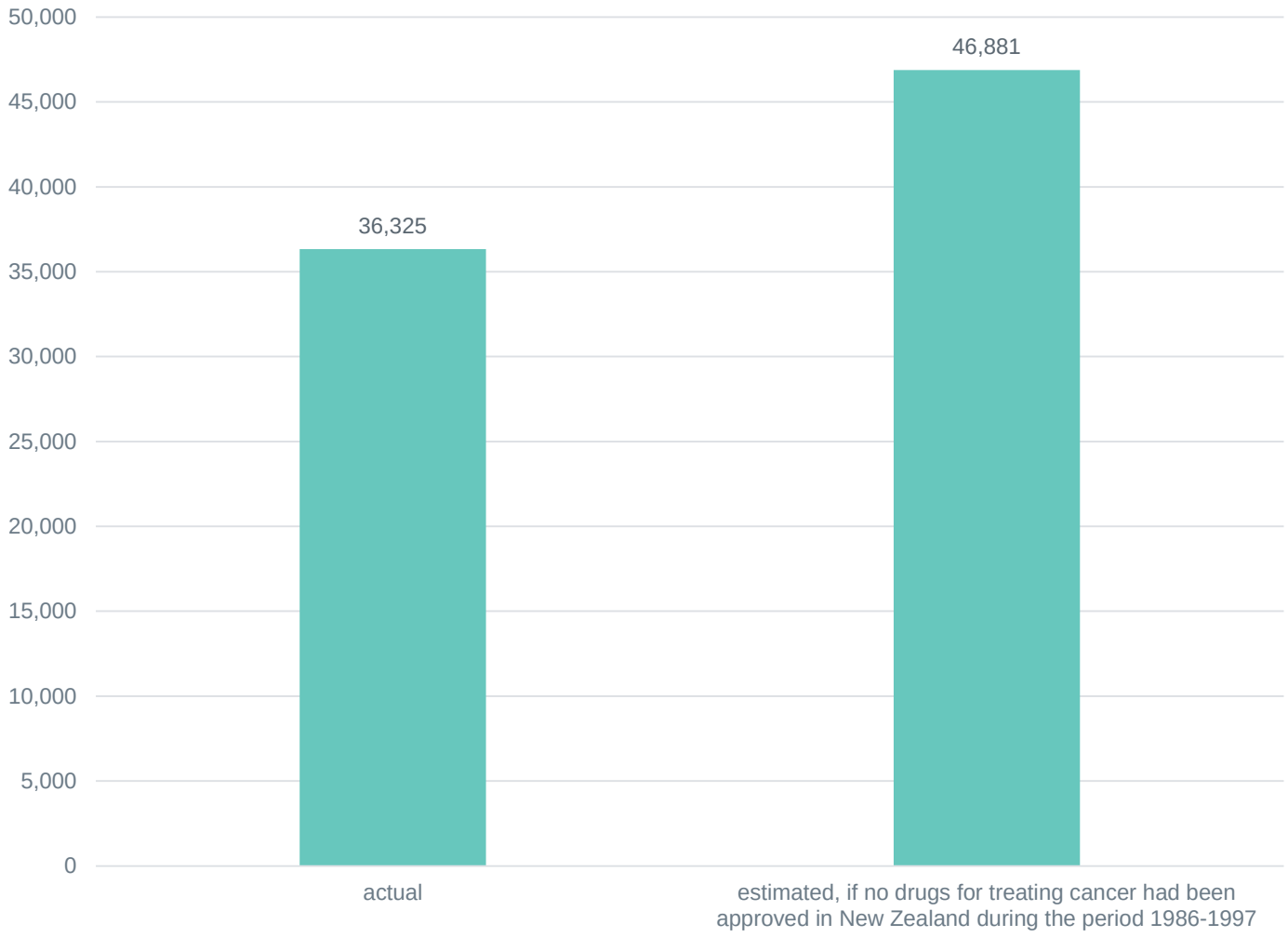
# Potential years of life lost to cancer before age 70 in 2011

