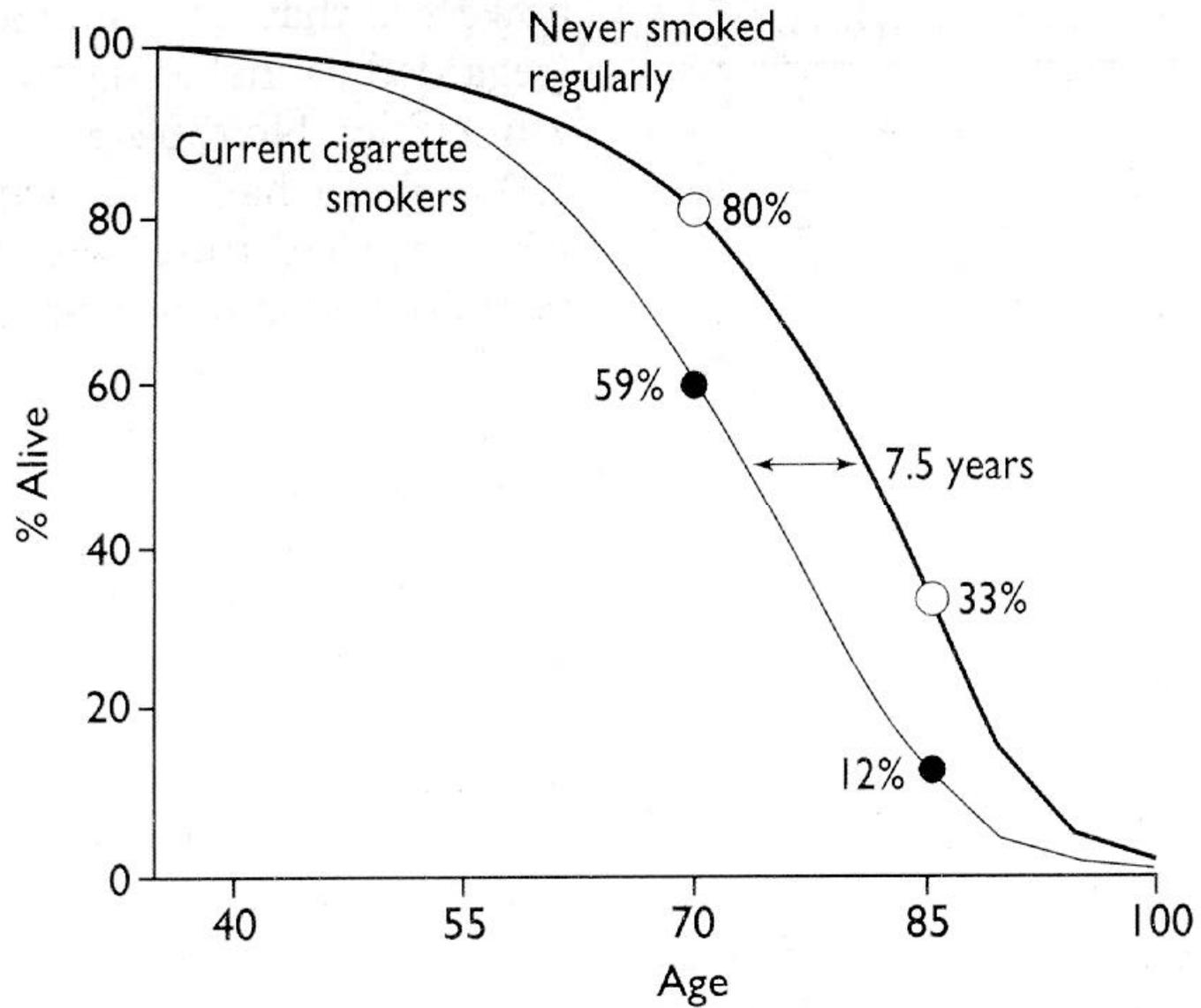


Anti-viral drugs – to lengthen ‘a man’s life’

Paul Moss

University of Birmingham





Doll, R et al. BMJ 1994;309:901-911

Study of lifespan for people in UK

- Sample of 530 people
- Age >65 years at recruitment
- Started in 1990
- 18 years of follow up

