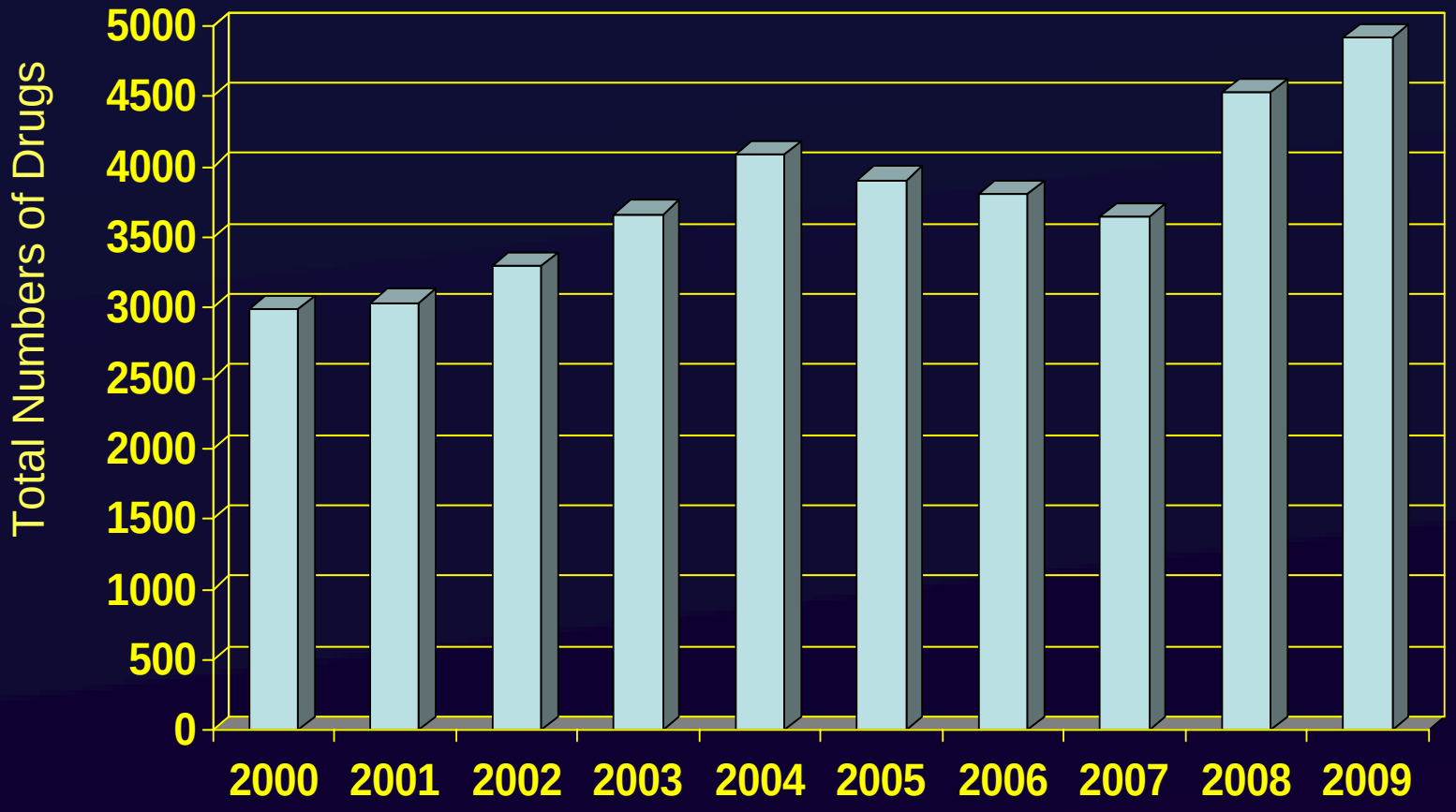
# UK attitude to cost-effectiveness:

# are we just being mean?

David Cameron

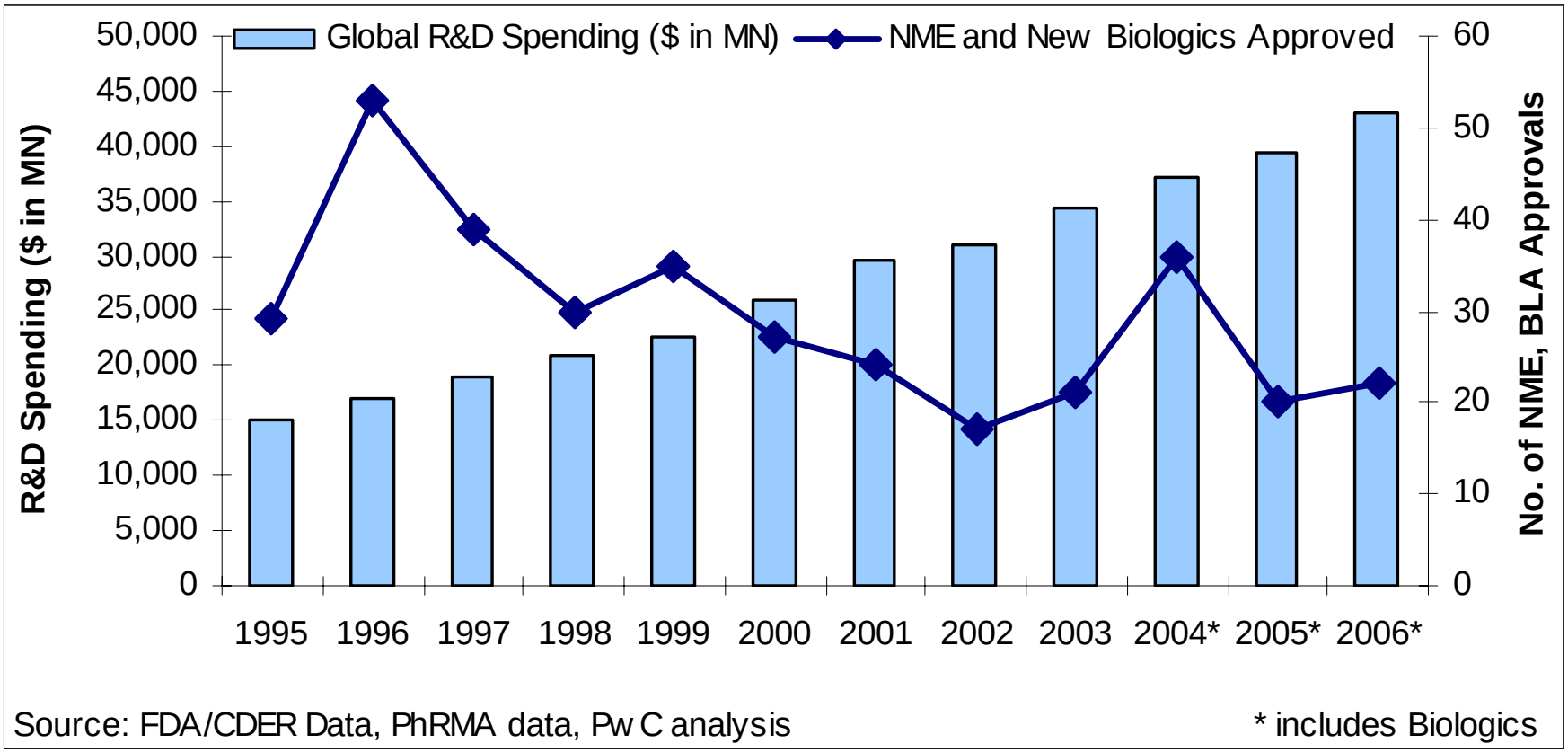
University of Edinburgh

# Numbers of Drugs in Pre-Clinical Testing; PhRMA World Wide




Source: PAREXEL'S Bio/Pharmaceutical R&D Statistical Sourcebook 2009/2010

# Productivity is falling…




**Even allowing for inflation, industry is investing twice as much in R&D as it was a decade ago to produce two-fifths of the new medicines…..**