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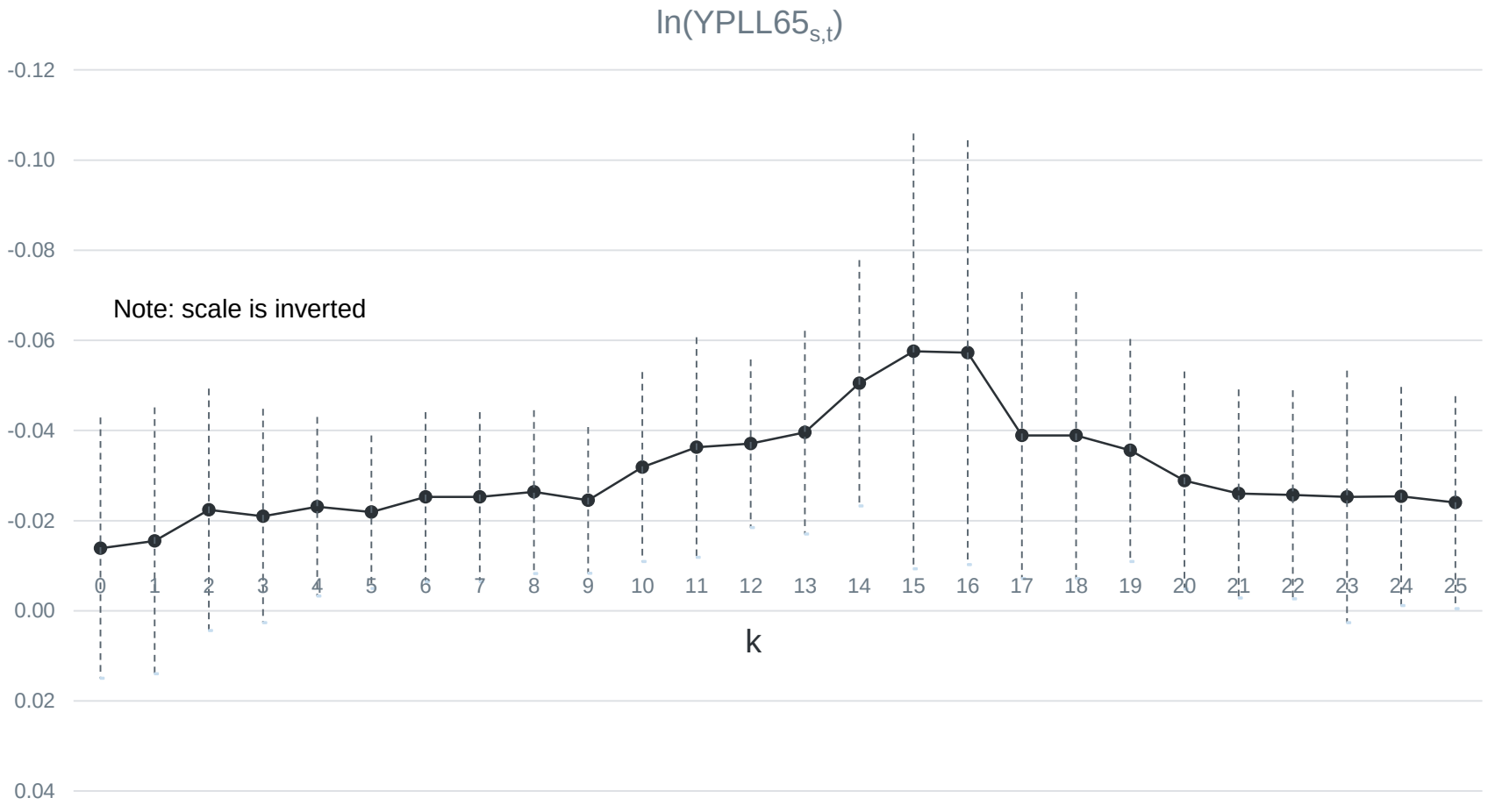
# Effect of number of drugs approved by the end of year t-k on potential years of life lost before age 65 in year t

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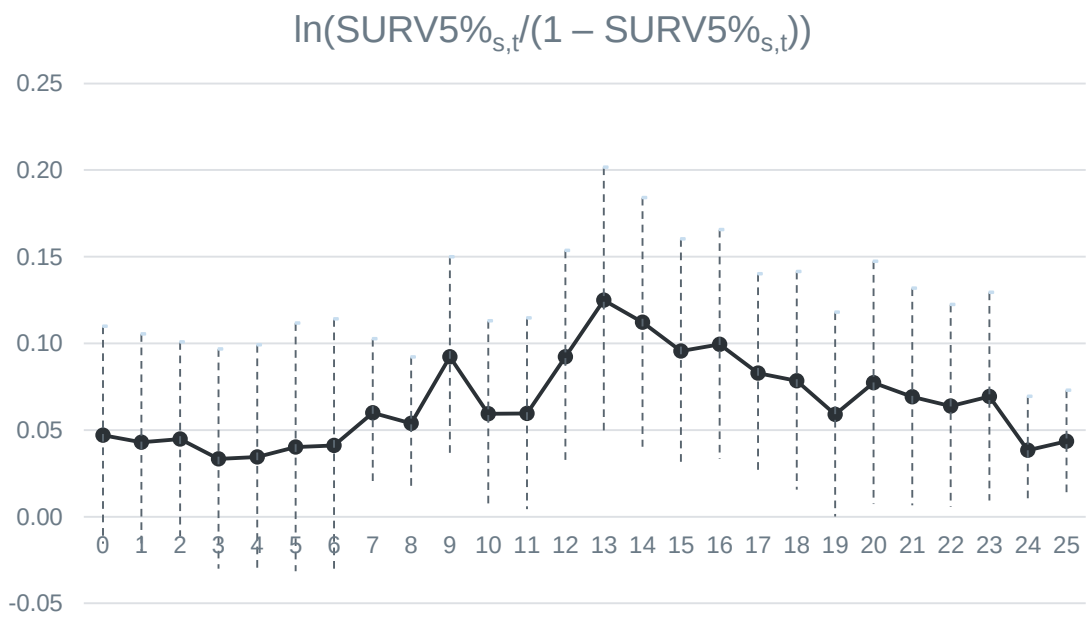
# Effect of number of drugs approved by the end of year t-k on odds of surviving 5 years from diagnosis in year t




The 5-year survival rate is significantly positively related to the number of drugs approved 7 to 25 years earlier, and is most strongly positively related to the number of drugs approved 13 years earlier

Between 1998 and 2010, the 5-year survival rate for all adult cancers increased from 57.7% to 63.3%. The estimates indicate that if no new drugs had been approved during 1985-1997, the 5-year survival rate would not have increased between 1998 and 2010.