Survival

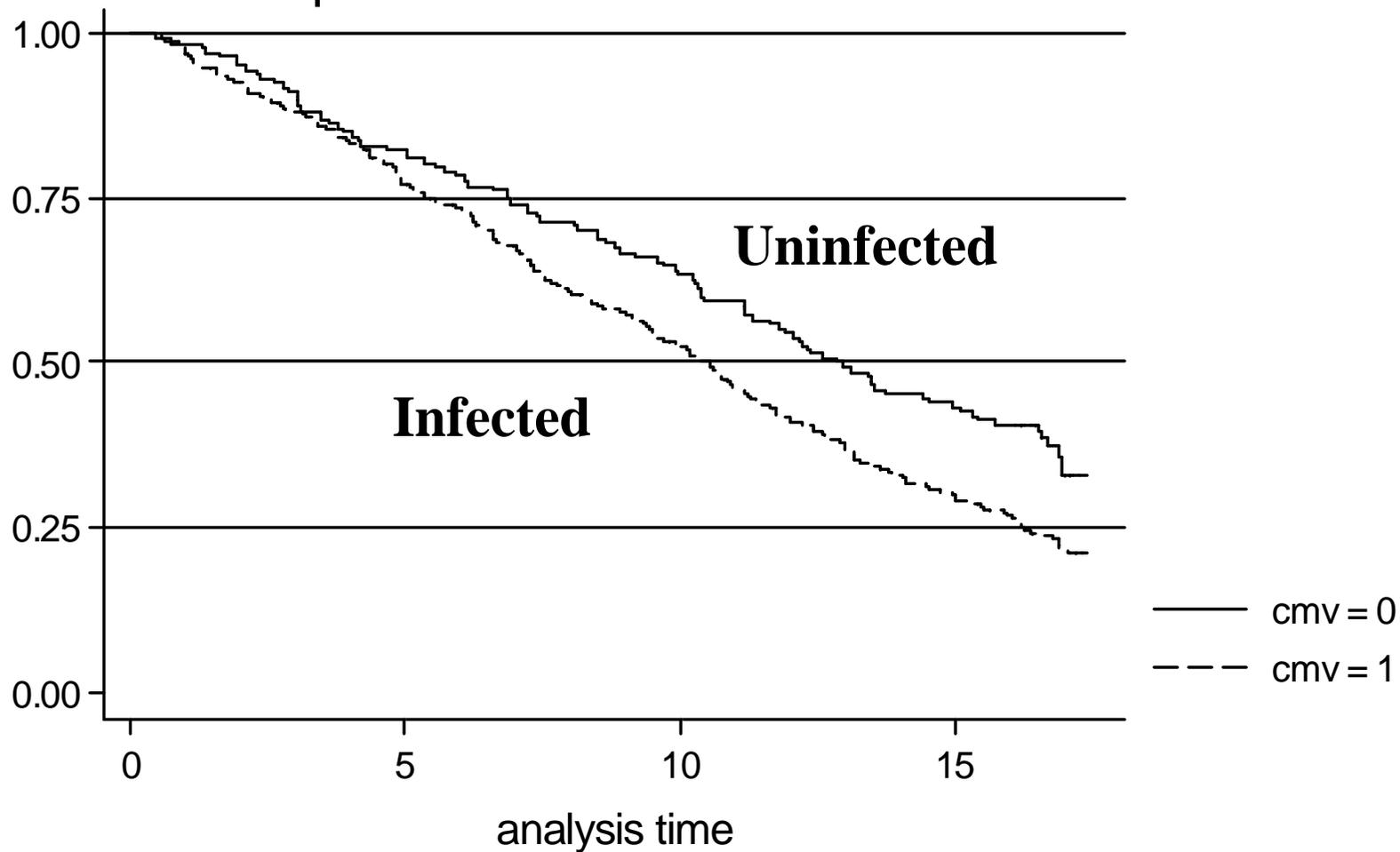
- **Men**

- **To 81 years** (if infected)
- **Or 85 years** (if not infected)

Women

- **To 85 years** (if infected)
- **88 years** (if not infected)

