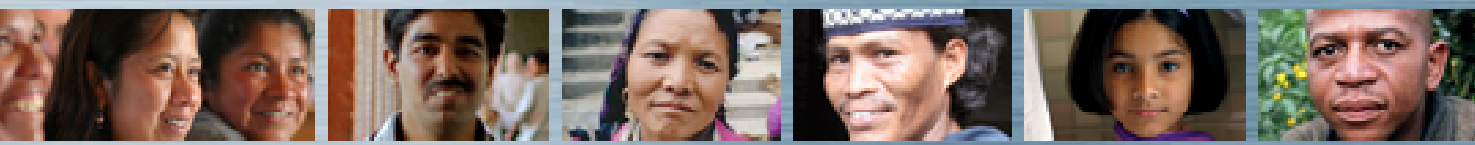


Analysis of the Global TB Drug Market and Country-Specific Case Studies of TB Drug Distribution Channels

UK Case Study



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- TB Control in the UK
- Procurement and Distribution of TB Drugs
- Value and Volume of the UK TB Market
- Appendix

After years of increases, the incidence of TB in the UK has only recently begun to plateau

- Prevalence and incidence of TB has been rising in the UK for more than 15 years
- This has been attributed to increased migration from countries with high TB burden
- The ageing UK population and increase in HIV/AIDS has also contributed

Prevalence and incidence of TB and HIV/AIDS in the UK

YEAR	NUMBER OF TB CASES	RATE OF TB (PER 100 000)	ANNUAL PERCENTAGE CHANGE IN TB		NUMBER OF HIV/AIDS CASES
			NO. OF CASES	RATE	
1999	5761	10.8	-	-	41 585
2000	6323	11.8	+9.8	+9.4	45 449
2001	6652	12.4	+5.2	+4.8	50 511
2002	6861	12.7	+3.1	+2.4	56 738
2003	6837	12.5	-0.3	-1.0	64 005

Distribution of age groups in the UK in 1971 and 2004

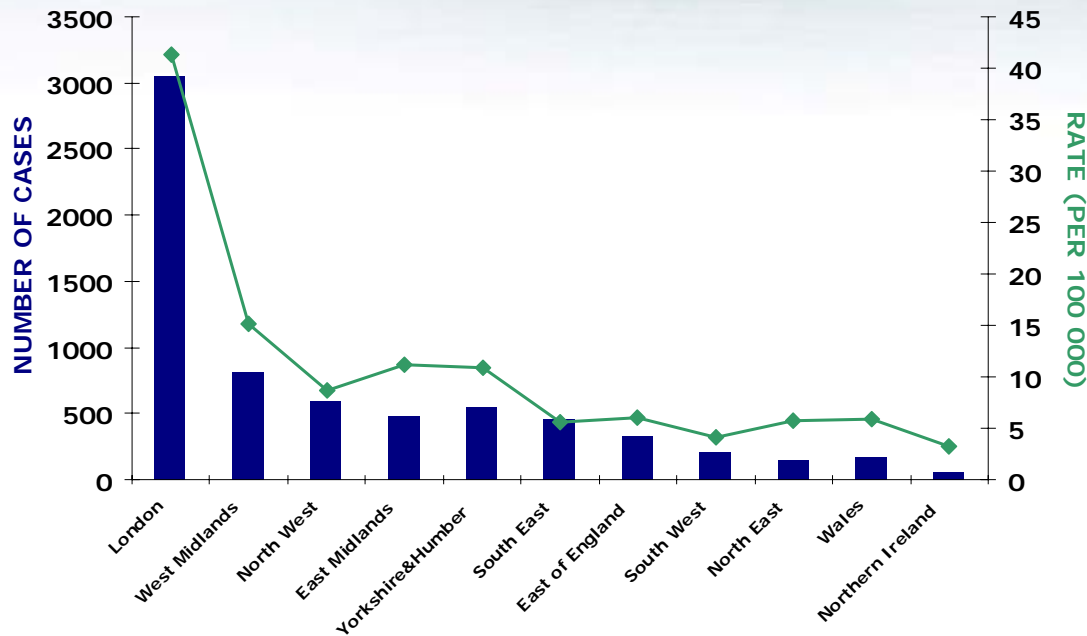
Age group	1971	2004
Under 16	25%	19%
16-65	62%	65%
Over 65	13%	16%

Source: Health Protection Agency; www.avert.org; Office of National Statistics



TB cases are concentrated in inner city areas -- London has by far the highest number of cases

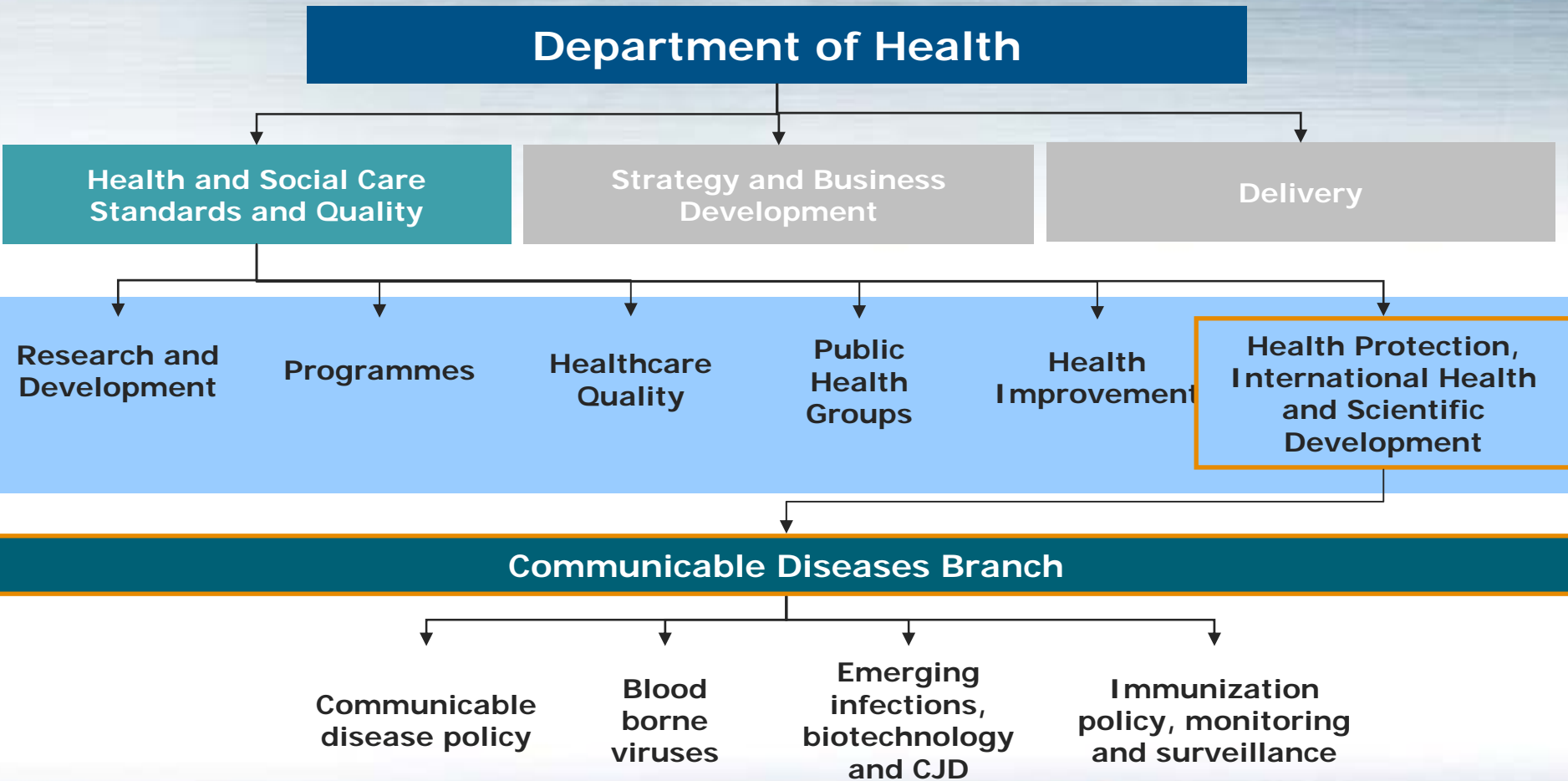
Prevalence and incidence of TB across the UK (2003)



- The largest proportion (45%) of TB cases reported in 2003 were located in London
- A majority of cases in the UK occur in inner cities (there is almost no incidence in rural locations). This is thought to be associated with the large immigrant populations and relatively high levels of poverty
- 70% of TB patients were born abroad, with the greatest proportion born in India, Pakistan and Bangladesh (36%)

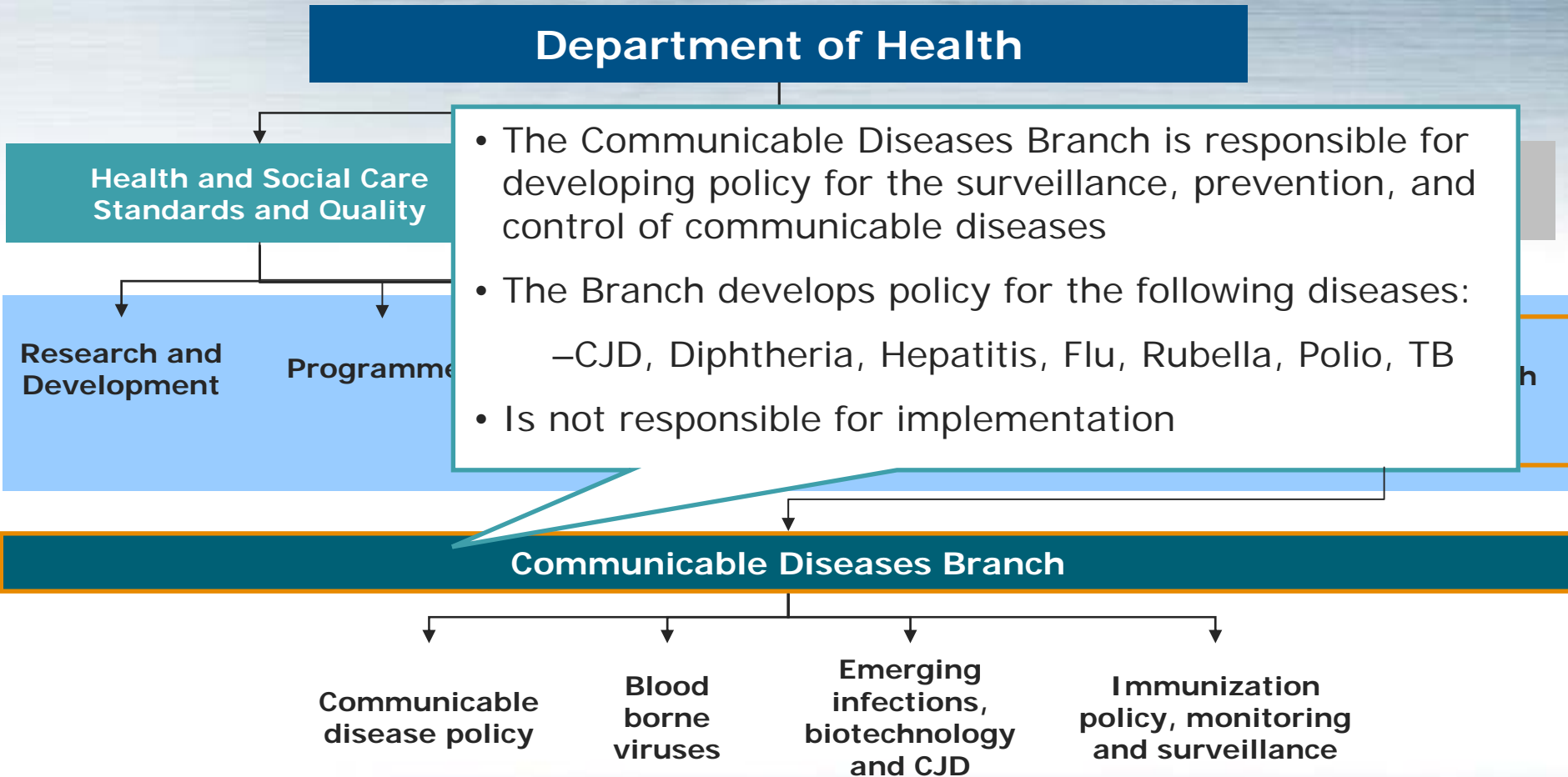
Source: Health Protection Agency

There is no National TB Control Programme in the UK. TB Control falls under the Communicable Diseases Branch of the Department of Health