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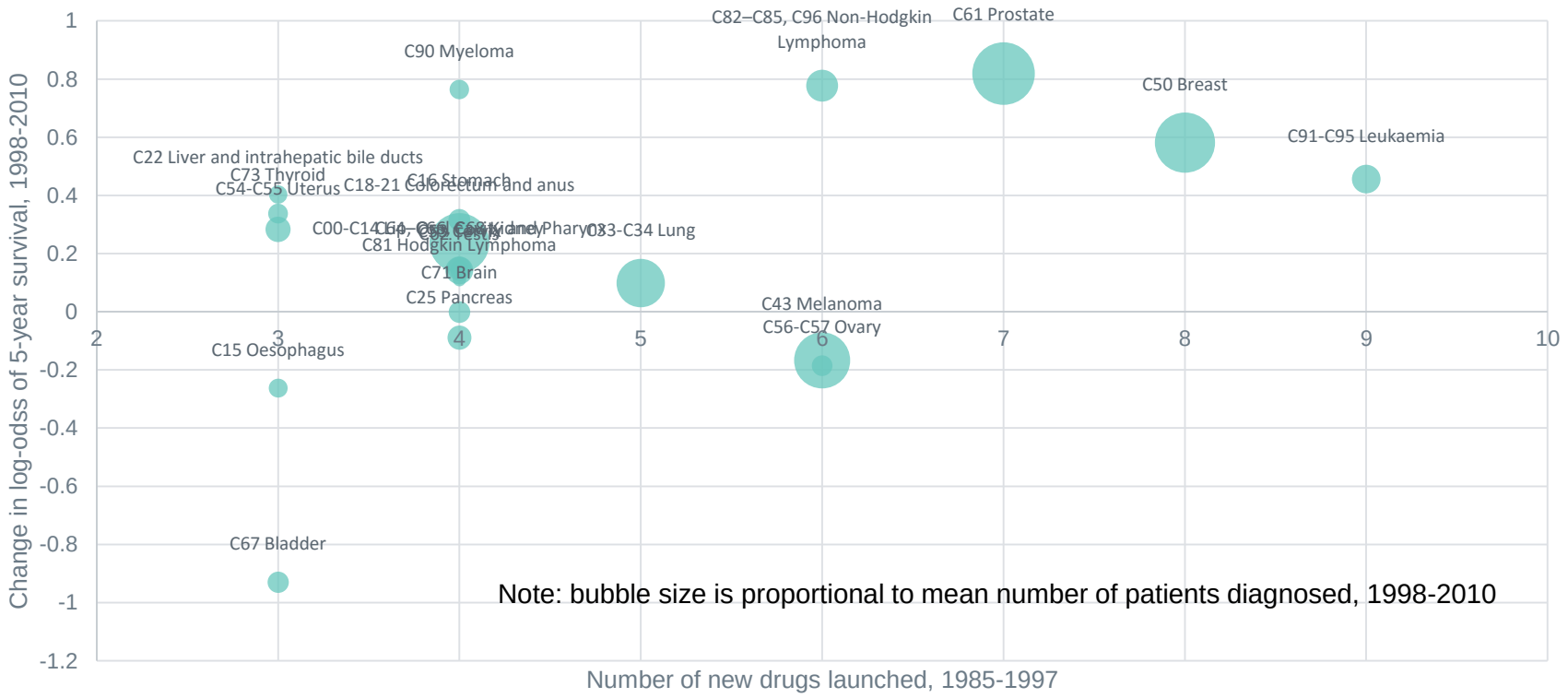
# Relationship across cancer sites between number of new drugs approved during 1985-1997 and the 1998-2010 change in log-odds of 5-year survival

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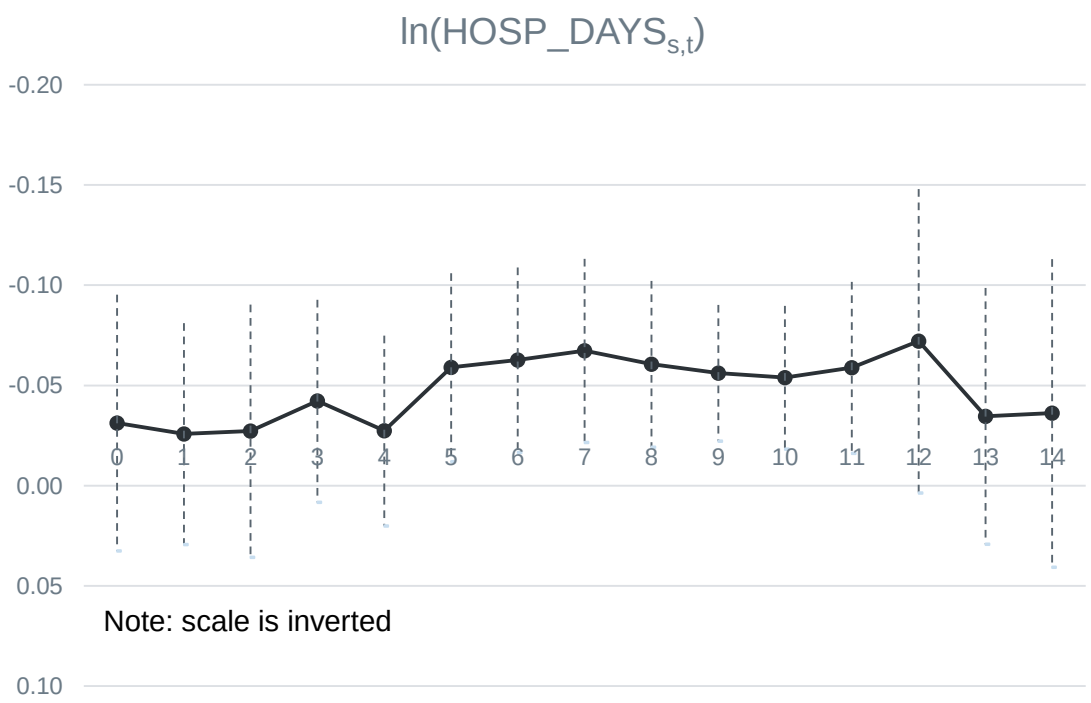
# Effect of number of drugs approved by the end of year t-k on number of hospital days in year t




