Dr John Petrie

Rheumatologist

Lakes Care Medical Centre, Rotorua

Professor Lisa Stamp

Rheumatologist

University of Otago, Christchurch

Dr Bryan Betty

General Practitioner

Porirua Union and Community Health Service, East Porirua

Dr Peter Chapman-Smith

Phlebologist

NZ Stem Cell Treatment Centre, Whangarei

FULLY BOOKED

Friday, August 12, 2016

16:30 - 18:30 WS #53: Rheumatology Forum: Gout; Biologics; Stem Cells; Early Intervention in RA (120mins not repeated)

(Room 2)

Biologics and Rheumatology: Why GPs should be interested

Dr Bryan Betty,

Deputy Medical Director, PHARMAC

GP Cannons Creek East Porirua

The funding environment

PHARMACEUTICAL INDUSTRY GETS HIGH ON FAT PROFITS

BBC News

KALYDECO – TOO HIGH A PRICE TO PAY?

Milwaukee Sentinel

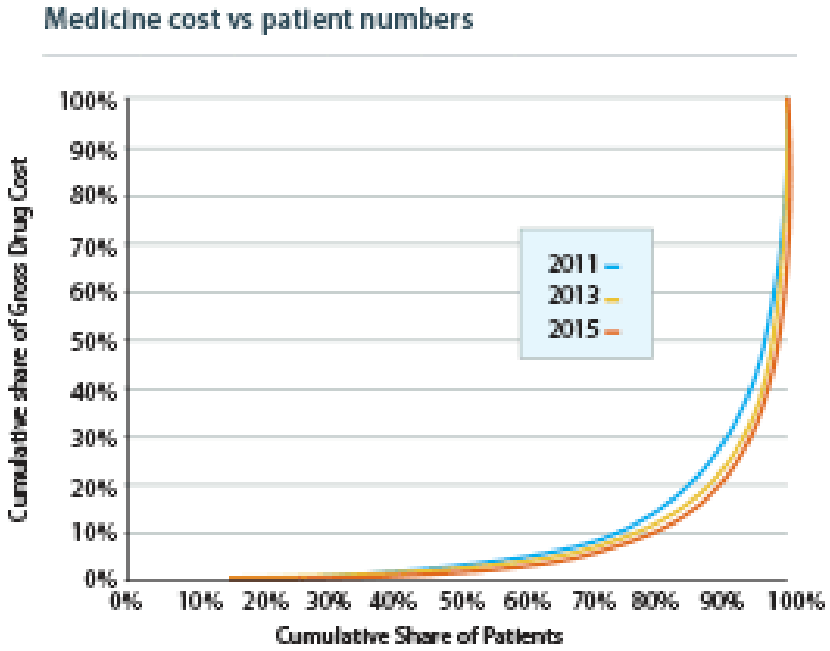
THE RACE TO CURE RISING DRUG COSTS

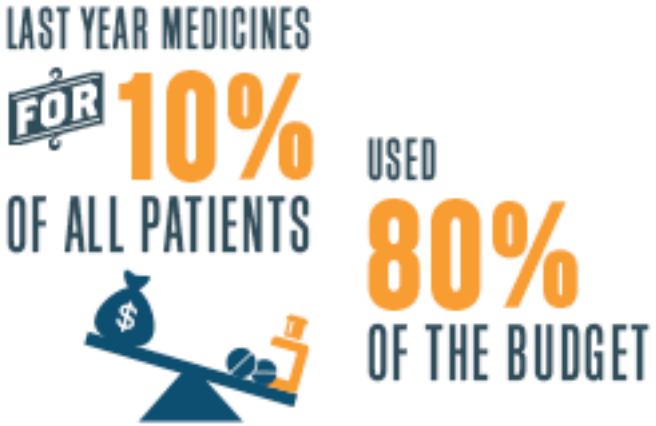
Financial Times

THE DRUG THAT IS BANKRUPTING AMERICA

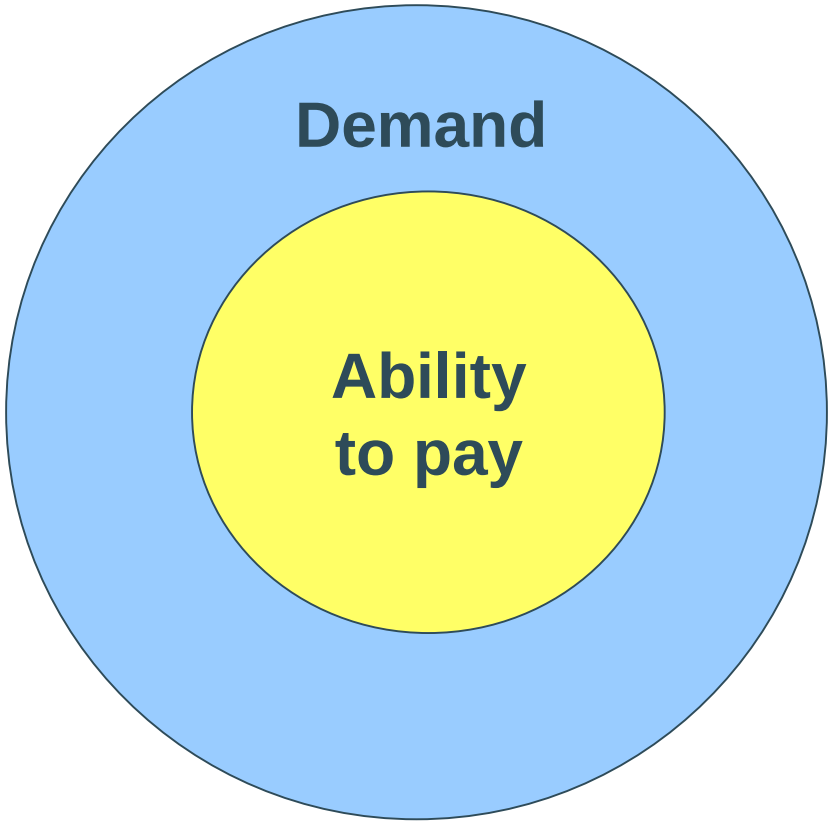
Huffington Post

Bang for the buck



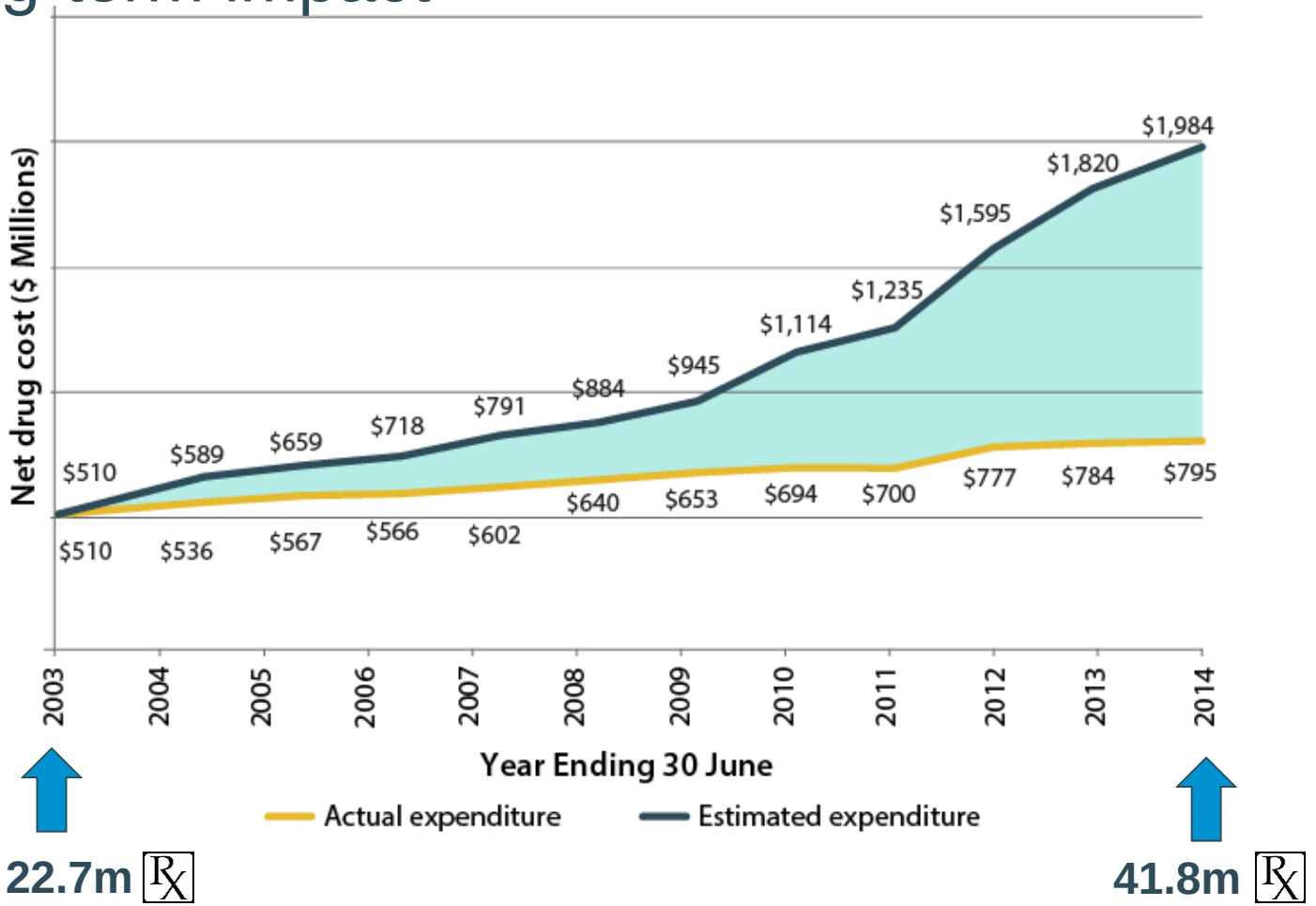


Health care wants exceed resources available…



… so choices need to be made

PHARMAC's long-term impact

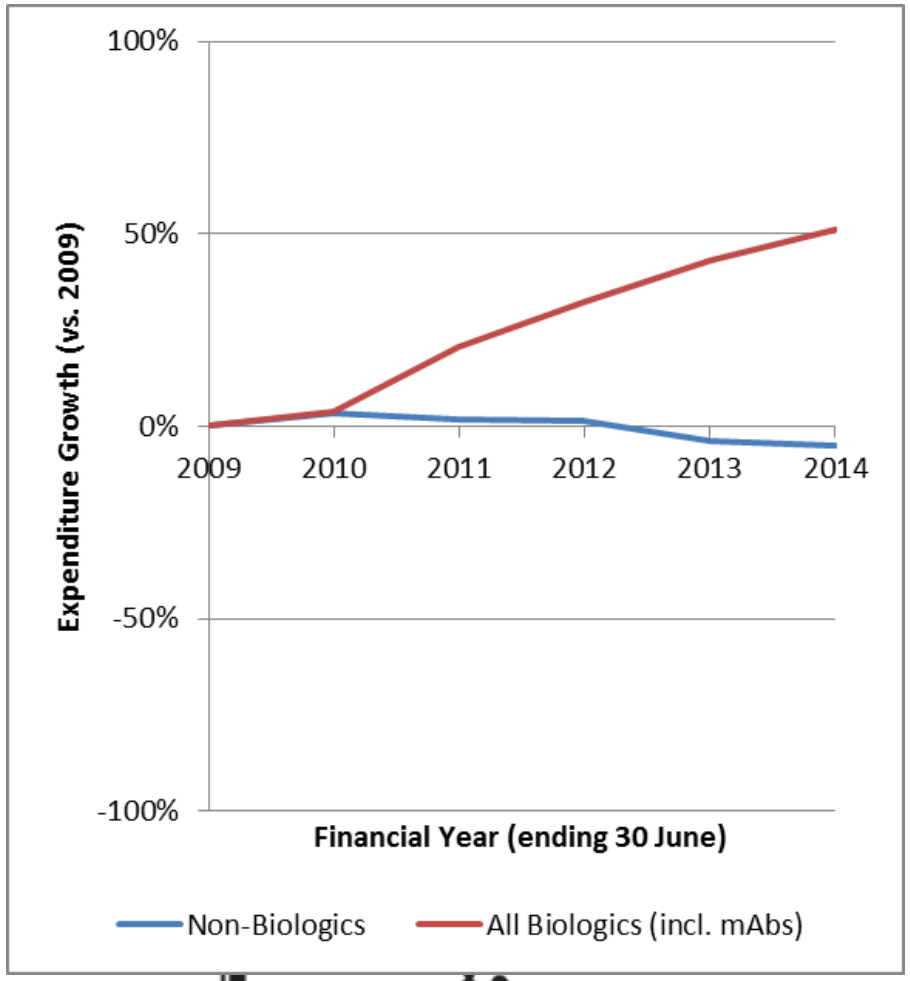


Biologics Challenge

The promise of biologics……