Source: Department of Health, interviews

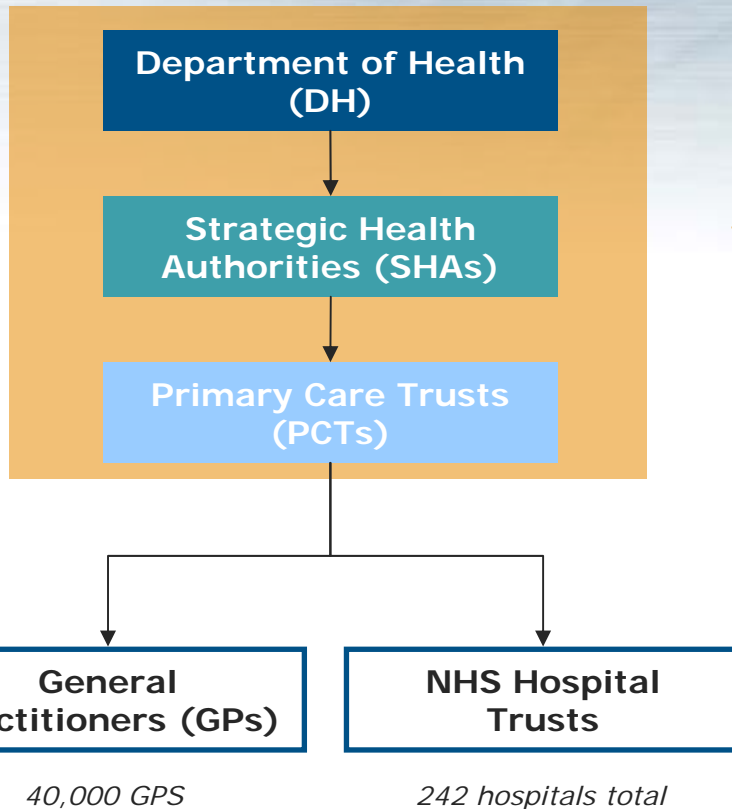
The role of the Communicable Diseases Branch is one of policy, not implementation



Source: Department of Health website, interviews

Within their region, the Primary Care Trusts (PCTs) set budgets for GPs and hospitals for all diseases, including TB

FLOW OF FUNDING



Department of Health (DH)

- Grants market access (Medicines and Healthcare products Regulatory Agency); approves price/regulating profitability; sets reimbursement status; develops healthcare policy

28 Strategic Health Authorities (SHAs)

- Ensure that healthcare policies are implemented by the Primary Care Trusts (PCTs)
- Oversee 1 of 28 regions

303 Primary Care Trusts (PCTs)

- Control 75% of the NHS budget and are responsible for commissioning healthcare in their area
- Required to ensure all types of healthcare are available, including; GPs, hospitals, dentists, pharmacies etc.
- Allocate budgets and implement new DH policies
- When hospitals and GPs receive their budgets they are free to allocate the money as they wish

As of 2005, the BCG vaccination is no longer routine in the UK and only high risk patients receive it

Pre-2005

- All children between the ages of 10 and 14 were vaccinated within schools through the School Vaccination Program
- Also offered to those who may be exposed at work, immigrants from countries in which TB is endemic and people going to live in countries in which TB is endemic
- Children at a particularly high risk received the BCG when <10 years old

Post-September 2005

- Offered to those who may be exposed at work, immigrants from countries in which TB is endemic and people going to live in countries in which TB is endemic
- School Vaccination Program was abolished
- Strongly recommended for:
 - All infants (0-12 months) living in areas where incidence is 40/100,000 or more
 - All infants with a parent or grandparent born in a country where incidence of TB is 40/100,000 or more

National Institute for Health and Clinical Excellence (NICE) is an independent advisory board to the NHS – they published guidelines for the treatment of TB in March 2006

National Institute for Health and Clinical Excellence (NICE)

Independent organisation responsible for reviewing clinical data and developing national guidance on drugs and therapy areas. The DH commissions NICE to develop clinical guidelines and guidance on public health and technology appraisals. NICE is funded primarily by the DH.

NICE guidance

Prepared by independent groups, the guidance is heavily influenced by health economic data. There is a high level of compliance with these

Positive recommendation

Funding must be made available by PCTs for at least a limited number of patients in all regions

Negative recommendation

Immediately implemented by NHS related organisations, drug will not be used

NICE recommends new patients are treated with a four drug regimen, this is supported by the British Thoracic Society

NICE and BTS Guidelines

<u>Category</u>	<u>Definition</u>	<u>Initial phase</u>	<u>Continuation Phase</u>
New patient	Patient not having previously received care	2HRZ* / 2HRZE	4HR
Single drug resistance	Infected with TB resistant to one of the 1 st line drugs (shown by DST)	2HRZE	4HR
Isoniazid resistance	Infected with TB resistant to isoniazid (shown by DST)	6R	
MDR TB	Infected with TB resistant to two or more 1 st line drugs (shown by DST)	5 drugs organism is susceptible to (at least 2 of which, preferably 3, should not have been used before) – until sputum negative	At least 3 drugs the organism is susceptible to for a further 9 months (up to 24 months)
Latent TB	Positive Mantoux test or interferon-gamma immunological test but without symptoms	6H / 3HR	-

BTS guidelines state that ethambutol can be omitted in previously untreated white patients who are known to be HIV negative and have not had contact with a case of known drug resistance. Drug sensitivity tests (DST) are performed by PHLS Mycobacterium Reference Units on all samples taken by specialists. Specialists suspecting a case of drug resistant TB administer 4/5 drugs the patient has not received before and then change to a tailored regimen when the DST results are available.

Source: National Institute for Health and Clinical Excellence, British Thoracic Society

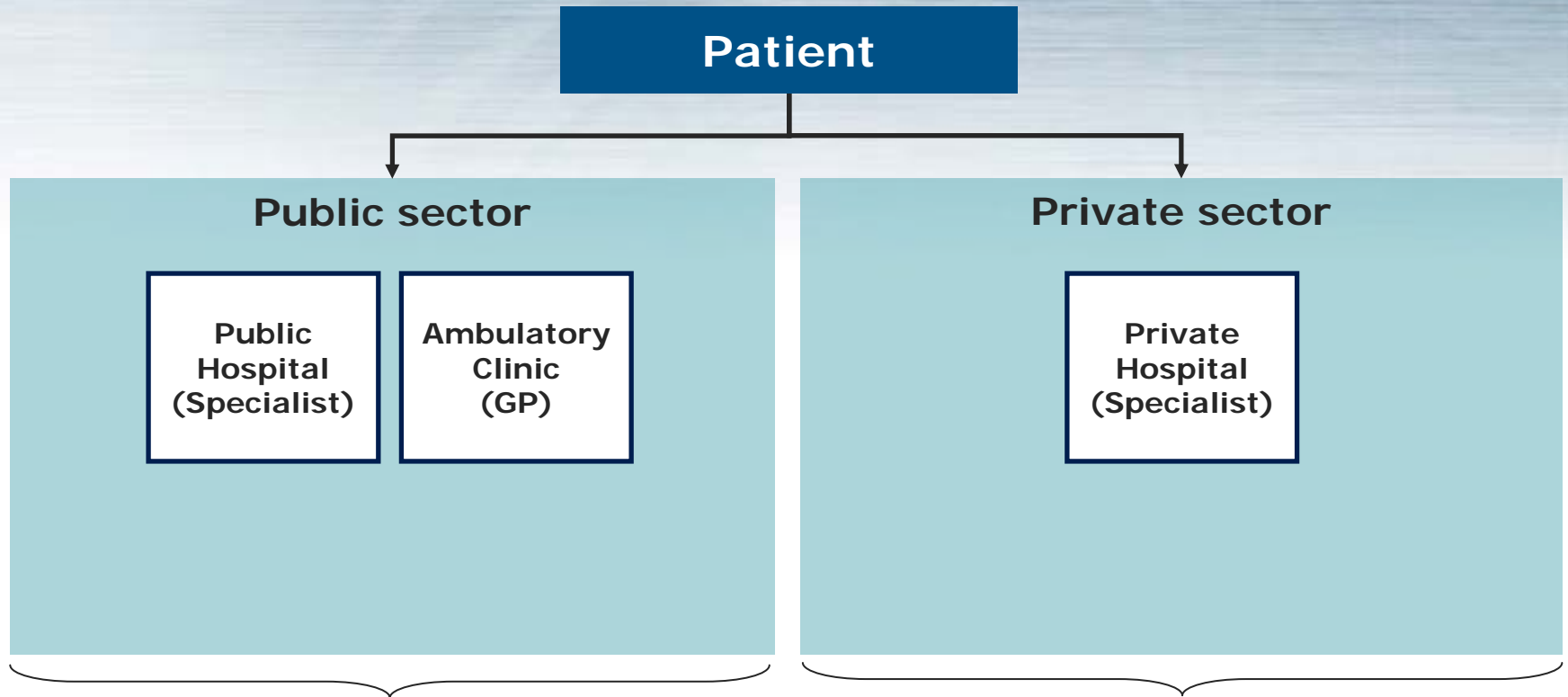
The British Thoracic Society (BTS) also specifies daily doses for 1st and 2nd line drugs

<u>1st line drug</u>	<u>Daily dosage</u>	<u>Thrice weekly dosage</u>
Isoniazid	300mg	15mg/kg
Rifampicin	<50kg – 450mg >50kg – 600mg	<50kg – 2g >50kg – 2.5g
Pyrazinamide	<50kg – 1.5g >50kg – 2g	<50kg – 3g >50kg – 3.5g
Ethambutol	15mg/kg	30mg/kg

<u>2nd line drug</u>	<u>Daily dose</u>
Streptomycin	15mg/kg
Amikacin	15mg/kg
Capreomycin	15mg/kg
Kanamycin	15mg/kg
Ethionamide	<50kg – 375mg twice daily >50kg – 500mg twice daily
Cycloserine	250-500mg twice daily
Ofloxacin	400mg twice daily
Ciprofloxacin	750mg twice daily
Clarithromycin	500mg twice daily
Rifabutin	300-450mg twice daily
Thiacetazone	150mg
Clofazamine	300mg
PAS	5g twice daily

Source: British Thoracic Society

TB patients can be treated in the public or private sector, although most remain in a public setting

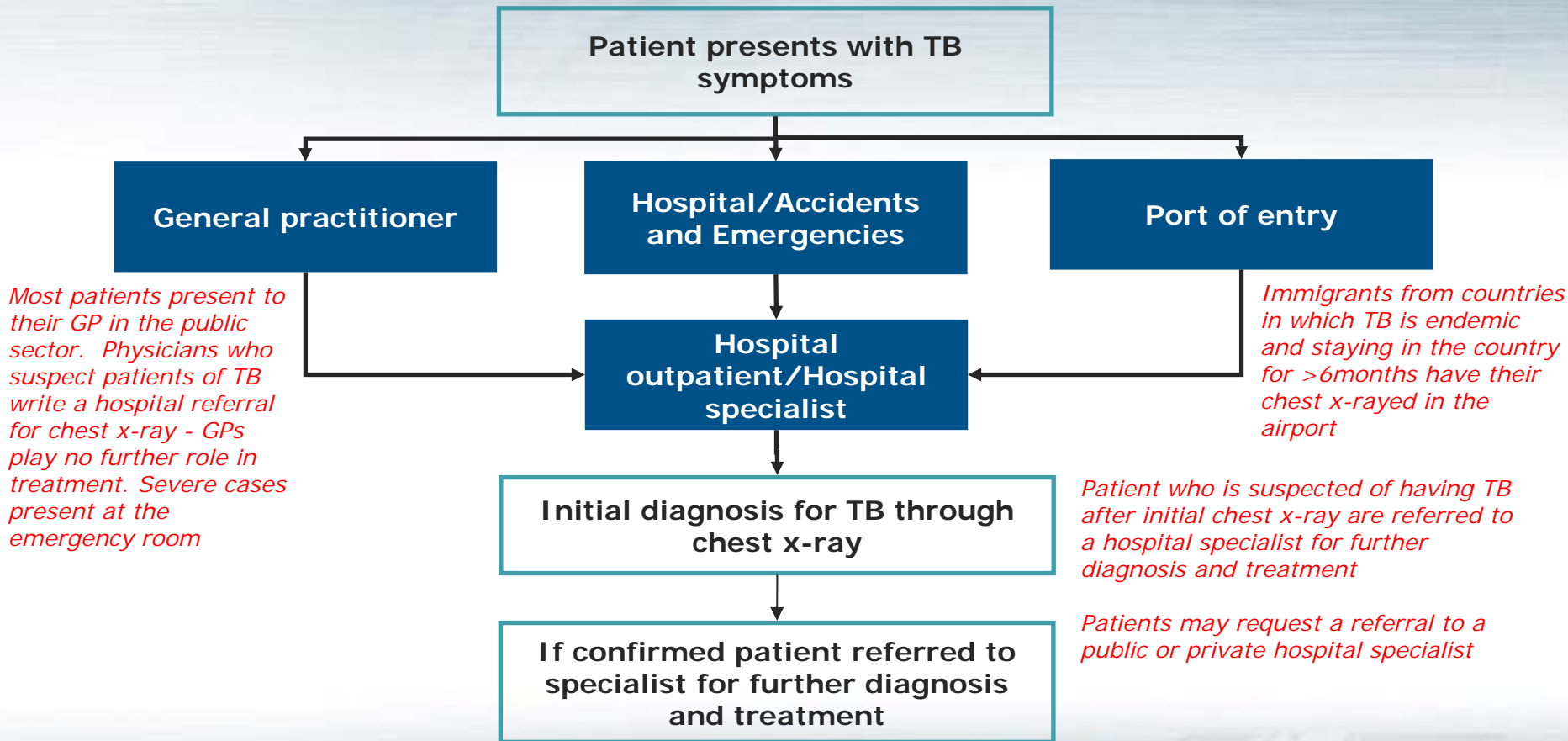


All patients must first be diagnosed by a GP in the public setting. Most patients remain in the public outpatient setting for treatment