The number of publicly-funded hospital days is significantly inversely related to the number of drugs ever approved 5 to 11 years earlier; it is most strongly inversely related to the number of drugs ever approved 9 years earlier

The approval of one additional drug for a cancer site is estimated to reduce the number of publicly-funded inpatient hospital days for cancer at that site by about 5.6% 9 years later.

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# Annual public price of all cancers registered with the New Zealand Cancer Registry in 2008

| | Cost (millions) | % of total |
|---|---|---|
| Public hospital discharges | $215 | 42% |
| Outpatient attendance | $112 | 22% |
| Community and hospital pharmacy dispensing | $51 | 10% |
| Other | $133 | 26% |
| Total | $511 | 100% |

In 2008, the cost of public hospital discharges was 4.2 times as great as the cost of pharmacy dispensing

This implies that a 5.6% decrease in hospital costs would offset a 23.6% increase in pharmacy costs.

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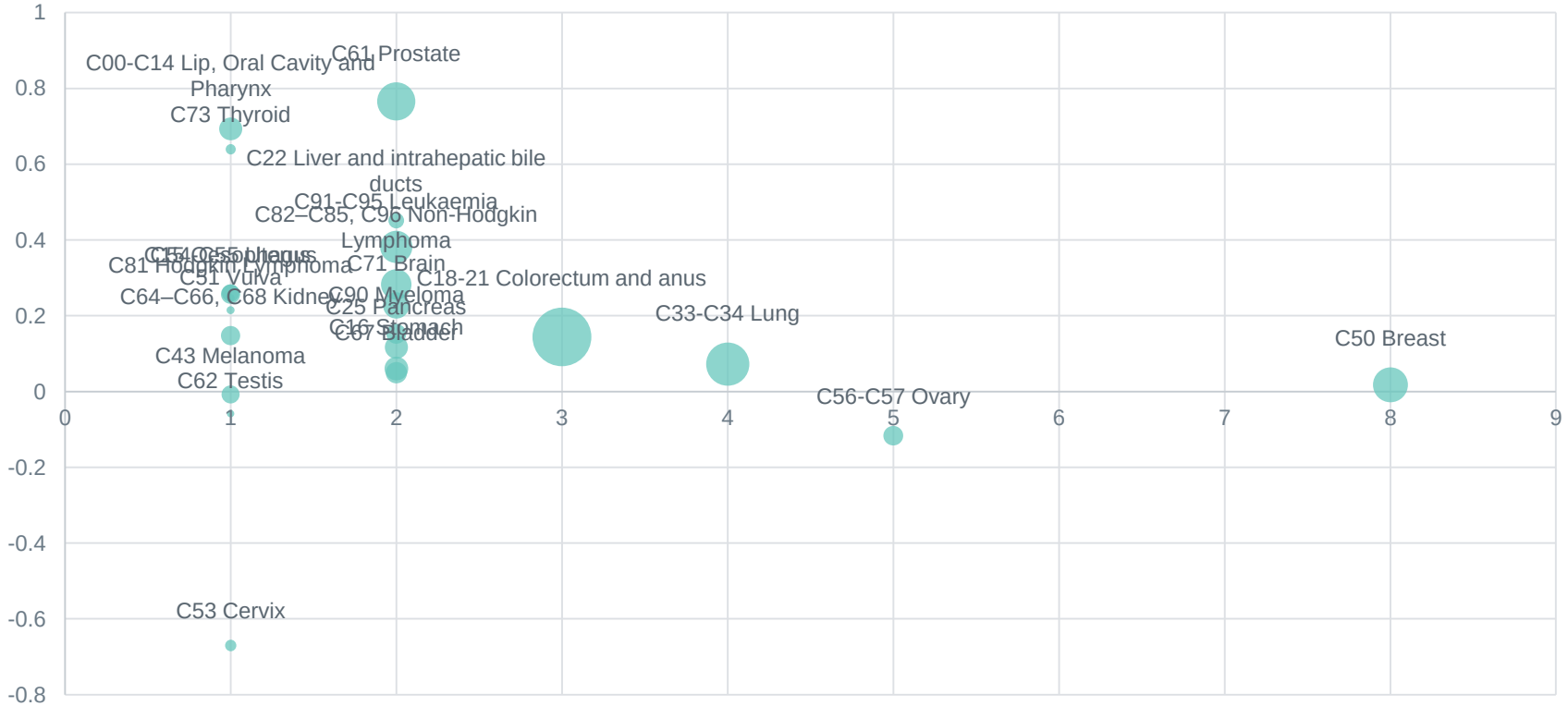
# Relationship across cancer sites between number of new drugs approved during 1995-2003 and the 2004-2012 log changes in the number of publicly-funded inpatient hospital days