- Biologics have had a profound effect health through treatment of many diseases
  - Primarily rheumatology, inflammatory conditions, diabetes and oncology
    - Filgrastim, pegfilgrastim, erythropoetin, somatropin, insulins
    - Adalimumab, etanercept, rituximab, trastuzumab (‘mAbs’)
  - Anti-TNF inhibitors for inflammatory conditions :
    - **Rheumatoid Arthritis**, psoriasis, IBD

NZ expenditure growth on biologics



Global spend on all medicines grew 24% from 2007-2012

Biologics spend grew 367% over the same time period

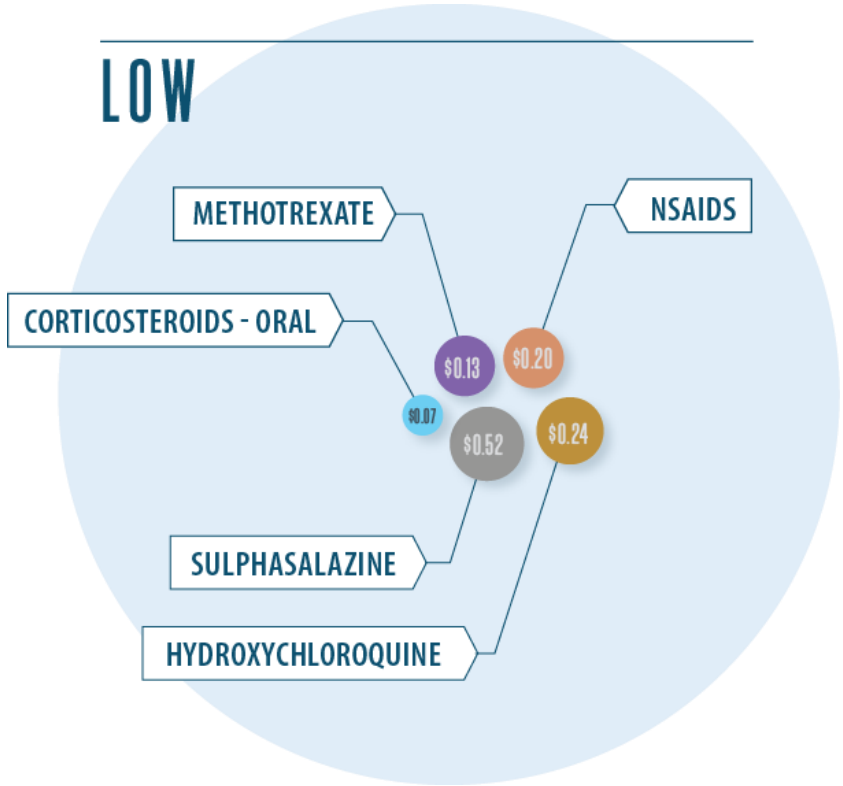
Global biologics sales forecast to grow to US$220 billion by 2017