However, patients can seek referral for a specialist in the private sector from a GP in the public setting once they have been diagnosed with TB

Patients may first visit their GP, a hospital Accident and Emergency department or be subjected to screening at their port of entry

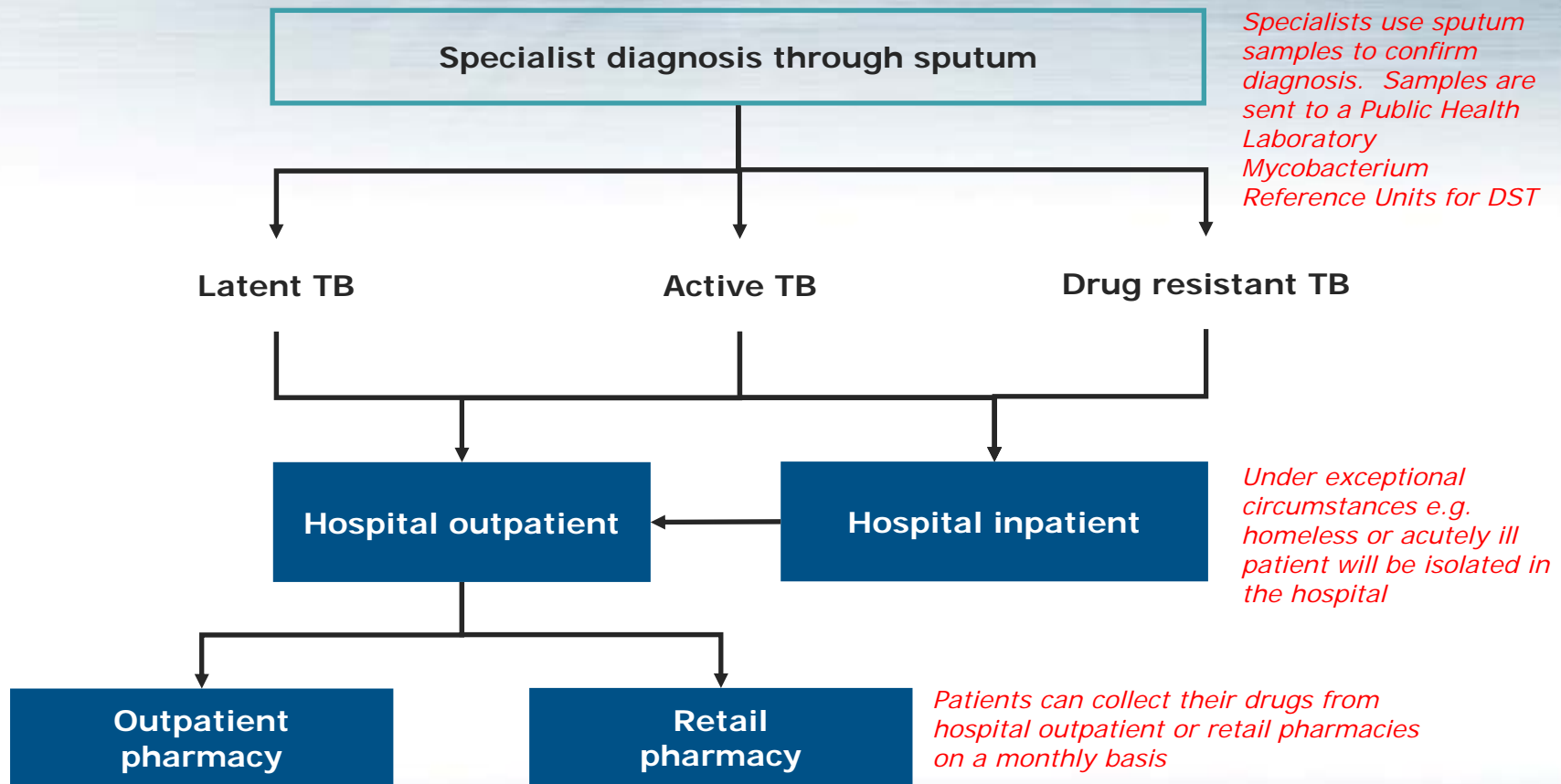
Patient flow through the public sector



Source: BTS Guidelines, Interviews

Once diagnosed, patients are referred to a specialist in the public or private setting for further diagnosis and treatment

Patient flow through the public or private sector



Source: BTS guidelines, interviews

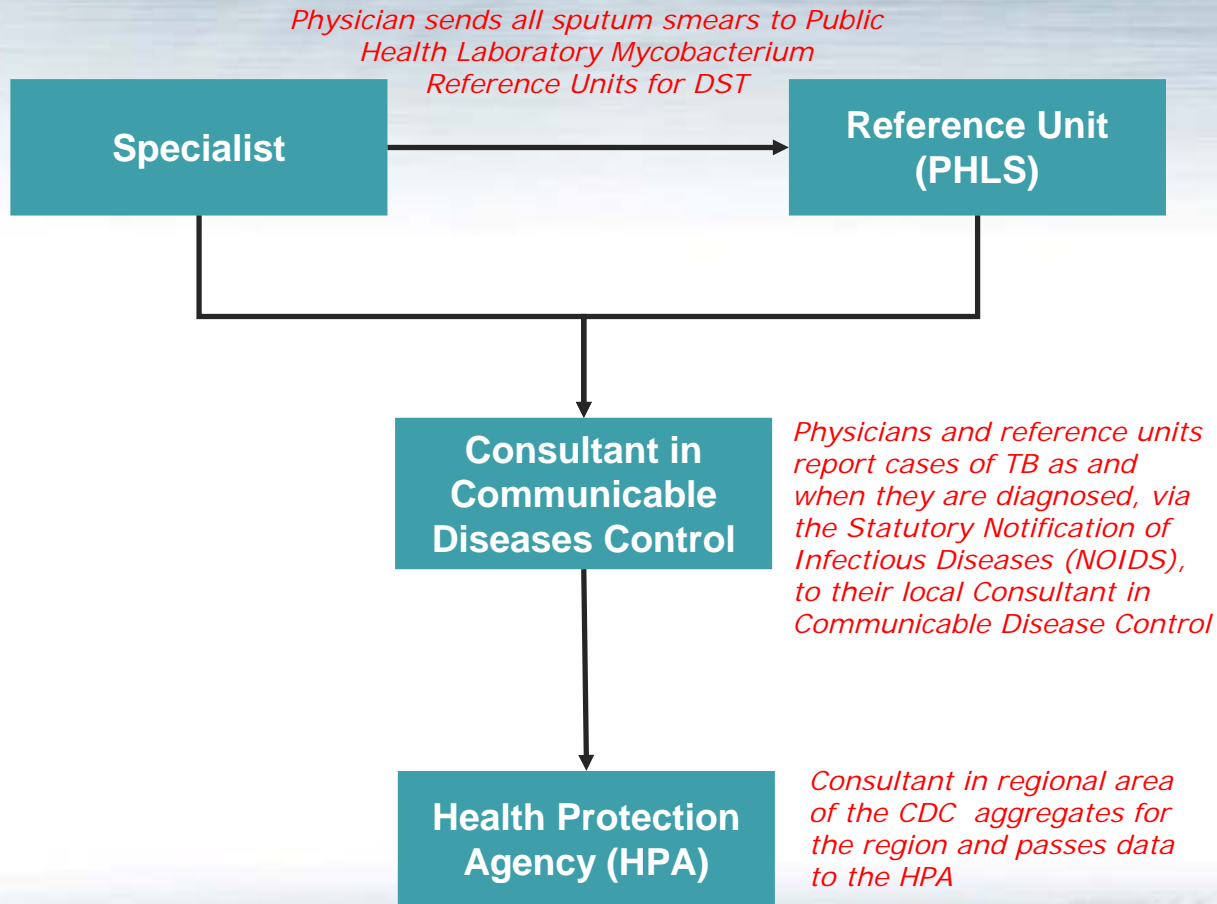
A further set of follow up tests are implemented to monitor TB patients during treatment

	Treatment initiation (Week 0)	Week 2	Week 8	Week 16	Week 24	Reason
Visit	✓	✓	✓	✓	✓	Check for S/Es Monitor change over in drug regimen
Chest x-ray					✓	To ensure treatment is working
Liver function tests	✓	✓	✓	✓	✓	Liver problems are most common S/Es – testing can be more frequent in high risk patients e.g. alcoholics
Visual tests (colour vision and visual acuity)	✓	✓	✓			S/E of ethambutol is vision damage – patient monitored whilst taking ethambutol

Source: Interviews

Physicians are required to report all detected TB cases to the Health Protection Agency

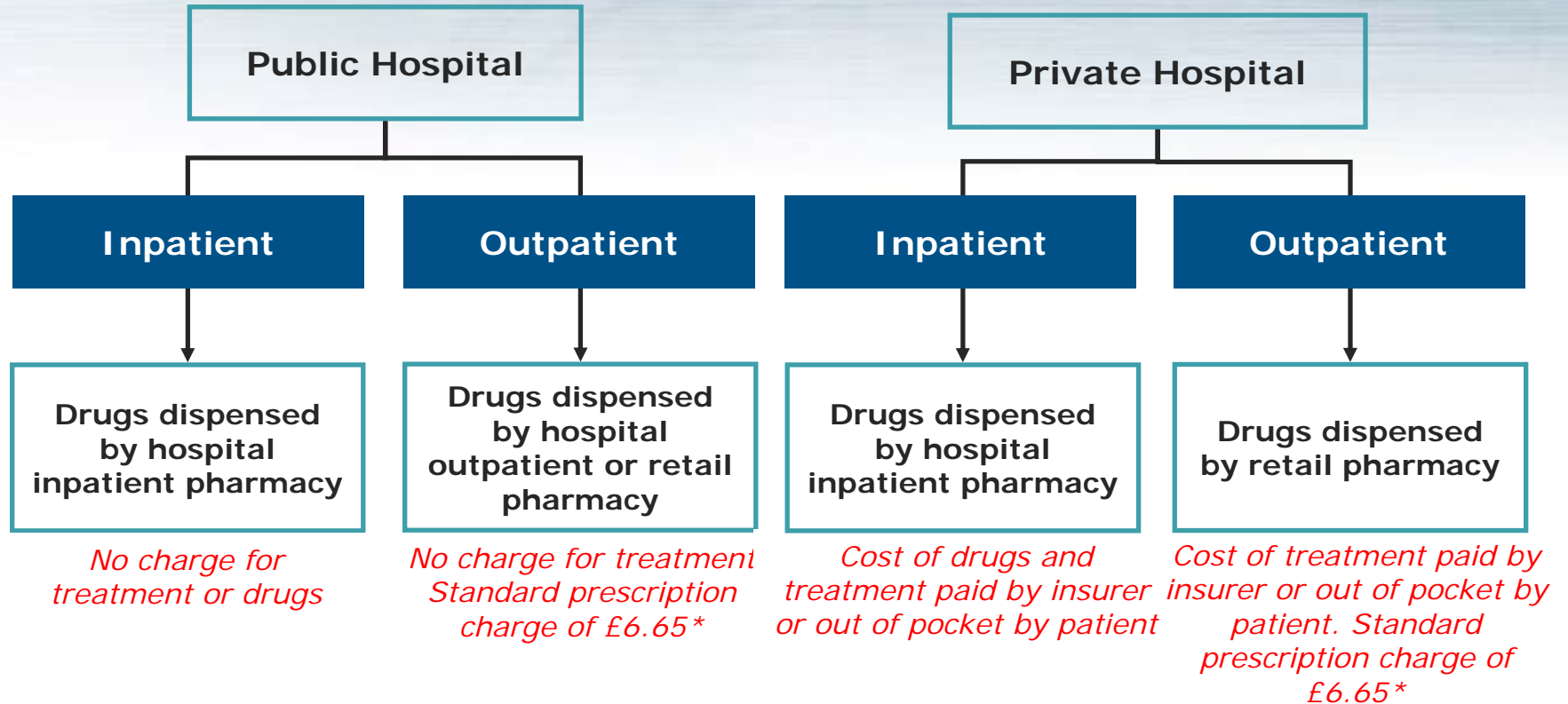
Flow of reporting



Source: Health Protection Agency Website, Interviews

TB treatment is free in the public sector but not the private sector; the cost of drugs in both sectors depends on treatment location