# New cancer medicines freely available in Europe

| | Reimbursement status | | | | | | Price comparisons (Cost per month £) | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | France | Germany | Italy | Neth'ds | Spain | Sweden | France | Germany | Italy | Neth'ds | Spain | Sweden | UK |
| Bevacizumab (first-line) for the treatment of advanced and/or metastatic renal cell carcinoma | 100% | 100% | Yes | Yes | Yes | No decision (available through hospital) | 4078 | 3932 | 3562 | 3465 | 3795 | 3271 | 2704 |
| Sorafenib (first- and second-line) for the treatment of advanced and/or metastatic renal cell carcinoma | 100% | 100% | Yes | Yes | Yes | Yes | 3471 | 3757 | 3118 | 3342 | 3443 | 3132 | 2402 |
| temsirolimus (first-line) for the treatment of advanced and/or metastatic renal cell carcinoma | 100% | 100% | Yes | Yes | Yes | No decision (available through | n.a. | n.a. | n.a. | 3855 | 3531 | 3094 | 2351 |

Source: European Trade Associations. IMS

# The changing picture of drug costs

- Molecular understanding ⇒ highly targetted drugs
- Registration trials cost €€€ €€€ €€€,€€
  - Target patient population smaller
  - Large phase III trials in many countries
    - HERA, Lapatinib, BEATRICE, Cetuximab trials……
  - FDA/ EMEA require high standard of monitoring
    - 100% source data verification
    - Costs time and people
  - Complex CRFs running to 100s of pages…….
- Many new agents fail long before phase III
- Investment in a drug by first registration ~ 1 billion ?

# Is this to our patients' benefit?

- Targetted agents
  - Better specificity
  - Better activity
  - Less off-target toxicity
  - Revolutionise natural history (Herceptin)
- Drugs get more expensive
- We often still don't know exactly the target population
- Novel side effects (herceptin, TKIs)
- Uncertain long-term benefits and toxicities


- National Health service
- €120 Billion per year
  - All consultations
  - All operations
  - All in patient stays
  - All hospital drugs
  - All screening
  - Out patient drugs for
    - Children
    - Pregnant women
    - Elderly
    - poor
- *Out patient drugs for the rest*
- *Private hospital care*

# So is it all done to money?

- UK health service has to balance all the new choices within the same pot of money
  - Hip replacements vs Herceptin
  - Bowel cancer screening vs Bevacizumab
  - Valve replacements vs Velcade
  - eLtrombopag vs Lapatinib

# 15 years ago

- What anti-cancer drug you got depended on local decisions
  - “post-code prescribing”
  - Cross the street and drug availability changed
  - Oncologist vs Orthopaedic surgeon fighting for the same bit of a hospital budget

So they invented NICE

# NICE

- What does NICE mean?

- To Shakespeare it mean PRECISE, or exact
- Now it means friendly, kind, amenable….
- National Institute for health and Clinical Excellence (http://www.nice.org.uk/)
  - something friendly to patients and doctors….
  - Decides what should and should not be available for the country
  - Guideline development to standardise care
- *National Institute for Cost Effectiveness ?*
  - *Something that* precisely *measures cost-benefit of therapy?*

# Who would not get Herceptin?

- 45 year old, grade 3, HER2+ Node+
- 65 year old, grade 2, HER2+, Node+
- 75 year old, grade 1, HER2+, Node-

- 45 year old, grade 3, HER2-, Node+

? 5 -10% are HER2+ve….?

We follow guidelines that balance the evidence for benefit vs the evidence for toxicity

# Toxicity

- Toxicity to the patient
  - Risk of serious morbidity
    - Infection, heart disease, death
  - Loss of quality of life
    - Alopecia, fatigue, mild diarhoea
- Toxicity to the health care system
  - Doctor and nurse time
  - In patient admissions
  - Extra treatments