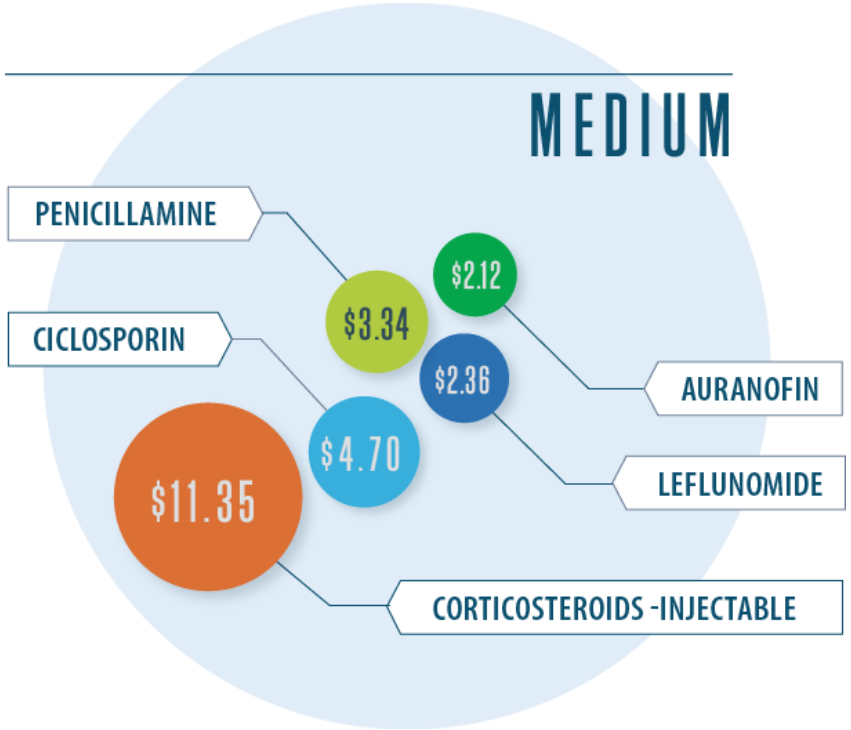
Top 20 CPB funded meds by cost

CHEMICAL NAME	COST	CURRENT RANKING
Adalimumab	$70,860,000	1
Dabigatran	$35,250,000	2
Fluticasone with salmeterol	$31,470,000	3
Trastuzumab	$30,870,000	4
Etanercept	$24,930,000	5
Budesonide with eformoterol	$21,170,000	6
Insulin glargine	$18,920,000	7
Rituximab	$17,090,000	8
Tiotropium bromide	$13,750,000	9
Bortezomib	$13,440,000	10
Blood glucose diagnostic test strip	$12,740,000	11
Efavirenz with emtricitabine and tenofovir disoproxil fumarate	$11,230,000	12
Sodium valproate	$9,900,000	13
Octreotide LAR (somatostatin analogue)	$9,450,000	14
Lamotrigine	$9,190,000	16
Mesalazine	$8,600,000	17
Varenicline tartrate	$8,580,000	18
Venlafaxine	$8,380,000	19
Dasatinib	$8,070,000	20

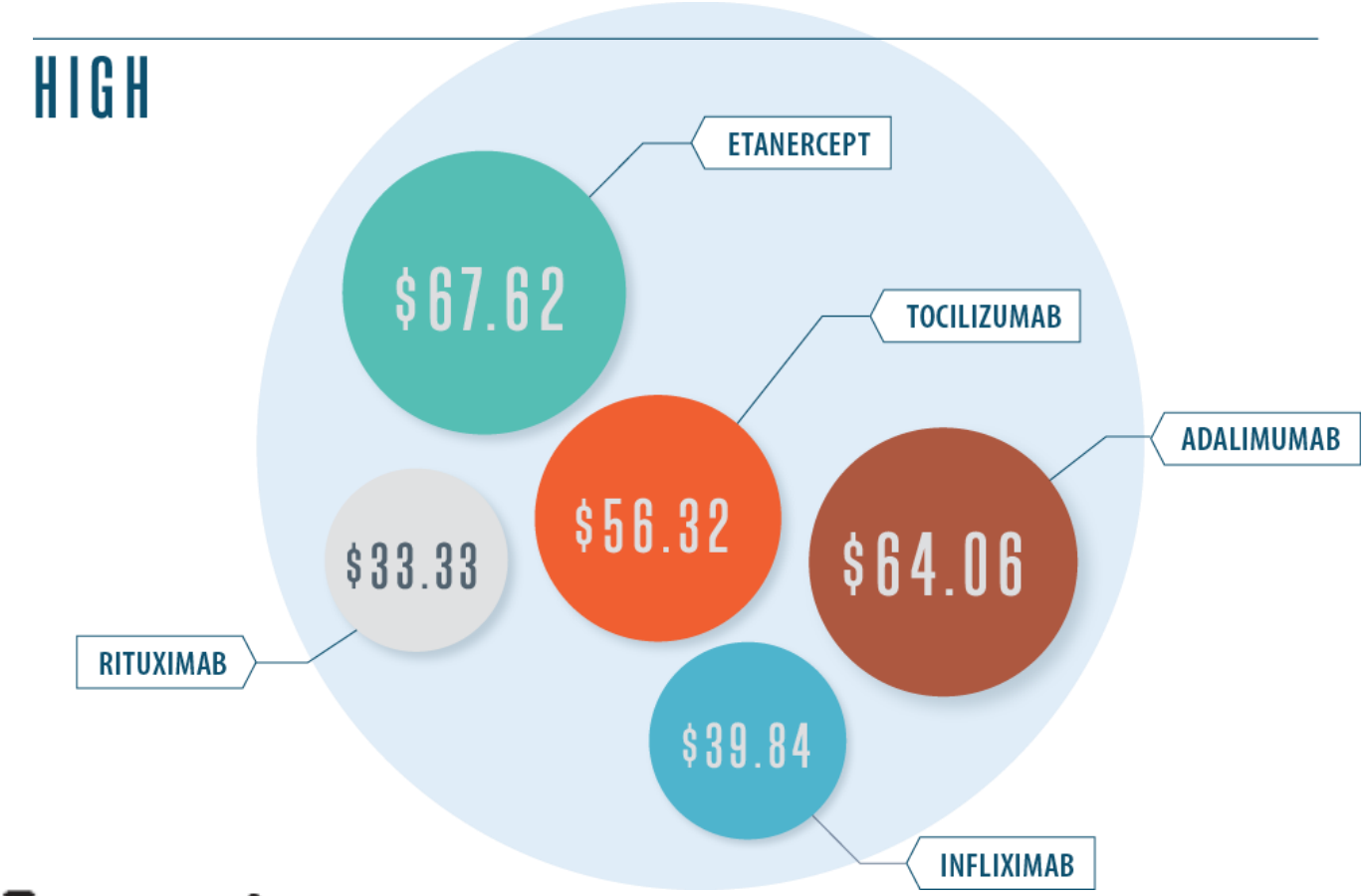
by ex manufacturer cost
(ex GST and rebates)
excludes vaccines