Charges for TB drugs in each healthcare setting



**Exceptions to these charges include pregnant women, children, war and service pensioners, children under 16, students aged 16, 17 or 18 in full-time education, men and women aged 60 and over, etc*

Immigrants, irrespective of legal status, are entitled to free treatment for TB within the public sector

Immigrant entitlement to healthcare within the public sector

<u>Status</u>	<u>GPs</u>	<u>Hospitals</u>
Asylum seekers Refugees Discretionary leave to stay Humanitarian protection	Access without charge Pay standard charge for Rx (unless exempt under normal rules)	
Failed asylum seekers	Emergencies or treatment which is immediately necessary is free Must pay for other treatment	Any course of treatment already underway remains free of charge Any new course is chargeable

- TB is included in a list of 'exempt diseases for which no charge is made', including malaria, plague, leprosy and cholera, etc
- All patients receive TB treatment for free irrespective of their immigration status
 - They must still pay the standard prescription charge, unless exempt under the normal rules
- There is no risk that an illegal immigrant will be reported to the authorities

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In the UK, 1st and 2nd line TB drug procurement mechanisms vary according to the setting in which drugs are administered

	<u>Pricing</u>	<u>Distribution</u>
Public Hospitals	<ul style="list-style-type: none">• <i>NHS Purchasing And Supply Agency Contract</i>• <i>PCT Pharmacy Purchasing Group</i>• <i>Direct Negotiations</i>	<ul style="list-style-type: none">• <i>Direct to Facility</i>• <i>Via Wholesaler</i>
Private Hospitals	<ul style="list-style-type: none">• <i>Pharmacy Purchasing Group</i>• <i>Direct Negotiations</i>	
Retail Pharmacies		<ul style="list-style-type: none">• <i>Via Wholesaler and/or Company Warehouse</i>

Source: PQ Systems, interviews

In the public hospital sector, the NHS Purchasing and Supply Agency (PASA) prices many 1st and 2nd line TB drugs via a bid and tender system

What PASA is

- NHS Purchasing and Supply Agency (PASA)
- Executive agency within the Department of Health that negotiates contracts with suppliers

How it works

- Uses a bid and tender system to select suppliers and determine prices of drugs
- Contracts apply to all NHS facilities
- Selects a supplier on a number of criteria:
 - Price
 - Quality
 - Record of supply

What it applies to

- A majority of TB drugs with the exception of pyrazinamide (imported)

Non-PASA drugs are procured by one of 14 Pharmacy Purchasing Groups that work on behalf of the Primary Care Trusts (PCTs)

- Each PCT is represented by one of 14 pharmacy purchasing groups
- Pharmacy purchasing groups consist of Chief Pharmacists from each of the hospitals covered by the group
- Pharmacy purchasing groups aggregate demand and operate a bid and tender system for all purchases >£100,000 (mandatory under EU law)
- Once a price is agreed with a supplier all hospitals within the group are able to purchase at that price

Additionally, public hospitals are also able to procure drugs not covered by PASA or Pharmacy Purchasing Group tenders direct from suppliers

- Chief pharmacists may negotiate individually with manufacturers and wholesalers in order to procure drugs not covered by a PASA contract or Pharmacy Purchasing Group
- Public hospitals must operate a bid and tender system for all purchases >£100,000 (mandatory under EU law)

Private hospitals and retail pharmacies are not entitled to prices negotiated by PASA or PCT Pharmacy Purchasing Groups and negotiate with suppliers individually

Direct negotiations

Pharmacy Purchasing Group

Private hospitals

- Negotiate purchases directly with suppliers

- May form chains to aggregate demand (e.g. the BUPA hospital group) in which one pharmacist is responsible for purchasing for the entire group

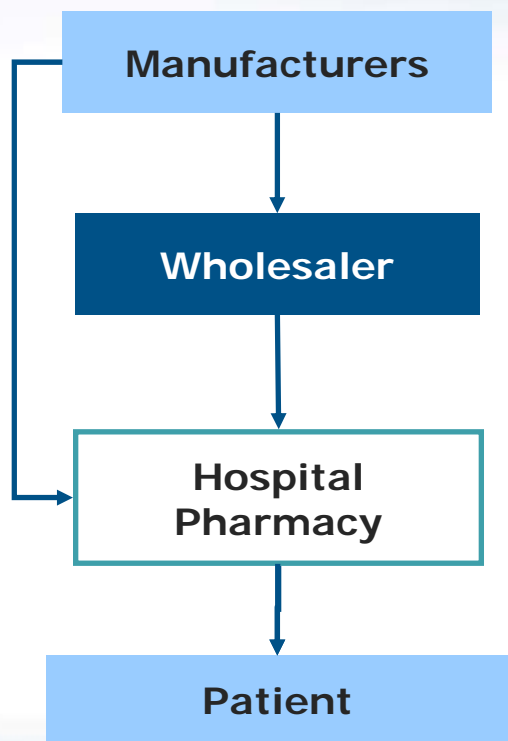
Retail Pharmacies

- Negotiate purchases directly with suppliers
- Suppliers may only offer authorised margins and discounts to pharmacists, in turn, pharmacists are only permitted to use specified mark-ups, thus profitability is limited

- May form chains to aggregate demand e.g. Boots

Public and private hospital distribution are similar to one another—the key difference lies in the mark-ups applied as the drugs flow to patients

Drug Flow:
Public/Private Hospitals

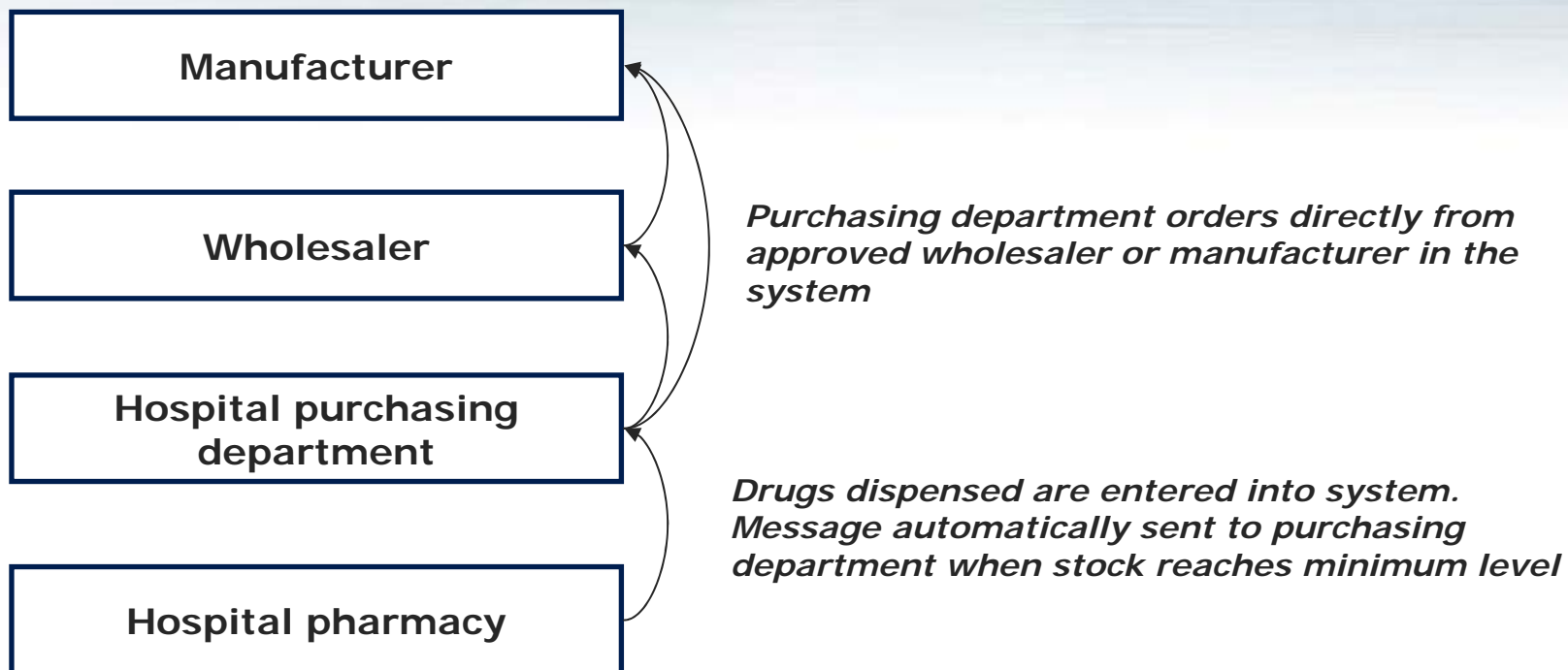


	<u>Public Hospitals</u>	<u>Private Hospitals</u>
1st point of sale	Manufacturers holding the contract supply 1st and 2nd line TB drugs at the agreed price direct to hospitals or, if they lack a distribution network, via a wholesaler	
Wholesaler sale	Wholesalers holding a PASA contract supply 1st and 2nd line TB drugs at the agreed price direct to hospitals. Free to set margins for generic products (covers most TB drugs) and limited to roughly 2.8% of ex-manufacturers price on branded products	Wholesalers supply 1st and 2nd line TB drugs at the agreed price direct to hospitals within the group. Free to set margins at any level when dealing with the private sector
Hospital sale	Hospitals then distribute 1st and 2nd line TB drugs to the patient either free of charge (inpatients) or for a standard prescription charge (outpatients)	Hospitals then sell 1 st and 2 nd line TB drugs to the patient at a marked up price

Source: PQ Systems, interviews

Once suppliers have been selected, the actual ordering process is automated through a computer system

**Order Flow: Hospital
Pharmacy Sector**



Source: Interviews

In the retail pharmacy sector, 1st and 2nd line TB drugs may flow through a centralized warehouse if procured through a group purchasing process

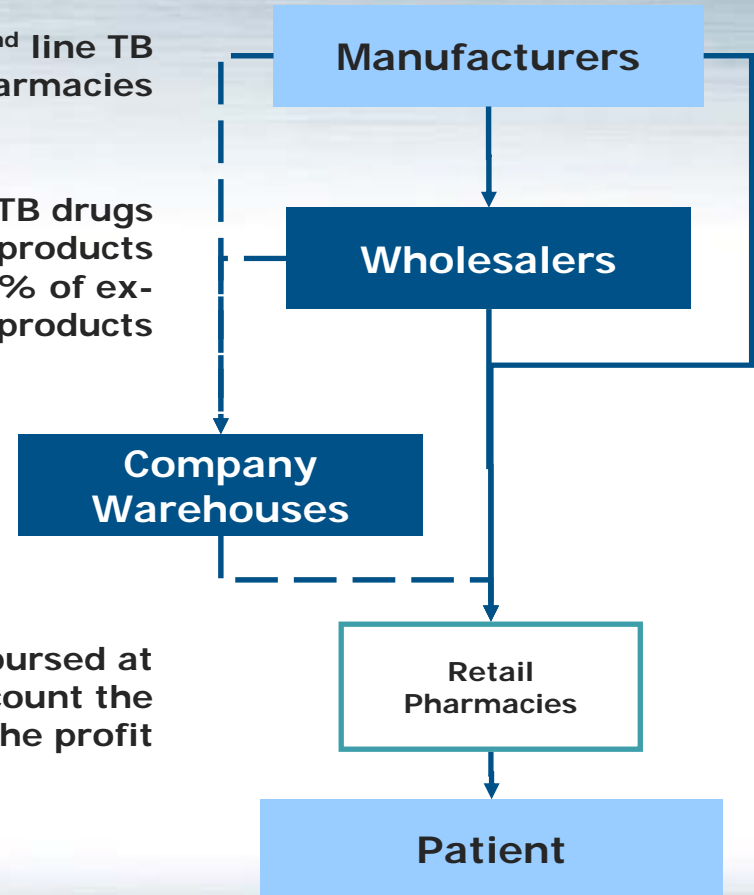
Drug Flow: Retail Pharmacy Sector

1st point of sale: Manufacturers supply 1st and 2nd line TB drugs to wholesalers or to pharmacies