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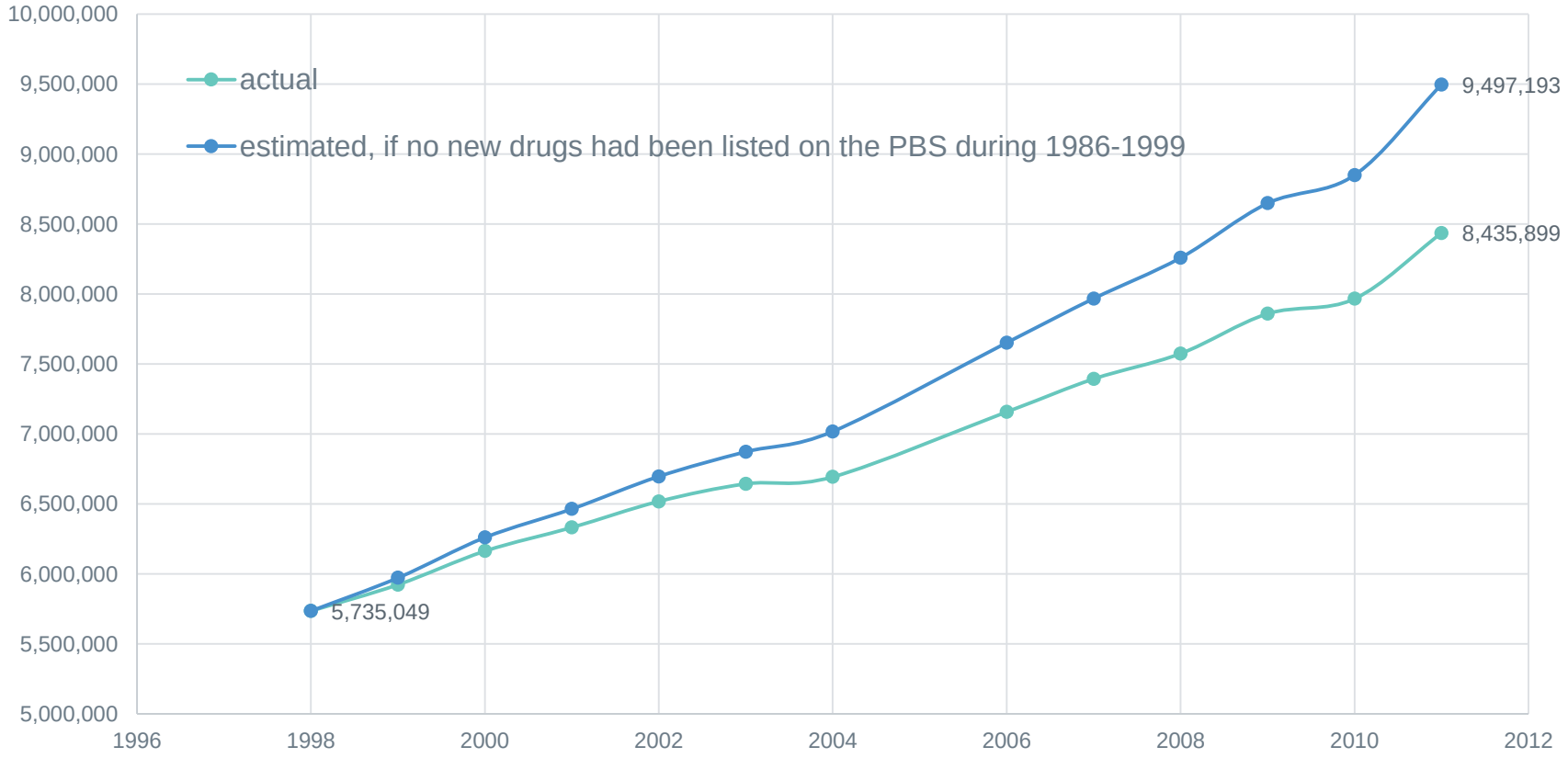
# Number of hospital discharges in Australia, 1998-2011: actual vs estimated, if no new drugs had been listed on the PBS during 1986-1999

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# Estimates of the effects of the number of drugs, the number of chemical subgroups, or both, on outcomes

| Model | | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Dependent variable | | ln($YPLL70_{s,t}$) | | | ln($YPLL65_{s,t}$) | | | ln($SURV5\%_{s,t}$/(1 – $SURV5\%_{s,t}$)) | | | ln($HOSP\_DAYS_{s,t}$) | | |
| Lag (years) | | 14 | | | 14 | | | 13 | | | 9 | | |
| $CUM\_NCE_{s,t-k}$ | Estimate | **-0.049** | | **-0.048** | **-0.051** | | **-0.062** | **0.125** | | **0.099** | **-0.056** | | -0.022 |
| | Z | **-3.56** | | **-2.32** | **-3.63** | | **-3.46** | **3.20** | | **3.32** | **-3.23** | | -1.02 |
| | Pr > \|Z\| | **0.000** | | **0.020** | **0.000** | | **0.001** | **0.001** | | **0.001** | **0.001** | | 0.310 |
| | | | | | | | | | | | | | |
| $CUM\_SUBGROUP_{,t-k}$ | Estimate | | **-0.086** | -0.006 | | -0.066 | 0.043 | | **0.411** | 0.232 | | -0.131 | -0.101 |
| | Z | | **-2.51** | -0.13 | | -1.57 | 0.96 | | **2.35** | 1.76 | | -1.92 | -1.16 |
| | Pr > \|Z\| | | **0.012** | 0.898 | | 0.117 | 0.335 | | **0.019** | 0.078 | | 0.055 | 0.245 |