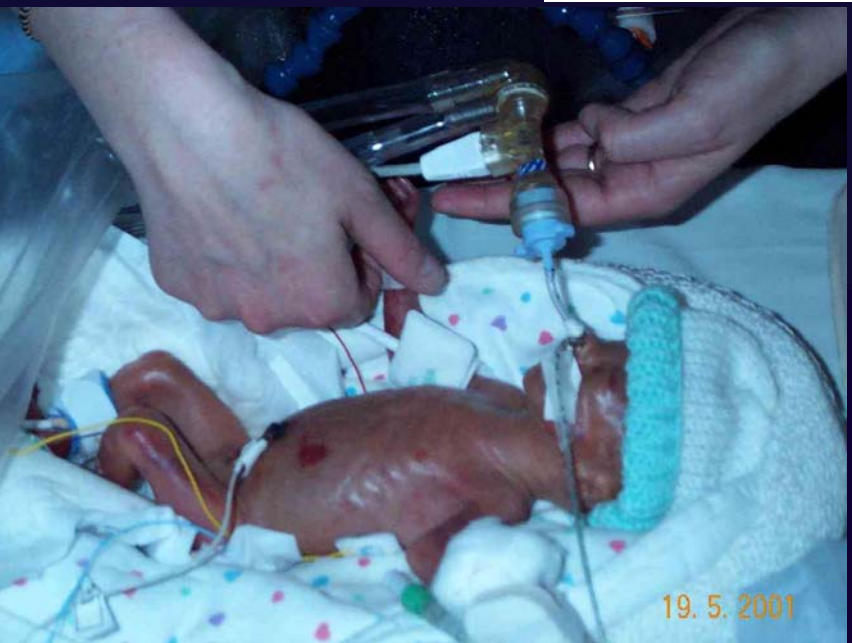
# Cost of Toxicity

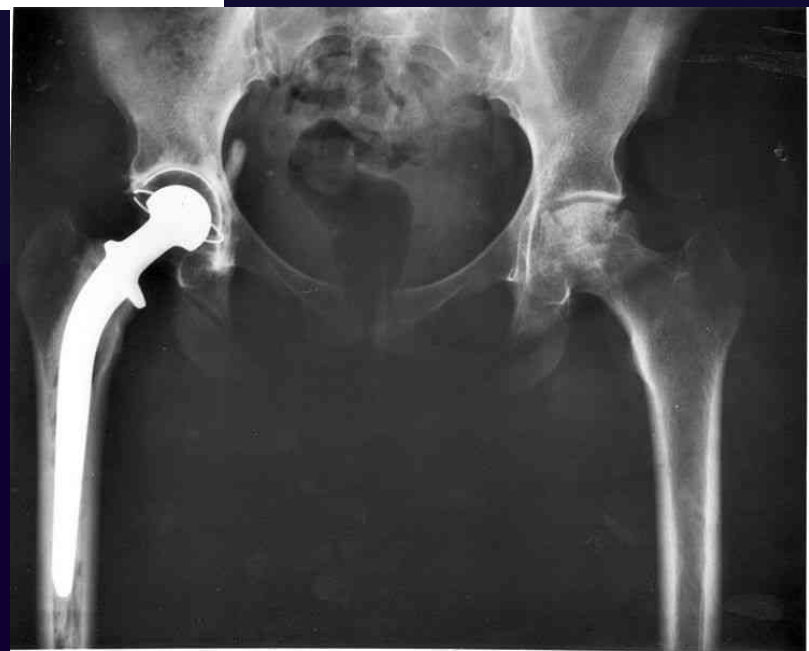
- Patient and family
  - Loss of income
  - Extra expenditure: Travel, comfort shopping
- Health care system
  - Doctor and nurse time
  - In patient admissions
  - Extra treatments
- National cost
  - Loss of GDP

# Choice in spending


I ♥ ITALIAN SHOES

# Choice in spending for a country

# So how to choose

- Cost per QALY
  - Quality adjusted life year
  - Perfect health = 1.0

    $\Rightarrow$ 1 year perfect health = 1 QALY
  - 1 year alive with Metastatic breast cancer:
    - Stable disease on therapy 0.72
    - Responding disease 0.79
    - Stable disease with toxicity ~ 0.57
- 6 month gain survival for stable metastatic breast cancer patient, no toxicity = 0.5 * 0.72 = 0.36 QALY

Lloyd A et al, British Journal of Cancer (2006) 95, 683 – 690

# Cost

- Threshold around £30 000/ QALY
- 6 month survival gain gives 1/3 QALY
  - Treatment (drug+nurse+pharmacy+doctor+..)
    - < £10 000……
- Saving the life of a tiny baby = 80 QALY
  - So we can spend £ 2.4 million……..
- Doing a hip replacement in an 80 year old?