2nd point of sale: Wholesalers sell 1st and 2nd line TB drugs to pharmacies. Free to set margins for generic products (covers most TB drugs), limited to roughly 2.8% of ex-manufacturers price on branded products

Warehousing: Centralised warehouses may be used to store 1st and 2nd line TB drugs procured on behalf of members of pharmacy chains

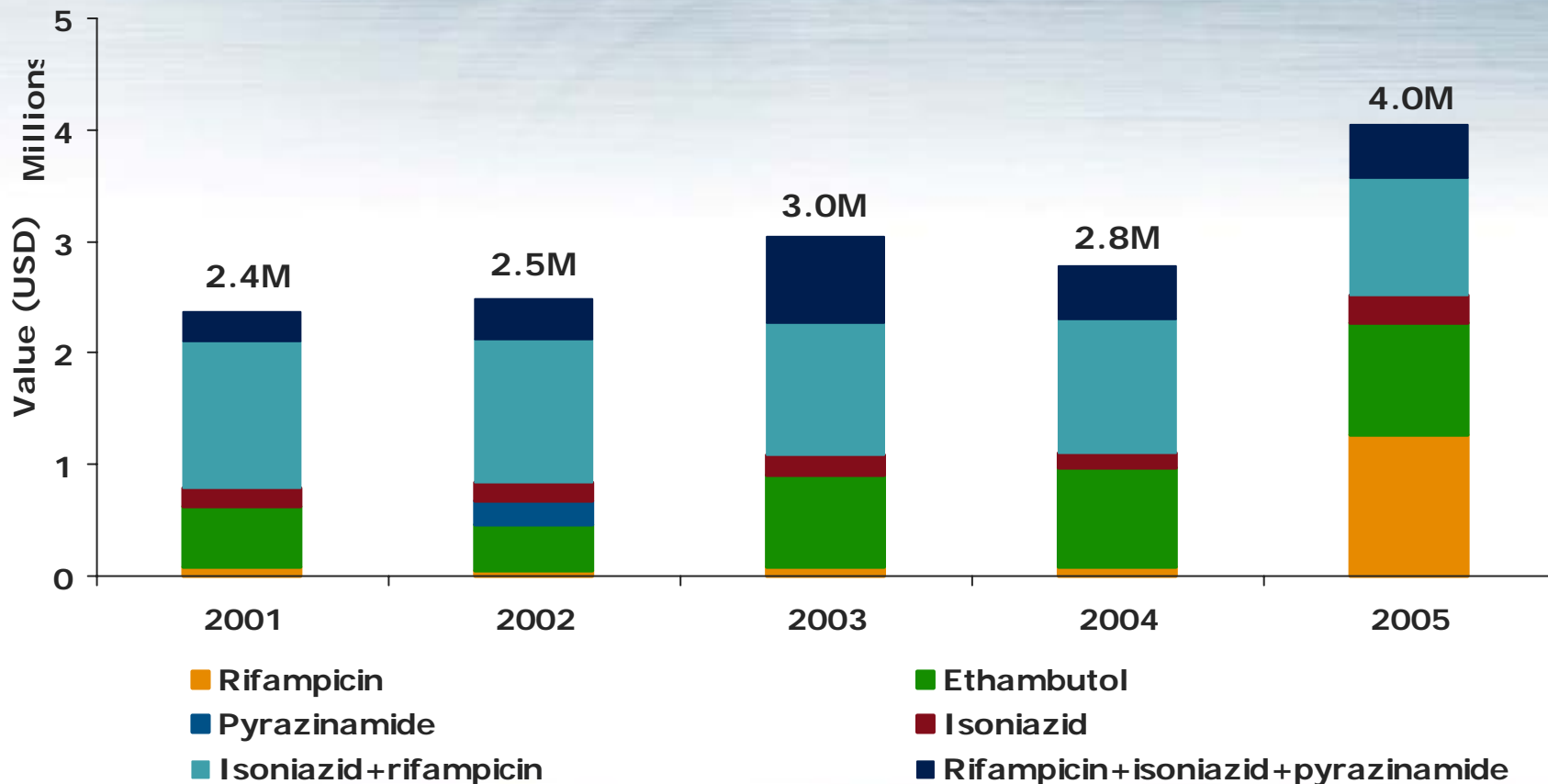
Pharmacy sale: Drugs are always reimbursed at the list price so the larger the discount the pharmacist can obtain the greater the profit



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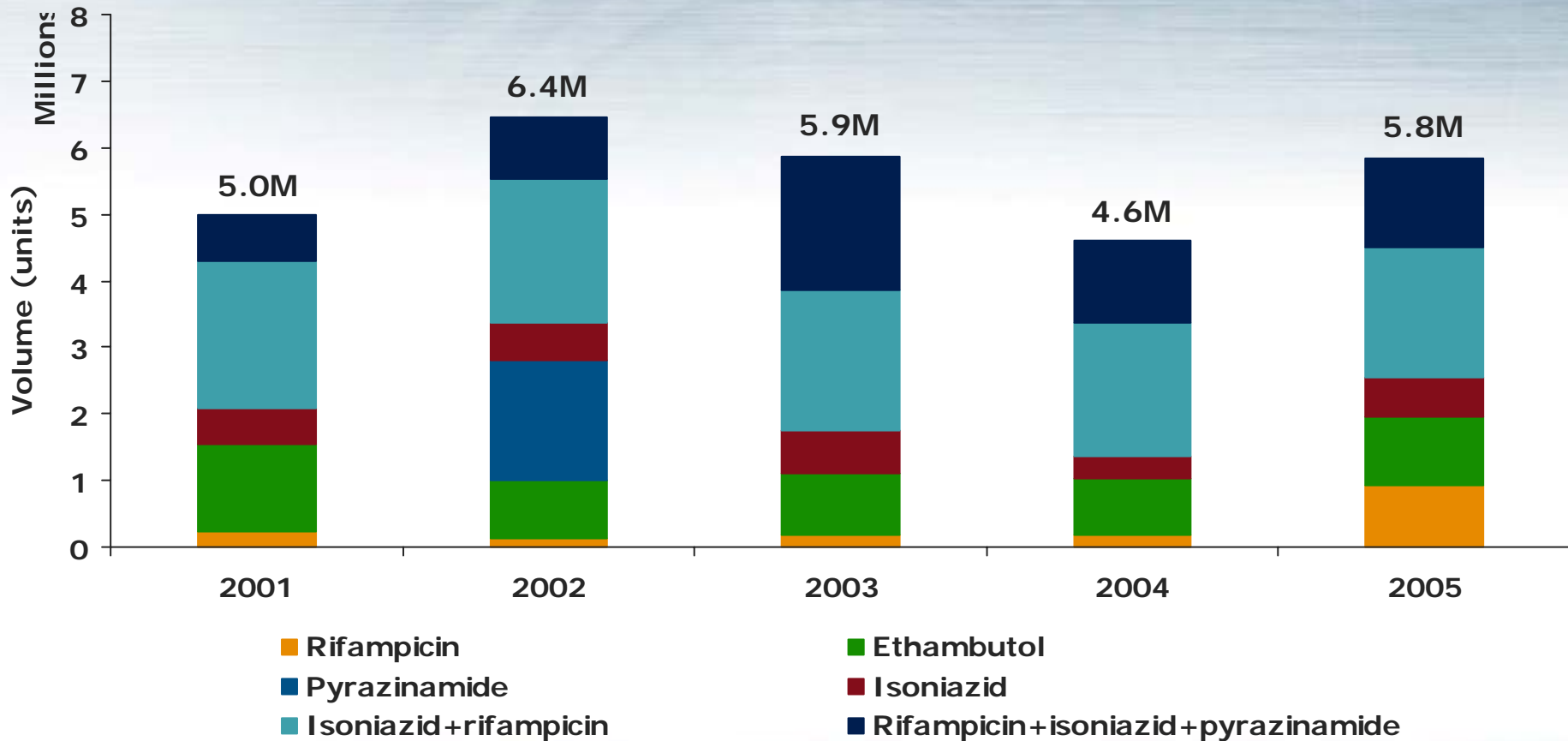
The overall 1st line drug market value has been increasing over the last five years and is currently 4M USD



Note: Includes 1st line drugs that may also be used in the 2nd line treatment

Source: IMS MIDAS data

Over that same time period, the volume of 1st line drugs dispensed has fluctuated

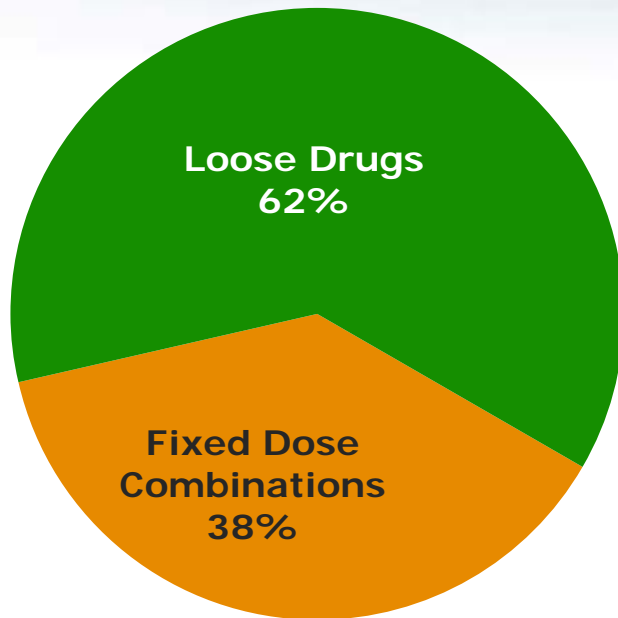


Note: Includes 1st line drugs that may also be used in the 2nd line treatment

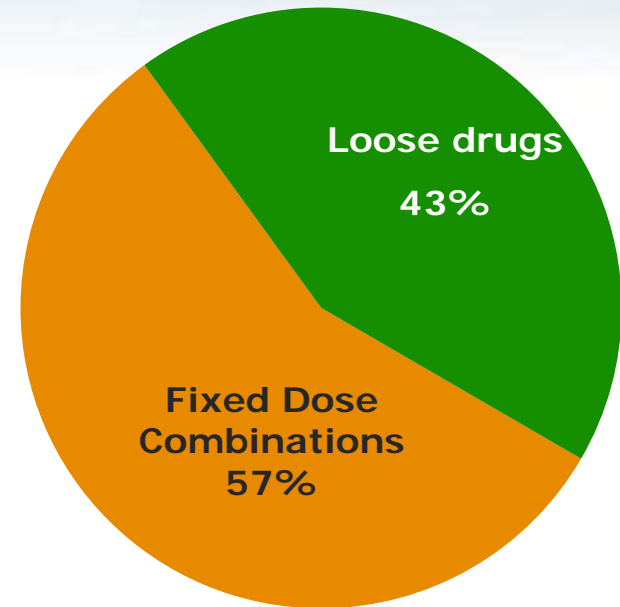
Source: IMS MIDAS data

FDCs currently account for 38% of the UK market by value at 1.5M USD and 57% by volume at 3.3M units

Total 1st Line TB Market Value by Drug in 2005 (4M USD)



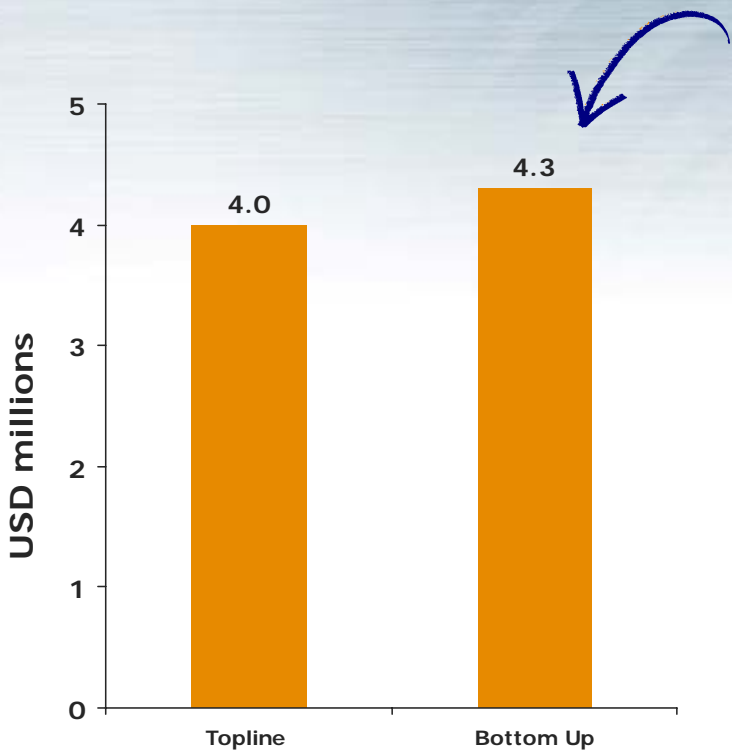
Total 1st Line TB Market Volume by Drug in 2005 (5.8M USD)