Average daily costs of rheumatology treatments in 2015

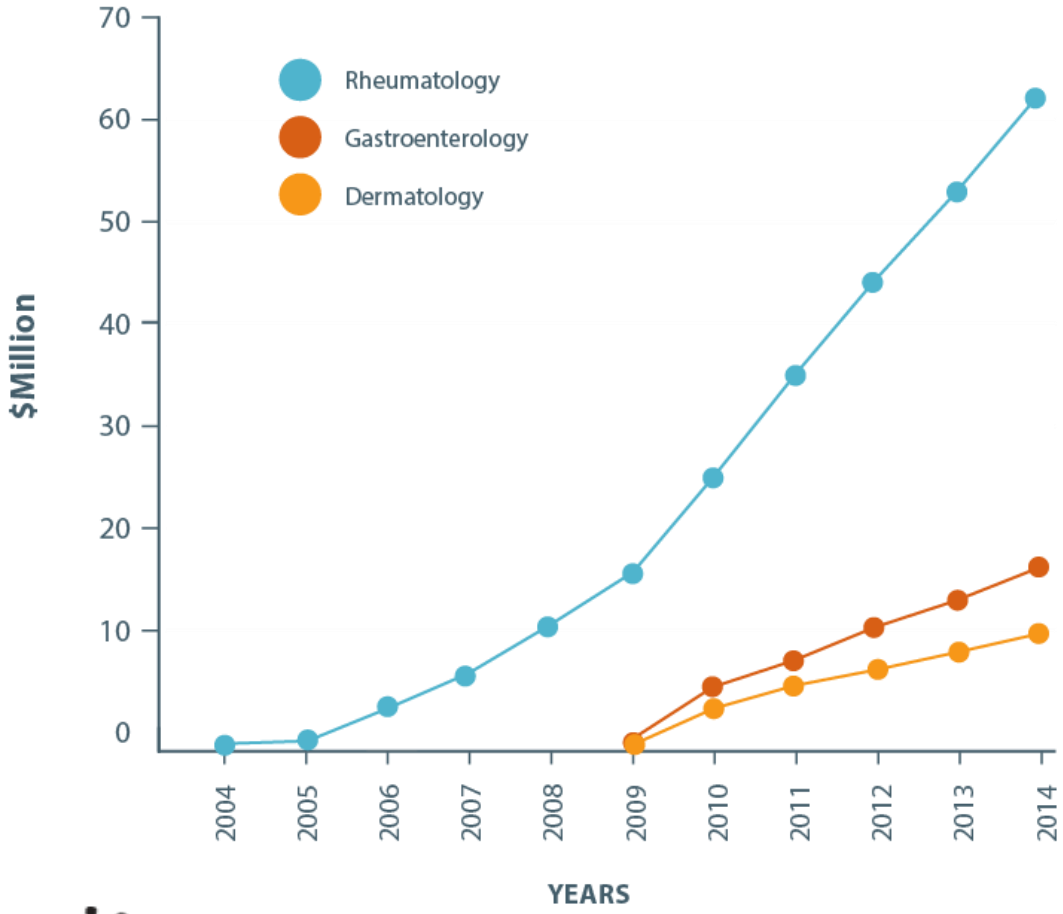




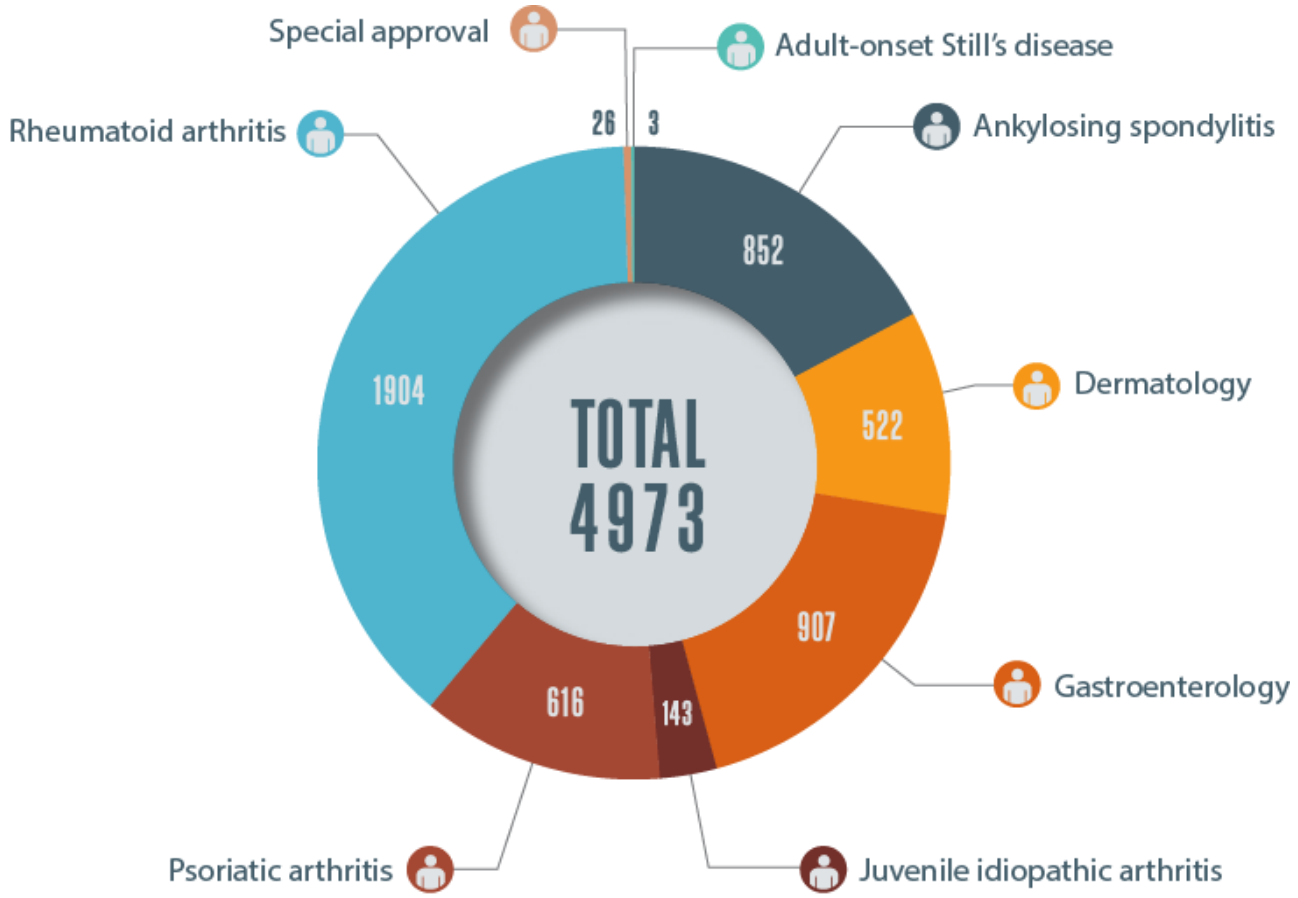
Average daily costs of rheumatology treatments in 2015