Overall, the estimates suggest that drugs (chemical substances) within the same class (chemical subgroup) are not “therapeutically equivalent,” i.e. they do not have essentially the same effect in the treatment of a disease or condition

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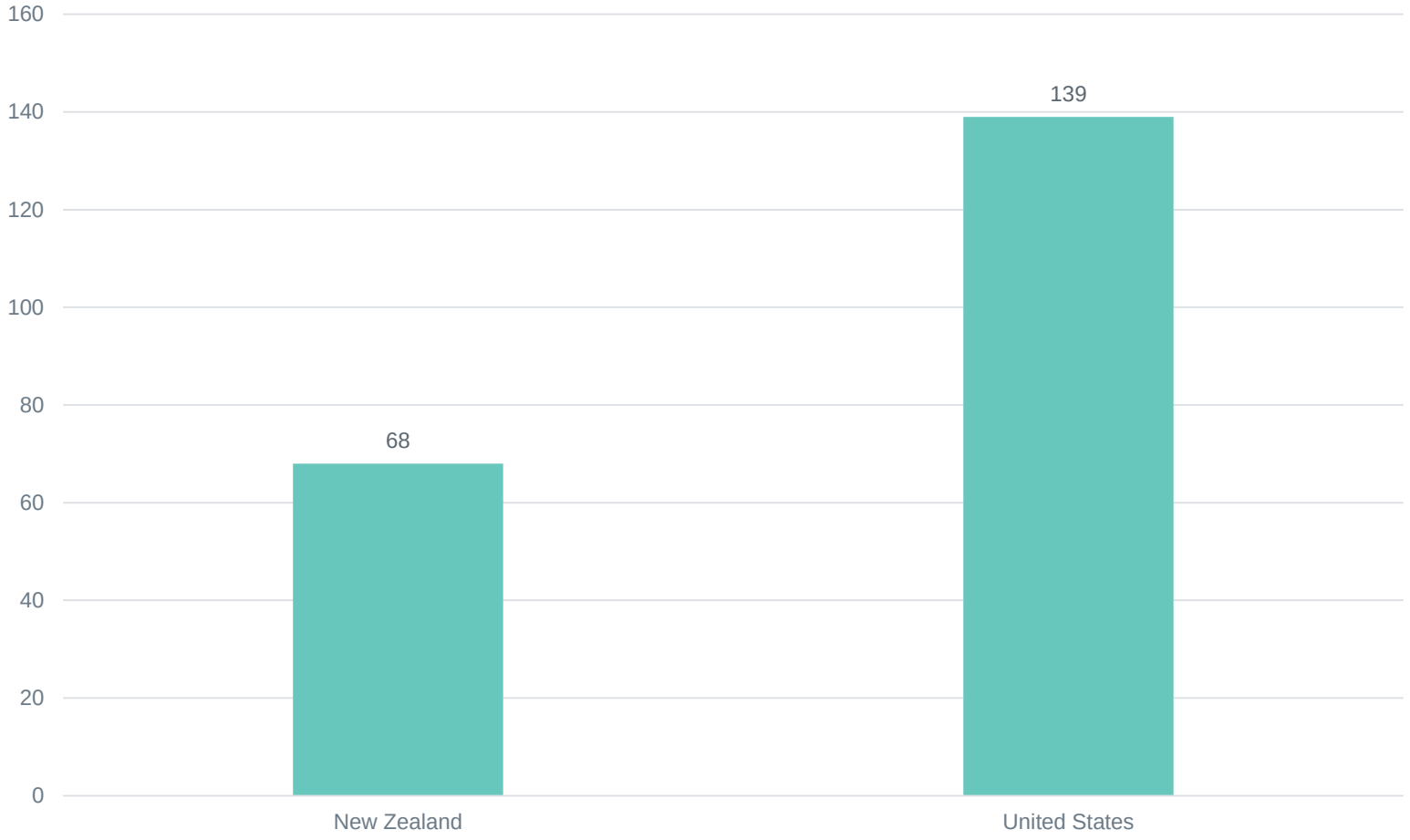
# Number of new cancer drugs launched, 1986-2015

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# Estimates of the effects of drug approvals on US premature (before age 75) cancer mortality

| Model | Parameter | Estimate | Standard Error | Z | Pr > \|Z\| |
|---|---|---|---|---|---|
| 1 | cum_drug (all drugs) | -0.0239 | 0.0061 | -3.93 | <.0001 |
| | | | | | |
| 2 | cum_nz (drugs launched in both the U.S. and NZ) | -0.0246 | 0.0122 | -2.03 | 0.0428 |
| 2 | cum_not_nz (drugs launched in the U.S. and not launched in NZ) | -0.0236 | 0.0068 | -3.48 | 0.0005 |

In general, the drugs that were not launched in New Zealand were no less valuable than the drugs that were launched in New Zealand