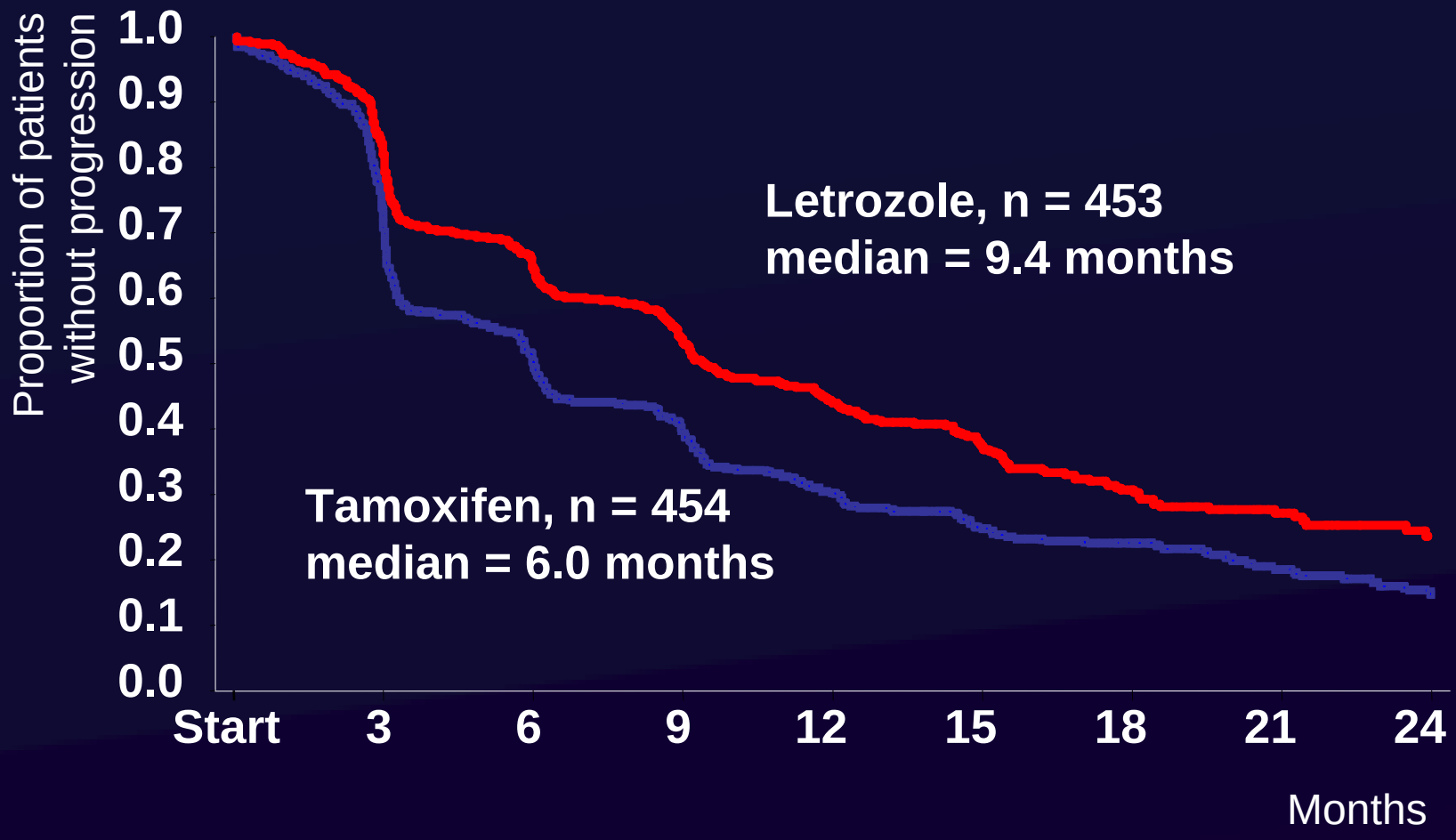
# Uneven approach

- Cancer
  - Most studies report OS so use the data
- Diabetes, paediatrics etc.
  - Rarely support survival $\Rightarrow$ use surrogates
- Terminal patients
  - < 2 years to live
    - 3 month gain in survival thought worthwhile
- If no other treatment (renal cancer)

# The future

- Value based pricing?
  - Drug price  = Y * QALY benefit
  - Would make Bevacizumab much cheaper than Trastuzumab for advanced disease
- Drug trials
  - 3 end-points?
    - Efficacy
    - Safety
    - Cost-effectiveness?