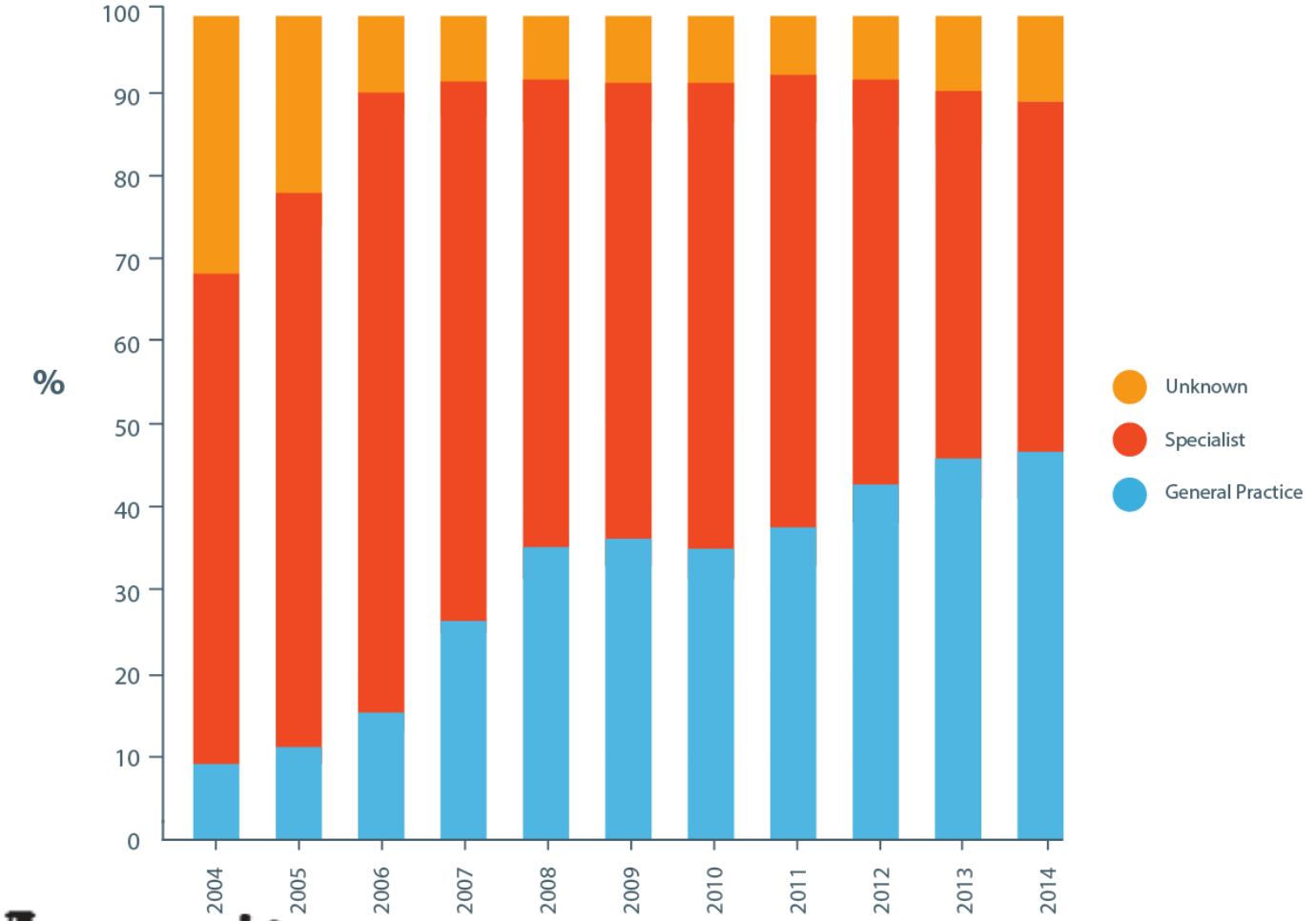
Expenditure on etanercept and aAdalimumab



Detailed breakdown of patients using etanercept and adalimumab in 2014



Who’s prescribing etanercept and adalimumab?