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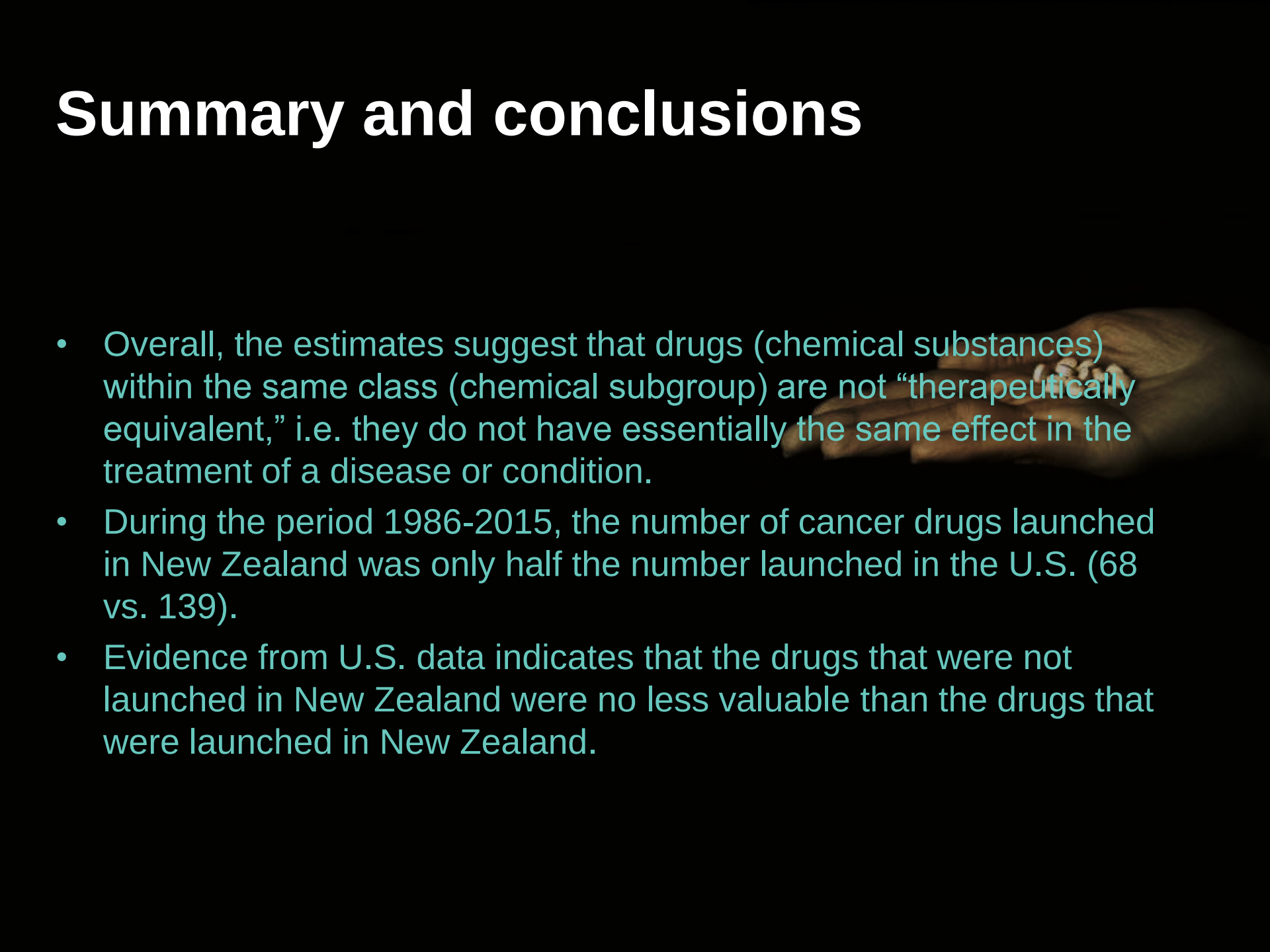
# Summary and conclusions

- Between 1998 and 2010, the 5-year survival rate for all adult cancers increased from 57.7% to 63.3%. The estimates indicate that if no new drugs had been approved during 1985-1997, the 5-year survival rate would not have increased between 1998 and 2010.
- Drugs for treating cancer that were approved in New Zealand during the period 1986-1997 are estimated to have reduced the number of life-years lost to cancer before age 70 in 2011 by 10,556.
- Even if we don't account for the apparent reduction in hospital utilization, the cost per life-year gained from previous pharmaceutical innovation (< $500) is well below the vast majority of estimates from the value-of-life literature of the value of a life-year.
- When the reduction in hospital utilization is taken into account, the evidence indicates that pharmaceutical innovation was cost-saving.

# Summary and conclusions



- Overall, the estimates suggest that drugs (chemical substances) within the same class (chemical subgroup) are not “therapeutically equivalent,” i.e. they do not have essentially the same effect in the treatment of a disease or condition.
- During the period 1986-2015, the number of cancer drugs launched in New Zealand was only half the number launched in the U.S. (68 vs. 139).
- Evidence from U.S. data indicates that the drugs that were not launched in New Zealand were no less valuable than the drugs that were launched in New Zealand.