# First line metastatic disease:
## Tam vs letrozole in the ER positive population



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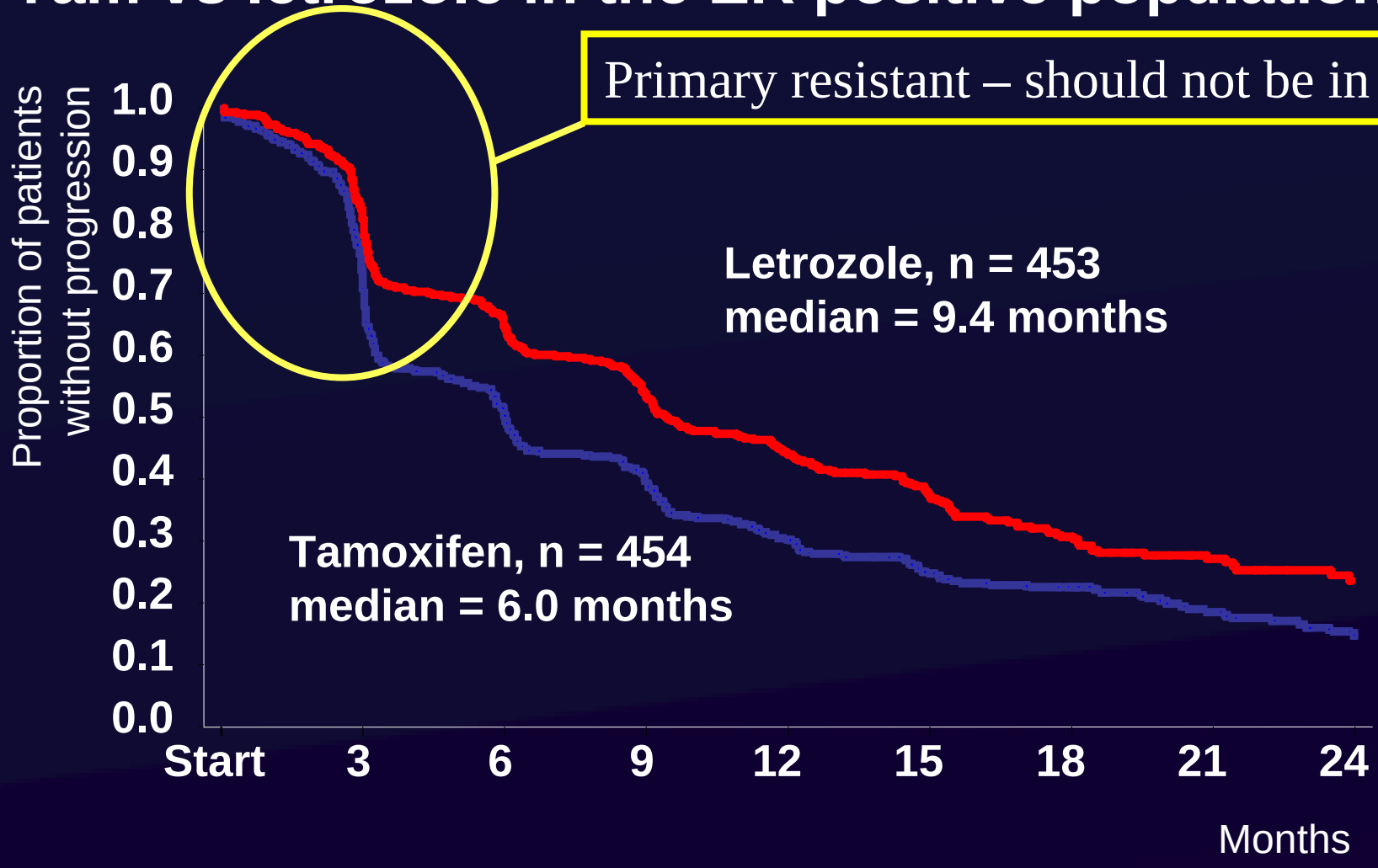
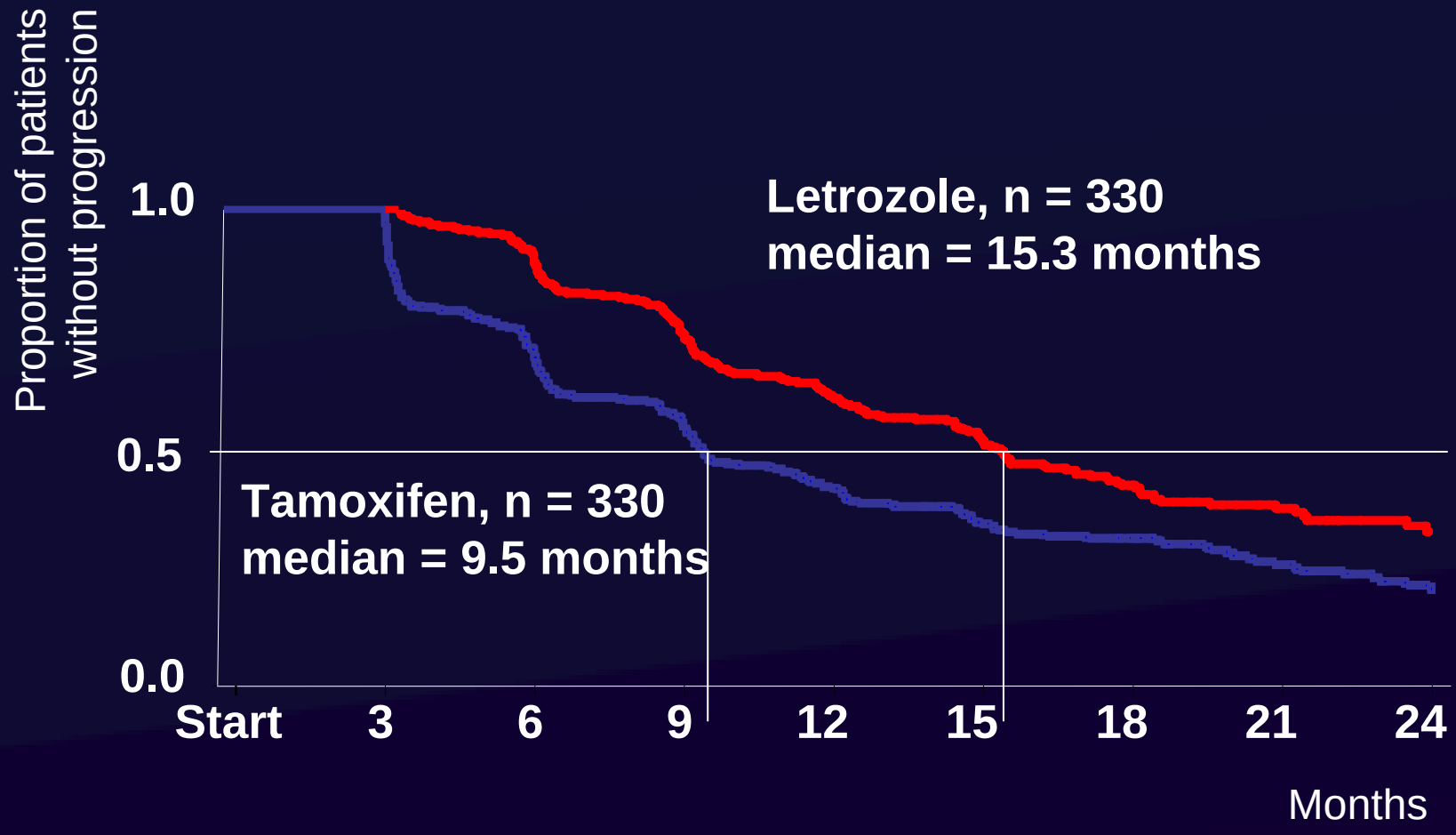


# Endocrine sensitive population




Making the drug look more effective could well change the Health economics…

# Cost-effectiveness ?

- Not in our lecture courses…..
- Never an end-point of clinical trials
- Clinical trials
  - Efficacy – DFS/ Time to progression/ Overall Survival
  - Toxicity – CTC graded toxicity
    - NOT what matters to a patient – have to be re-interpreted
  - Cost-effectiveness – derived data, increased uncertainty…

# Comprehensible

- Who understood all that?

- We understand clinical trials
  - Efficacy and toxicity

- We now have to rely on health economists to tell us if it is worth using new drugs…..