The Challenge…

Biologics are the fastest growing category of medicines in NZ

48% increase over the last five years

Monoclonal antibodies (mAbs) largest and fastest growing segment

Approx. 10% of total NZ medicines expenditure

<1% of prescriptions funded

120% growth over last 5 years

High costs of biologics may limit access and health gains

- This is not just an NZ issue

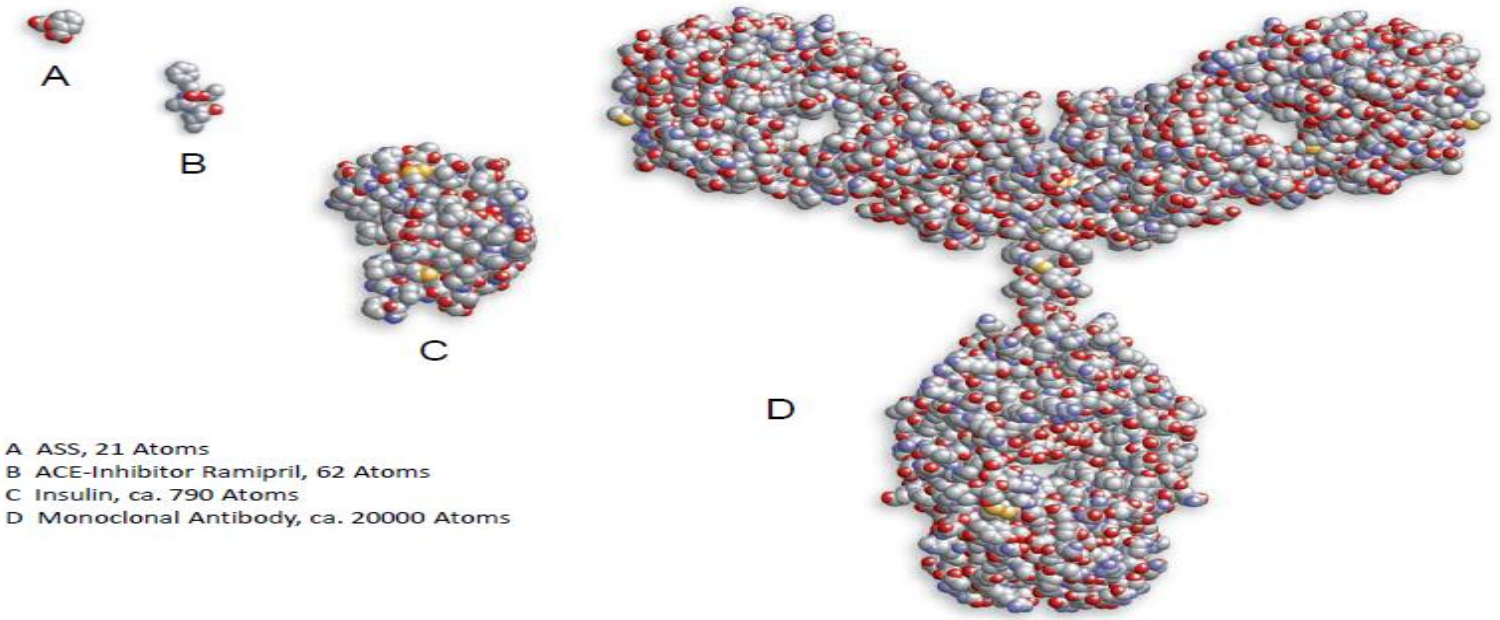
What are Biologics?

Biopharmaceuticals aka “Biologics”

- Produced by, or extracted from, living organisms(as opposed to synthesized chemical process)

- Many made using recombinant DNA technology in bacteria, yeast or mammalian cells

Biologics Vary in complexity



A ASS, 21 Atoms
B ACE-Inhibitor Ramipril, 62 Atoms
C Insulin, ca. 790 Atoms
D Monoclonal Antibody, ca. 20000 Atoms

Monoclonal Antibody can be 800 times an aspirin molecule.

So what is a Biological product?

A glass of milk

Biologics

- **Innovator small molecules**
  - **Chemically** synthesized to identical molecular structure

- **Innovator biologics**
  - Both made in living systems therefore have inherent variability

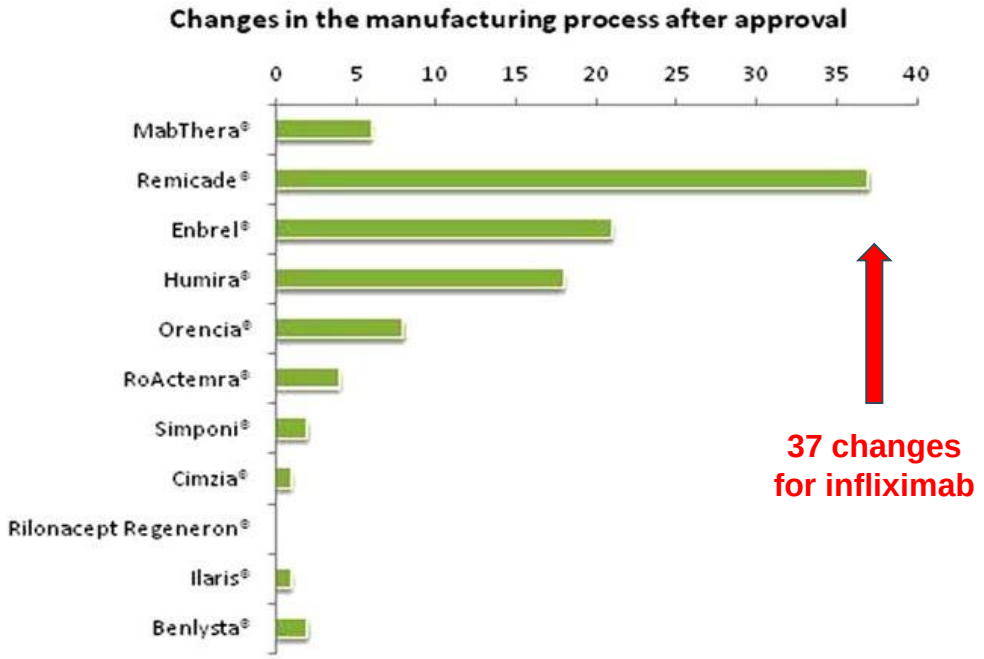
- **Micro- heterogeneity**: small differences between batches.