Note: Includes 1st line drugs that may also be used in the 2nd line treatment

Source: IMS MIDAS data

Bottom up estimates confirm the top line value data and give a 1st line market estimate of between 4-4.3M USD

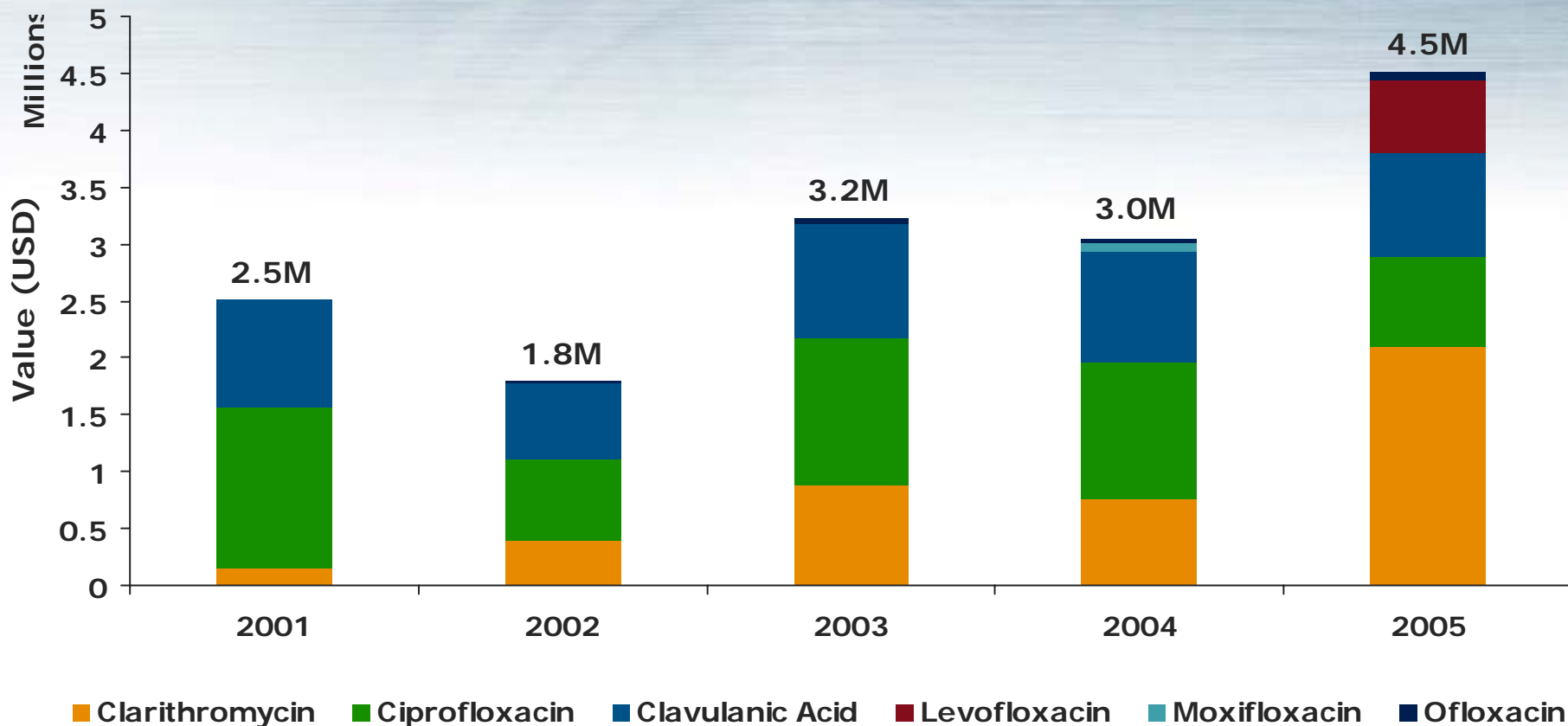


	Active	Resistant	Latent	Retreated
Total patients treated	8,585			
Patients per category*	7,172	412	622	379
Average cost per patient	489.83	1139.10	170.19	468.24
Total cost per category	3,513,013	469,308	105,859	177,464
1st line estimate	4,265,644			

Note: Includes 1st line drugs that may also be used in the 2nd line treatment

Source: HPA, IMS MIDAS data, IMS analysis, BNF. See appendix for details of calculation

The market value of all 2nd line TB drugs is growing overall - the market is currently valued at 4.5M USD

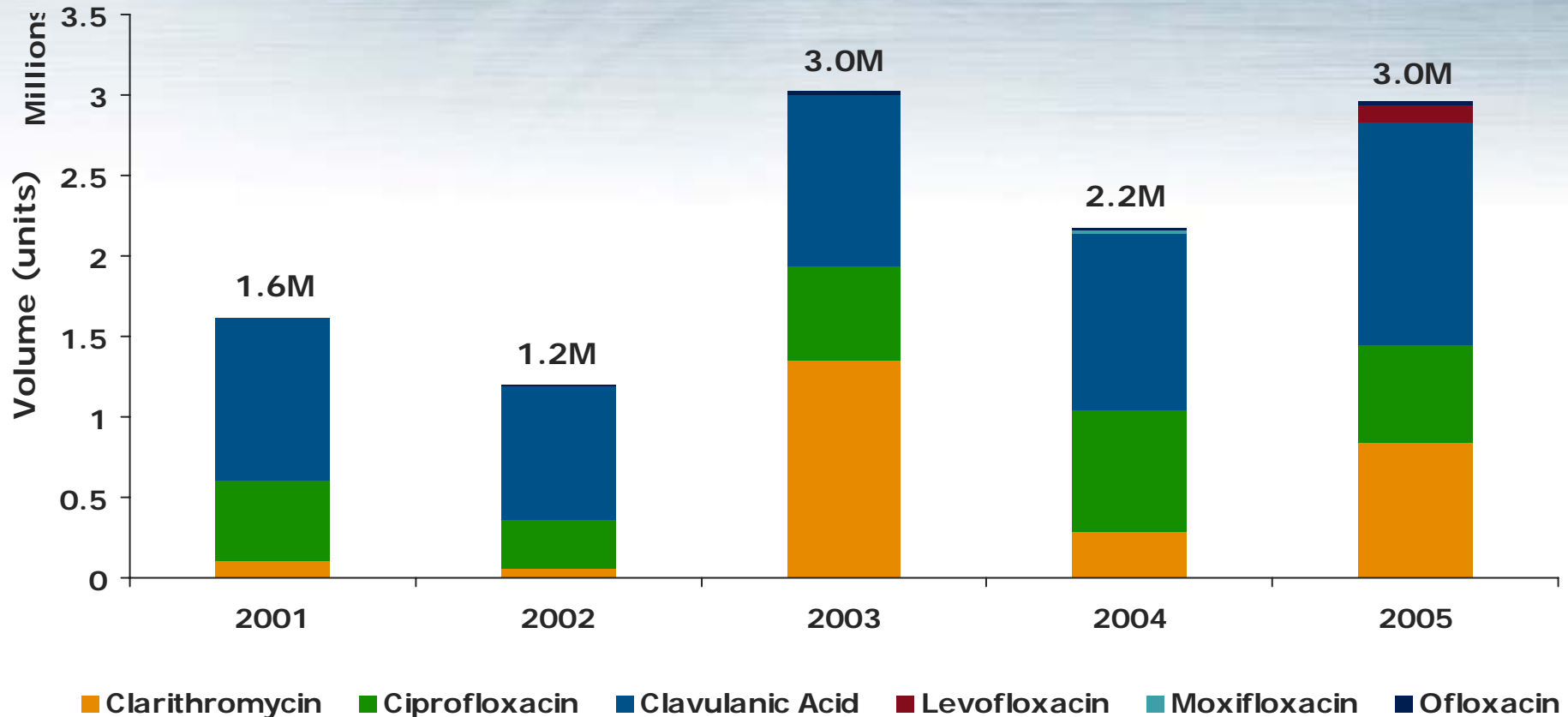


Source: IMS MIDAS data

Note: Does not include 1st line drugs that may also be used in the 2nd line treatment

*Data was not available for all 2nd line drugs used in this country. Drugs listed do not comprise full 2nd line treatment regimen in this country.

The volume of 2nd line TB drugs dispensed has fluctuated widely and currently stands at 3M units



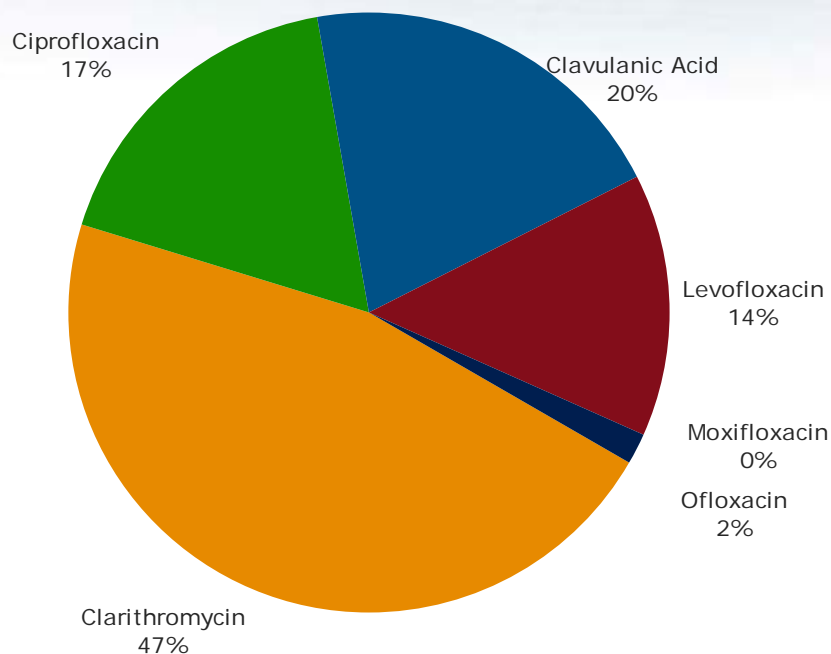
Source: IMS MIDAS data

Note: Does not include 1st line drugs that may also be used in the 2nd line treatment

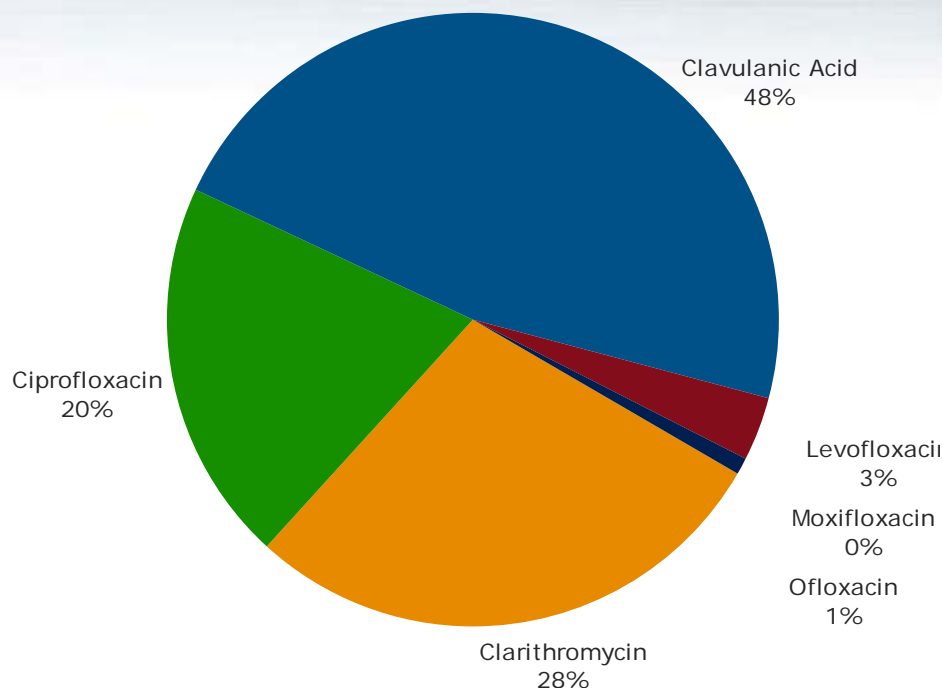
*Data was not available for all 2nd line drugs used in this country. Drugs listed do not comprise full 2nd line treatment regimen in this country.