# Pharmaceutical innovation also reduces disability and increases ability to work:

## evidence based on U.S. data

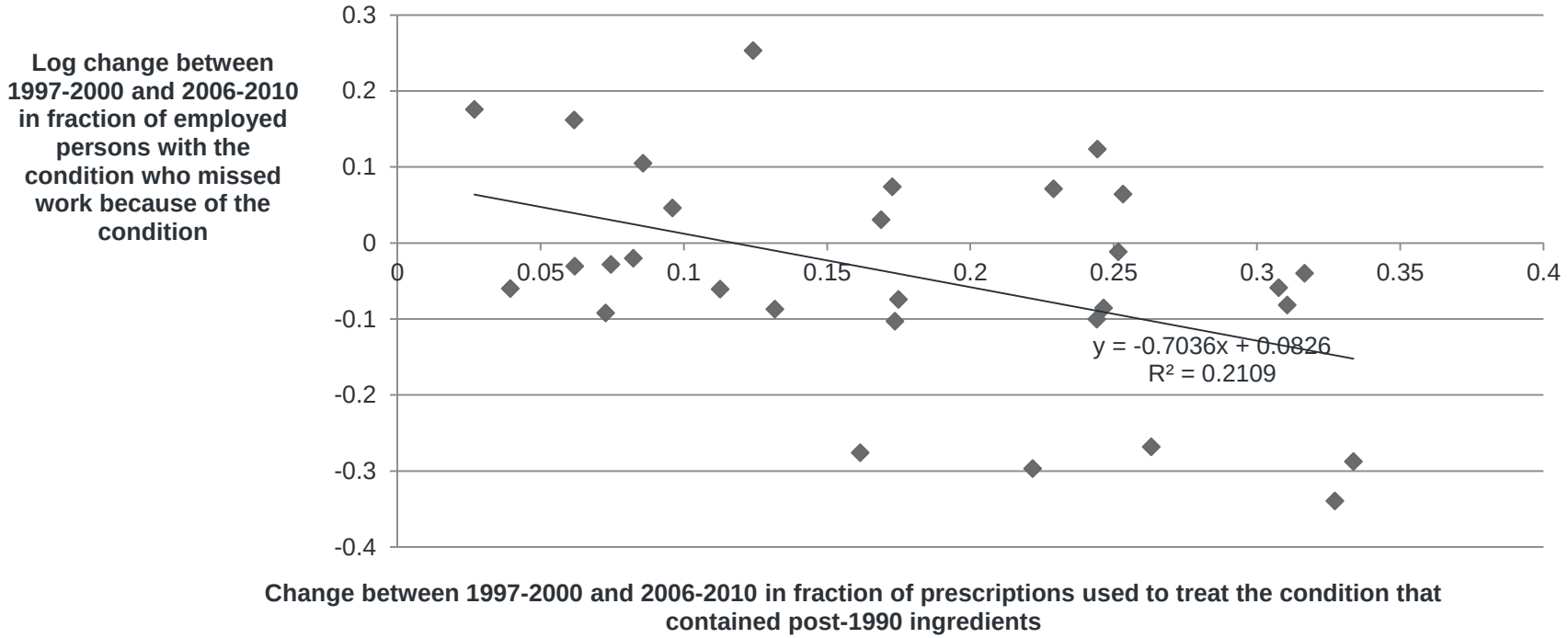
- Longitudinal state-level data during the period 1995– 2004 were analyzed to investigate whether use of newer prescription drugs reduced the ratio of the number of workers receiving Social Security Disability Insurance benefits to the working-age population (the “DI recipiency rate”).
- All of the estimates indicated that there is a significant inverse relationship between disability recipiency and a good indicator of pharmaceutical innovation use: the mean vintage (FDA approval year) of Medicaid prescriptions.
- From 1995 to 2004, the actual disability rate increased 30%, from 2.62% to 3.42%. The estimates imply that in the absence of any post-1995 increase in drug vintage, the increase in the disability rate would have been 30% larger: the disability rate would have increased 39%, from 2.62% to 3.65%.
- This means that in the absence of any post-1995 increase in drug vintage, about 418,000 more working-age Americans would have been DI recipients.

# Pharmaceutical innovation also reduces disability and increases ability to work:

## evidence based on U.S. data

- The mean number of work loss days, school loss days, and hospital admissions declined more rapidly among medical conditions with larger increases in the mean number of new (post-1990) prescription drugs consumed.
- The value of reductions in work loss days and hospital admissions attributable to pharmaceutical innovation was estimated to be three times as large as the cost of new drugs consumed.

# Correlation across conditions between pharmaceutical innovation and change in probability of work-loss, top 30 conditions (ranked by number of employed persons who missed work because of the condition during 1997-2000)

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# PHARMAC expenditure on chemotherapeutic agents, 2007-2012

| Year | Expenditure ($millions ex GST and rebates) |
|---|---|
| 2007 | $16.6 |
| 2008 | $21.1 |
| 2009 | $23.4 |
| 2010 | $26.2 |
| 2011 | $33.9 |
| 2012 | $61.3 |

# PHARMAC expenditure on chemotherapeutic agents, 2007-2012

| Age group | Estimated incidence, 2012 | % of total |
|---|---|---|
| 0-14 | 100 | 0% |
| 15-39 | 937 | 4% |
| 40-44 | 659 | 3% |
| 45-49 | 1047 | 5% |
| 50-54 | 1573 | 7% |
| 55-59 | 2106 | 10% |
| 60-64 | 2778 | 13% |
| 65-69 | 2981 | 14% |
| 70-74 | 2765 | 13% |
| 75+ | 6391 | 30% |
| Total | 21337 | 100% |

# The impact of pharmaceutical innovation on the longevity and hospitalization of New Zealand cancer patients, 1998-2012

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