Variability of Innovator Biologics

Changes include:

- Change in supplier of cell culture media
- New purification methods
- New manufacturing sites

Changes for innovator molecules approved by comparability exercise – rarely require clinical trials



" the medicine that a clinician administers to a patient today is not 'identical' (but comparable) to the medicine authorised years ago"

"no batch of any reference product is 'identical' to the previous one - 'non-identicality' is a normal feature of biotechnology"

From Schneider C K Ann Rheum Dis 2013;72:315-318

GP Issues

Specific GP clinical issues with biologics

1. Initially Majority of mAb biologics in GP practice are immunomodulatory (Inflammatory disease)

   - Anti-TNFs adalimumab (Humira) , etanercept (Enbrel)
   - Rheumatoid arthritis, Psoriasis, Crohn's Disease, Ulcerative Colitis

2. Specialist Rx, follow-up scripts + monitoring GP's
   - Capacity

Immunogenicity

All biologics confer a risk of **immunogenicity**

Neutralizing antibodies (anti-drug antibodies)

- Loss of efficacy e.g. infliximab 17-60%, often methotrexate co-prescribed
- Anaphylaxis (rare) , Red Cell Aplastic Anaemia(1990's) erythropoietin

Ongoing real world pharmacovigilance undertaken for biologics to assess any potential rare reactions

Specific GP clinical issues with biologics/biosimilars

1. Contraindicated in patients with :
   - **severe active infection (**sepsis, active tuberculosis)

2. Caution in patients with:
   - **active infections:** including chronic or localised infections patients who have been **exposed to tuberculosis**,
   - **Hepatitis B virus (HBV) infection, (reactivation can been fatal)**
   - **moderate to severe alcoholic hepatitis**
   - **moderate to severe heart failure (NYHA class III/IV).**
   - **Malignancy within 5 years**

Specific GP clinical issues monitoring

1. Develop serious infection: Prompt action contact specialist
2. Heart failure developing or worsening with mild CCF
3. Interstitial lung disease - dry cough, increase SOB
4. Periodic skin exam for non - melanoma skin cancers

Specific GP clinical issues monitoring

1. **Vaccination prior to commencing, avoid live vaccines during treatment (MMR, varicella, BCG)**
2. **Not proven in pregnancy: Contraception**
3. **Surgery with-held prior + started 2 weeks post**
4. **Bloods may Include: FBC (cytopenias), CRP, LFT**
5. **Long term: Lymphoma risk (2-2.5* risk)**

GPs: Biologics Take Home

1. Cost issues

2. GPs will have patients on biologics into the future

   Increasingly see patients on these medications and expected to review

3. **Immunogenicity** and micro-heterogenicity important concepts.

4. **Monitoring**: Serious infection developing, CCF, interstitial lung, non-melanoma skin ca, vaccinations. (Fluvax), pregnancy, surgery.

Questions

More Information

www.pharmac.govt.nz

Fact sheet

Biologics and biosimilars

Biologics are a relatively new form of medicines that are increasingly being used. They include products like vaccines, insulin to treat diabetes, hormones such as human growth hormone, and many modern medicines used to treat cancer, arthritis and other auto-immune disorders.

Unlike most traditional medicines that are made through chemical processes, biologic products are made of, or from, living things like yeasts, bacteria or animal cells. They usually have a more complex structure than other medicines.

Biologics are being used more and more around the world. While global spending on all medicines grew 24 percent from 2007-2012, spending on biologics grew 367 percent over the same period. Currently approximately US$170 billion is spent on biologics worldwide, and this is forecast to grow to approximately US$220 billion by 2017.

In New Zealand, expenditure on biologic medicines has increased 48 percent over the last five years. By comparison total expenditure on other medicines decreased 5 percent over the same period. The class of biologic medicines called 'monoclonal antibodies' accounts for around $150 million per annum, mostly for treating cancer, arthritis and related disorders. These medicines account for approximately 10 percent of all the spending on medicines in NZ for less than one percent of prescriptions funded.

The rapid growth in spending on biologic medicines is unsustainable. PHARMAC, and health care providers worldwide, must work to reduce these costs in order to maintain existing services and provide new pharmaceuticals to patients.

Biosimilars

If you want to replicate a traditional chemical medicine you produce a generic – an expert copy made by companies that didn't develop the original medicine themselves. You can't make an exact copy of a biologic medicine because they are made from living things and there is natural variability in all living things, just like two apples are never exactly alike.

The generic equivalents of biologics are called 'biosimilars.' A biosimilar is a highly similar, comparable version of an approved biologic medicine. New biosimilar medicines undergo clinical trials to demonstrate that they work just as well as the approved biologic medicine.

Biologic medicines are often very expensive due to the lack of competition. Biosimilars will help PHARMAC to increase competition which will reduce costs, improve access for patients to these important medicines, and provide access to other medicines.

Biosimilars have been available for many years and are used extensively overseas. Countries with a high acceptance of biosimilars include Austria, Germany, UK and Sweden.

Australia and New Zealand regulators have approved a number of biosimilar medicines. From 2012 PHARMAC funded a biosimilar form of filgrastim, a medicine used to treat low white blood cell count in people going through chemotherapy treatment, and in 2014 PHARMAC funded a biosimilar somatropin, a human growth hormone.

EXPENDITURE ON BIOLOGIC MEDICINES HAS INCREASED 48% OVER THE LAST FIVE YEARS

www.bpac.org.nz