Clarithromycin dominates the 2nd line market with sales of 2.1M USD, whereas clavulanic acid has the greatest volume of sales with 1.4M units in 2005

Total 2nd Line TB Market Value by Drug in 2005 (4.5M USD)



Total 2nd Line TB Market Volume by Drug in 2005 (3M units)

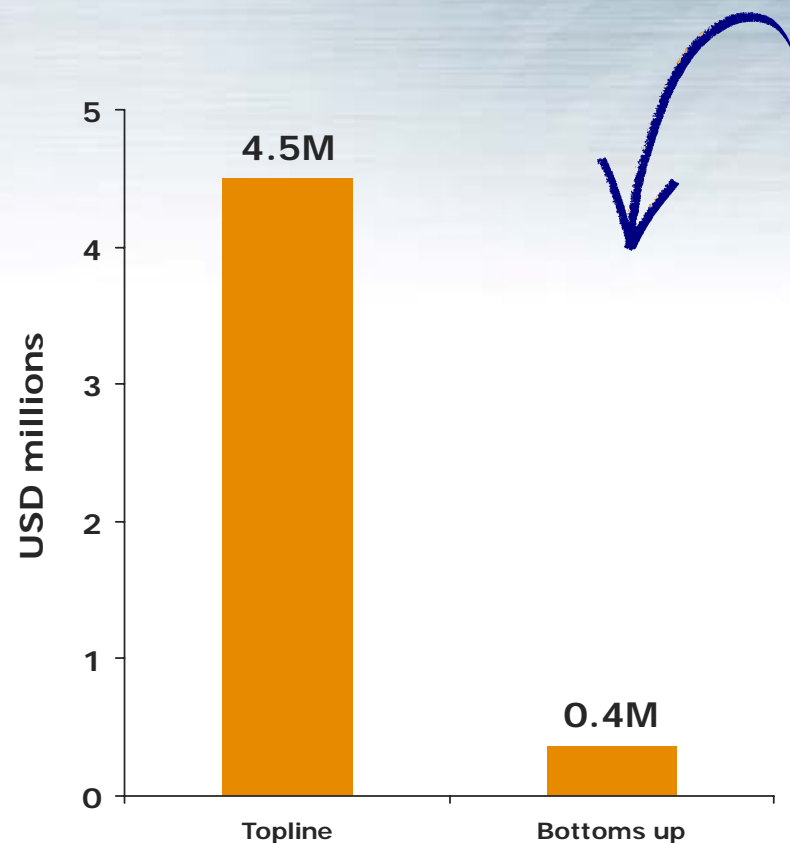


Source: IMS MIDAS data

Note: Does not include 1st line drugs that may also be used in the 2nd line treatment

*Data was not available for all 2nd line drugs used in this country. Drugs listed do not comprise full 2nd line treatment regimen in this country.

Top line value figures and bottom up calculations suggest the 2nd line market value is 0.4M to 4.5M USD



	Diagnosed in 2003	Diagnosed in 2004
Total patients receiving treatment in 2004	84	
Patients per category*	49	35
Average cost of treatment	1,665	7,242
2nd line estimate	357,379	

Note: Does not 1st line drugs that may also be used in the 2nd line treatment

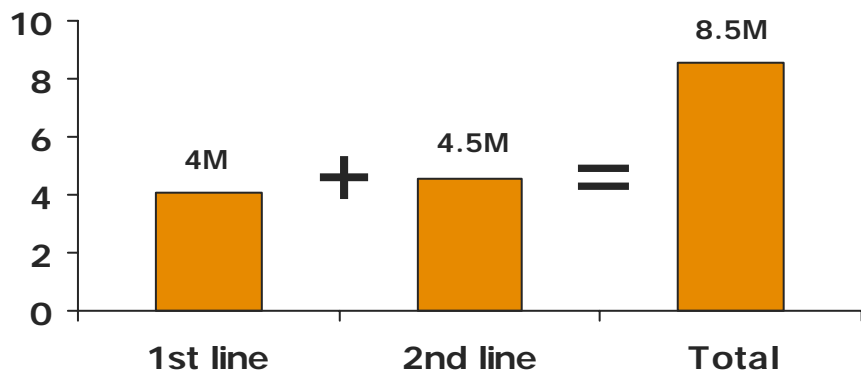
Source: *HPA, IMS MIDAS data, IMS analysis, WHO. See appendix for details of calculation

However, it is impossible to perform an accurate bottom up calculation for 2nd line drugs due to large numbers of uncertainties, hence, value is estimated to be 4.5M USD

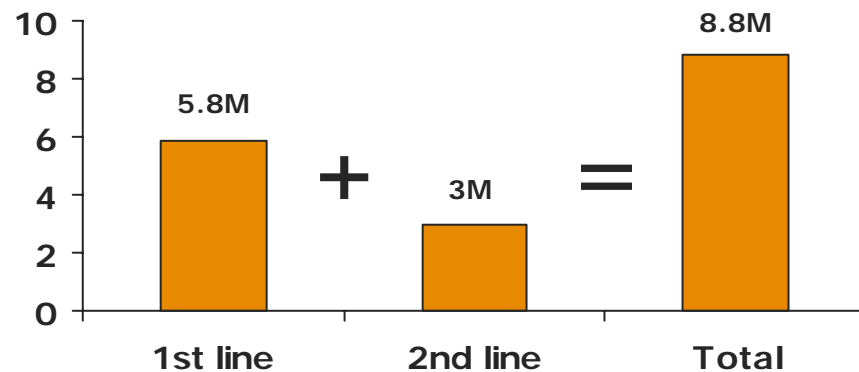
- A bottom up calculation involves assumptions about which drugs are administered to 2nd line patients, the dose at which they are given and the duration of treatment, all of which vary widely between patients
- Additionally, in 1st line patients suffering from side effects the 1st line drug responsible for those side effects is often substituted for a 2nd line drug
- Physicians estimated the incidence of side effects to be between 5-30%, however it is impossible to be certain how many 1st line drugs are substituted in these cases and which 2nd line drugs they are substituted for
- Hence, there are too many uncertainties for an accurate bottom up calculation and value is estimated to be \$4.5M USD (based on IMS MIDAS figures)

If we combine the value and volume of 1st and 2nd line drugs we have a market value of between 8.5M USD and volume of 8.8M units

Total UK TB drug market value (8.5M USD)



Total UK TB drug market volume (8.8M units)



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Total market value and volume figures for all 1st line drugs in 2005

<u>1st line drug</u>	<u>Volume (units)</u>	<u>Value (USD)</u>
Rifampicin	929,214	1,267,431
Ethambutol	1,037,371	996,554
Isoniazid	568,680	248,733
Pyrazinamide*	1,803,960	213,816
Rifampicin/isoniazid combination	1,979,166	481,640
Rifampicin/isoniazid /pyrazinamide combinations	1,329,845	1,055,033

Source: IMS MIDAS

*Figures for 2005 not available so 2002 figures used

Total market value and volume figures for all 2nd line drugs in 2005

<u>2nd line drug</u>	<u>Volume (units)</u>	<u>Value (USD)</u>
Clavulanic acid	1,392,107	913,849
Ciprofloxacin	604,311	782,092
Clarithromycin	838,599	2,101,591
Ofloxacin	26,393	76,633
Levofloxacin	99,928	644,369
Moxifloxacin*	19,869	71,798

Source: IMS MIDAS

*Figures for moxifloxacin were not available for 2005, thus data from 2004 were used

Manufacturers of 1st line drugs in the UK

<u>1st line drug</u>	<u>Manufacturers</u>
Rifampicin	Generics UK; Hillcross; Novartis
Ethambutol	Genus Pharm; Lederle
Isoniazid	IMS Labs; Novartis; UCB Pharma; Ivax; Martindale; Celltech Pharma
Pyrazinamide	Merck Sharpe and Dohme
Isoniazid+Rifampicin	Aventis
Isoniazid+Rifampicin+Pyrazinamide	Aventis

Source: IMS MIDAS

Manufacturers of 2nd line drugs in the UK

<u>2nd line drug</u>	<u>Manufacturer</u>
Levofloxacin	Aventis
Ofloxacin	Aventis; Hillcross; Sandoz; Teva UK; Generics UK
Ciprofloxacin	Hillcross; Sandoz; Teva UK; Generics UK; Ivax
Clarithromycin	Teva UK; Hillcross

Source: IMS MIDAS

Method of calculating cost of treating 1st line TB patients

- Patient numbers were sourced from the EuroTB website
- Cost of the regimen (for a 70kg patient) was calculated using prices of the most popular brand and pack size (by units sold) for each of the 1st line drugs
- Patient population was split into active, drug resistant, latent and retreated
- The size of each subpopulation of TB patients was then multiplied by the cost of the regimen they receive
- These figures were then summed to give a top-line value
- The low end estimate was derived by summing the lowest cost regimen to treat each of these subpopulations of patients
- The high end estimate was derived by summing the highest cost regimen to treat each of these subpopulations of patients

Method of calculating cost of treating 1st line TB patients (USD)

	Active	Resistant	Latent	Retreated
Total patients treated	8,585			
Patients per category	7,172	412	622	379
Average cost per patient	489.83	1139.10	170.19	468.24
Total cost per category	3,513,013	469,308	105,859	177,464
First Line estimate	4,265,644			

Source: IMS MIDAS, IMS Expertise

Method of calculating cost of treating 2nd line TB patients

Hospital

	Drug	Price per day	Price for one year
Initial Phase	Levo	4.99	1821.04
	Cipro	0.55	201.95
	Clarith	2.01	733.98
	Clav	1.00	364.31
	Ofx	6.94	2534.19
Cont. Phase	Cipro	0.55	201.95
	Clarith	2.01	733.98
	Clav	1.00	364.31
total cost of treatment euros			6956
total cost of treatment USD			8907
Cost of initial phase			7242
Cost of continuation phase			1665

Retail

	Drug	Price per day	Price for one year
Initial Phase	Levo	4.99	1821.04
	Cipro	1.98	722.25
	Clarith	4.01	1465.28
	Clav	1.00	364.31
	Ofx	0.58	213.22
Cont. Phase	Cipro	1.98	722.25
	Clarith	4.01	1465.28
	Clav	1.00	364.31
total cost of treatment euros			7138
total cost of treatment USD			9141
Cost of initial phase			5873
Cost of continuation phase			3268

Source: IMS MIDAS, IMS Expertise

MIDAS data in the UK is collected in public hospitals and retail pharmacies

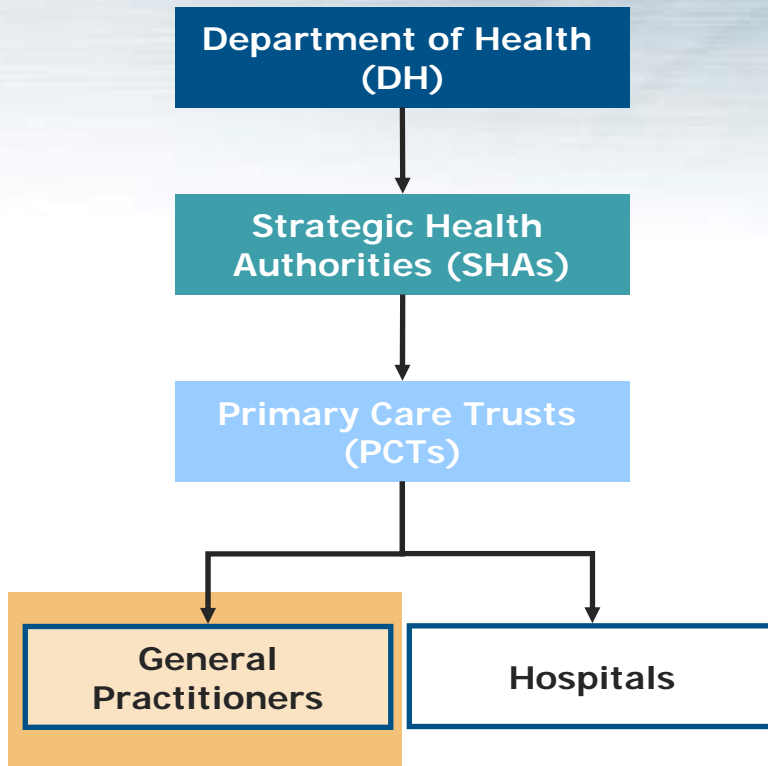
- MIDAS data in the UK is collected for public hospitals and retail pharmacies – drugs dispensed by private hospitals are not included
 - All prescriptions dispensed by pharmacies in public hospitals and retail pharmacies are captured in the data
 - Public hospital data includes prescriptions dispensed by both hospital inpatient and outpatient pharmacies
- The value data we have used is collected at an ex-manufacturer price and so represents the value of drug sales when sold by the manufacturer (not the value of sales to the end user)
- The volume data we have used collects units sold. The figure given covers the number of individual units sold. In most cases a unit is a single tablet. For injectables, it is a single pre-filled syringe

PharmaQuery Systems is IMS's unique online database of Pricing and Reimbursement regulations in 22 key world markets

- PQ Systems provides detailed coverage, on a country by country basis, of 22 key pharmaceutical markets
 - Argentina, Australia, Belgium, Brazil, Canada, Chile, China, Denmark, France, Germany, Hungary, Italy, Japan, Mexico, Netherlands, South Korea, Spain, Sweden, Switzerland, UK and the USA
- It contains detailed information about pricing and reimbursement regulations in each country
 - This information is divided into 4 areas; facts and figures, healthcare system, pharmaceutical market and useful information
- Information is updated daily by a network of multilingual pricing analysts

Source: www.imshealth.com

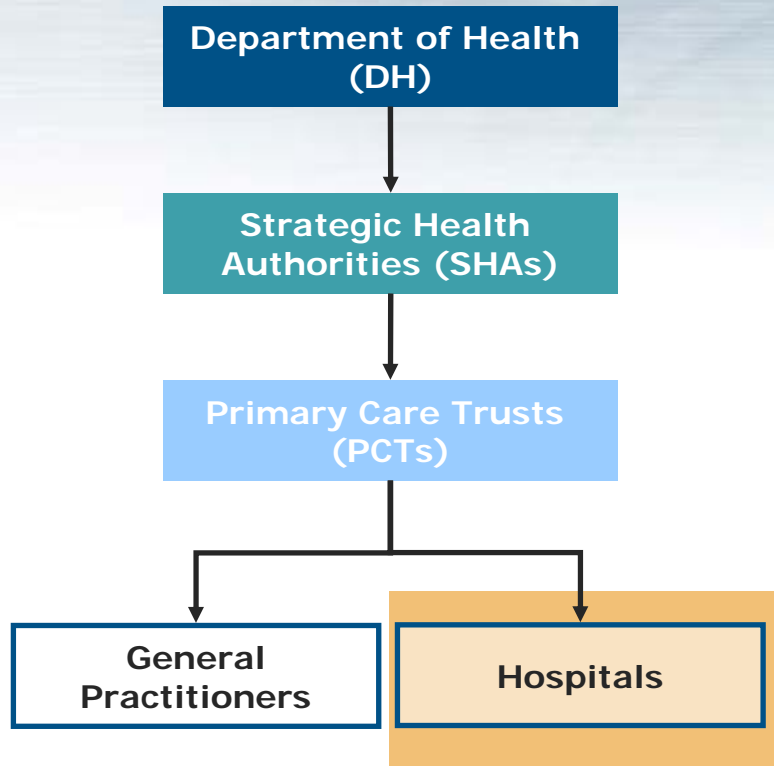
In all diseases patient care begins in the ambulatory setting - GPs either treat patients or refer them on to the hospital specialists



General Practitioners

- Primary care is delivered by General Practitioners (GPs) on an outpatient basis
- Services rendered are free of charge
- Referral is needed to gain access to hospital/specialist care

Patients can gain access to specialists in either the private or public hospital setting



Public Hospital

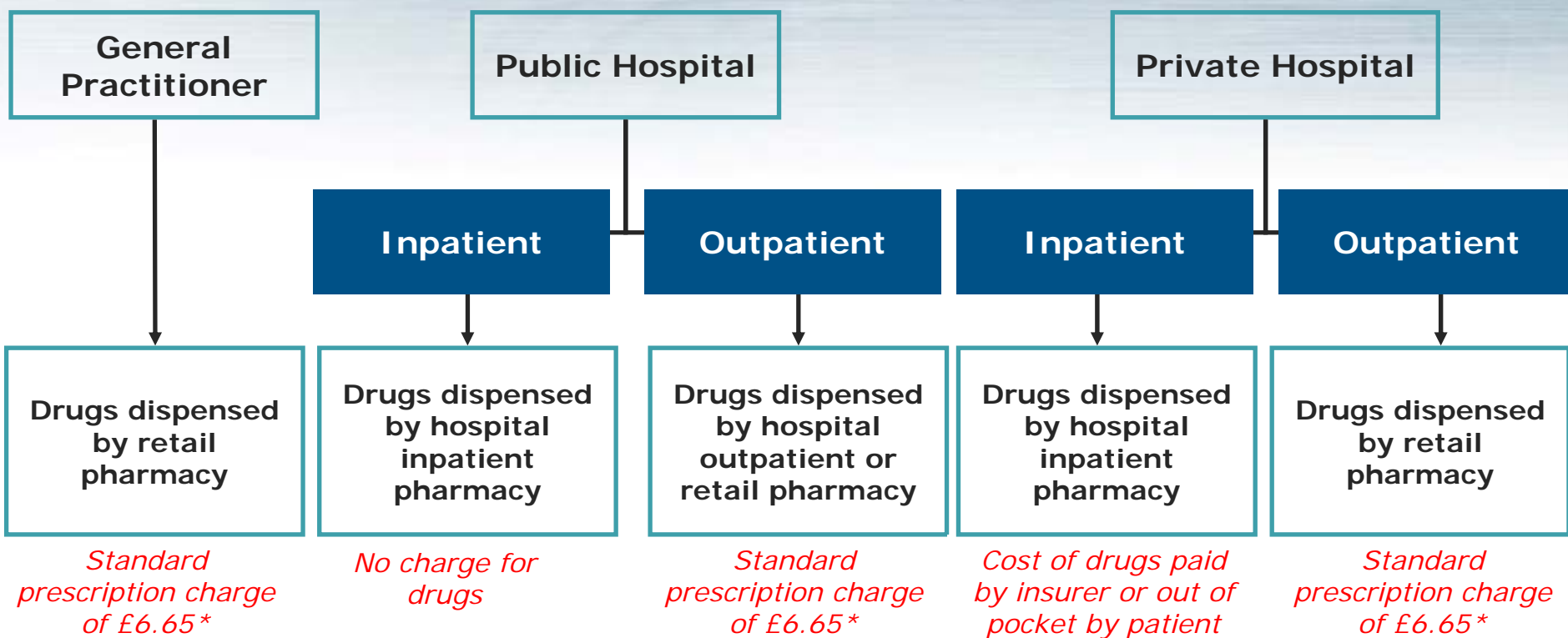
- Managed by Hospital Trusts that are contracted by PCTs to provide secondary care in exchange for funding
- Services rendered are free of charge

Private Hospital

- Not under the jurisdiction of the NHS
- Patients with private health insurance (13%) or who wish to pay out of pocket may be referred to private hospitals by their GPs
- Patients pay fees for services and treatments rendered at these facilities

The fee patients must pay for their drugs varies between treatment settings

Charges for drugs in each healthcare setting



**Exceptions to these charges include pregnant women, children, war and service pensioners, children under 16, students aged 16, 17 or 18 in full-time education, men and women aged 60 and over etc*

In the UK, marketing approval for all drugs occurs through one of three routes

Marketing Approval Routes in the UK

Centralised Procedure

- The European Medicines Agency (EMA) reviews applications
- Grants access throughout the EU

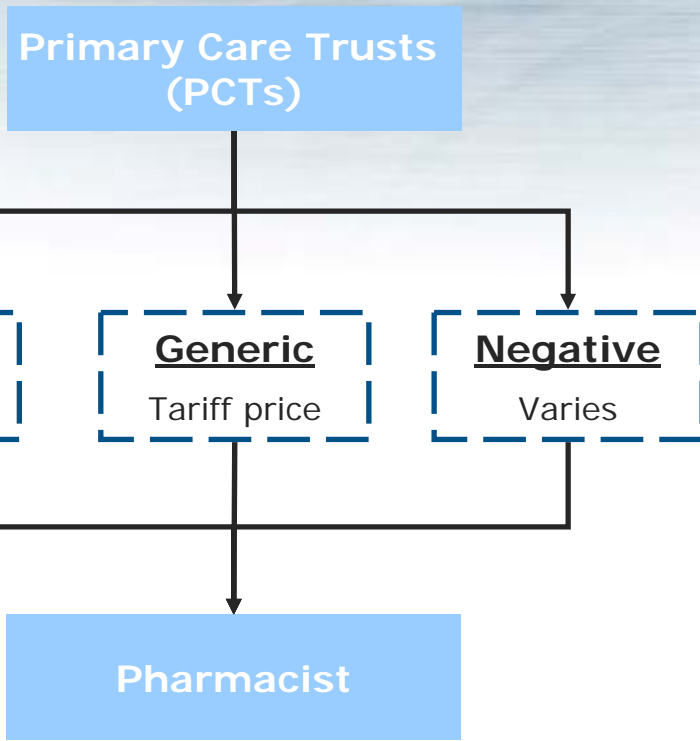
Mutual Recognition Procedure

- Applies only to all EU member states
- When a drug is authorised through one country's national scheme, it is automatically approved in all states who participate in the agreement

National Procedure

- MHRA (Medicines and Healthcare products Regulatory Agency) reviews application
- Grants access in the UK only
- This would result in access being granted in all other EU member states via the mutual recognition procedure

Reimbursement — or coverage by the NHS — is normally granted automatically for all drugs



- Pharmacists are reimbursed by the NHS for prescription drugs they dispense:
 - They receive the manufacturer’s list price for branded products
 - The tariff price for generics
- Some products are on the “negative lists”
 - Either not reimbursed or only reimbursed for special populations
 - E.g. lifestyle products such as erectile dysfunction drugs are only reimbursed for a small population identified as having a clinical need

Profits of all branded drugs sold to the NHS are controlled

The Pharmaceutical Price Regulation Scheme (PPRS) applies to branded drugs....

- Cost control measure negotiated between the Department of Health and the Association of the British Pharmaceutical Industry (ABPI)
- Limits the profit a manufacturer can make across all of its branded products sold to the NHS
 - Manufacturers must submit annual data on sales, costs, assets and profitability
- Those manufacturers exceeding the limit must reduce profitability the following year

...but not to generics, OTC drugs or private prescriptions

- Certain drugs are exempt from profit controls:
 - Generics
 - Over the counter (OTC) drugs
 - Private prescriptions
 - Normally issued for drugs which are not reimbursed e.g. prescriptions of Viagra to those not considered eligible by the state
 - Issued with the understanding the cost of the drug is to be paid in full by patients

Actual drug utilization for all diseases is restricted by the PCTs, who limit funding and issue formularies

	<u>General Practitioners</u>	<u>NHS Hospitals</u>
Budgetary constraints	<ul style="list-style-type: none">• PCTs provide each GP within their area with an annual budget with which they must operate their practice<ul style="list-style-type: none">– PCTs set prescribing budgets for each GP practice– These budgets limit the number of prescriptions a GP can issue which can then be 'cashed' in a pharmacy	<ul style="list-style-type: none">• NHS hospitals are managed by NHS Hospital Trusts: self-governing, not-for-profit organisations operating within the NHS• PCTs form agreement with trusts and provide funding for treatment of a certain number of patients per year
Formulary constraints	<ul style="list-style-type: none">• A series of formulary committees—all of which include at least one PCT representative—also review drugs on the market and generate formularies• These formularies indicate when particular drugs can be used and in which patients	

Pharmaceutical procurement, including that for TB drugs, is negotiated at a local level by pharmacists

Retail pharmacy procurement

- Negotiate their purchases directly with manufacturers and wholesalers
- Sometimes form chains to aggregate demand and negotiate volume savings
- Suppliers may only offer authorised margins and discounts to pharmacists, in turn, pharmacists are only permitted to use specified mark-ups, thus profitability is limited

Hospital pharmacy procurement

- Entitled to procure drugs at a PASA negotiated price – if a PASA contract exists the hospital must purchase from that supplier at that price
- Additionally, there are 14 pharmacy purchasing groups working on a geographical basis to procure drugs not covered by PASA
 - Negotiate with suppliers to set a price at which all hospitals in the group may procure drugs
 - Each PCT is represented by one of these groups
- In rare cases they may also negotiate their purchases directly with manufacturers and wholesalers

Specialists use sputum smear tests to confirm the diagnosis and check for drug resistance

SPECIALIST

Sputum smears are taken (bronchoscopes are used to retrieve pleural fluid if patient is not producing sputum)

Lymph node biopsies

Samples are sent to a PHLS Mycobacterium Reference Units for DST

Results are used to advise the specialist what to prescribe

- Unlike other healthcare providers specialists use sputum samples to diagnose TB, rather than chest x-rays
 - Approx 10% of chest x-ray diagnoses are incorrect, sputum smears are a more reliable method of diagnosis
- Smears are tested for drug resistance using drug sensitivity testing (DST)
- The results of the DST are used to tailor the drug regimen to the patient
 - If the DST is normal then the specialist will follow the NICE/BTS guidelines
 - If the DST is abnormal, i.e. the smear shows drug resistance, then the specialist tailors the regimen to maximise the chance of treatment success