Kaplan-Meier survival estimates

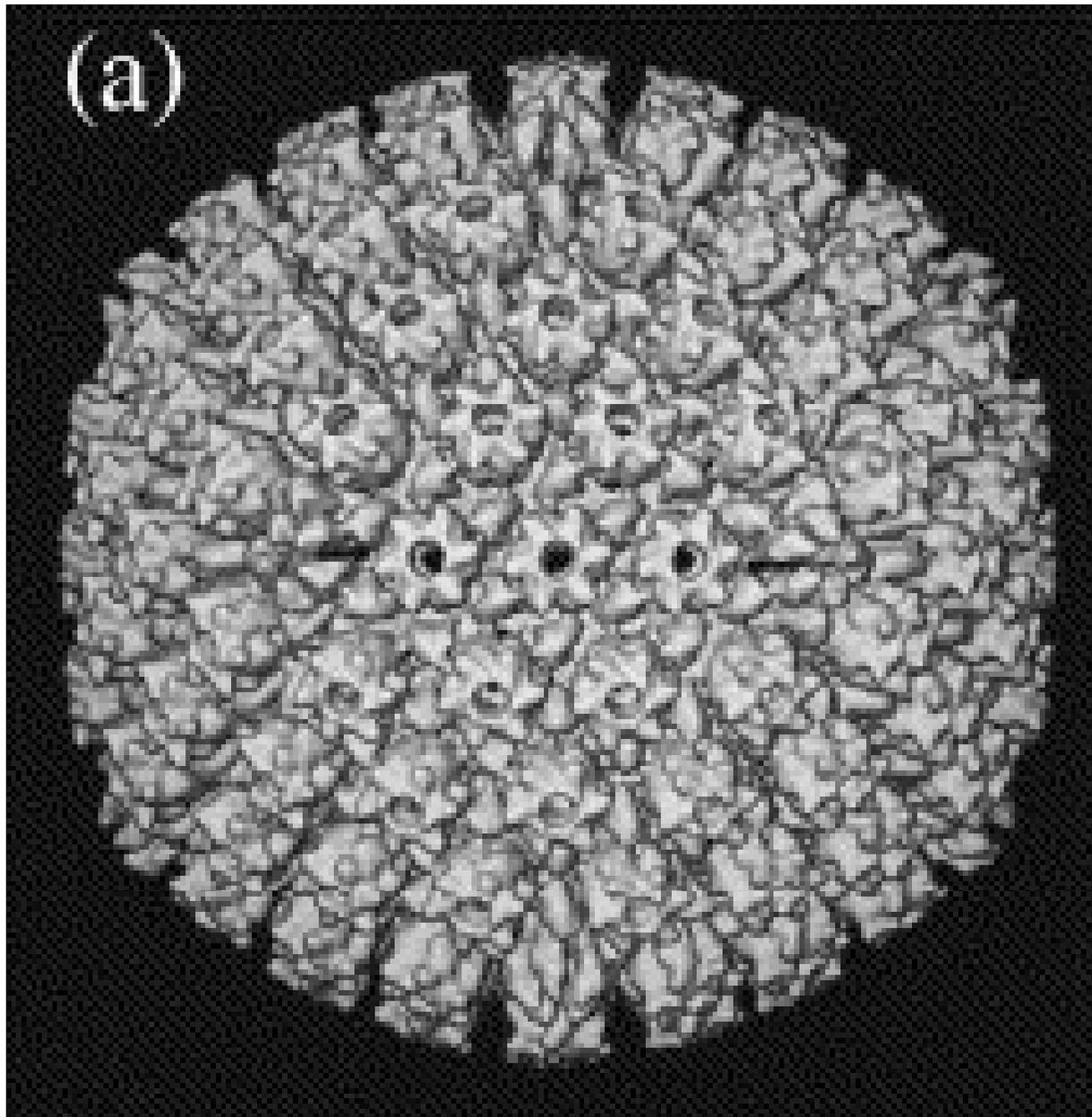


Number at risk

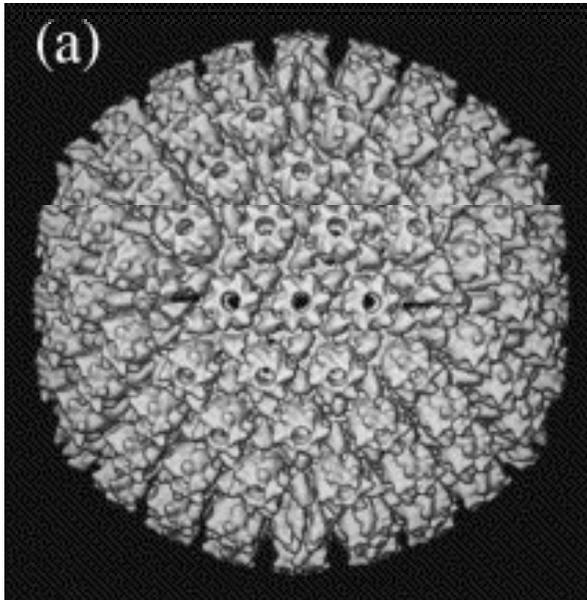
cmv = 0	148	(26)	122	(28)	94	(30)	64
cmv = 1	323	(73)	250	(81)	169	(75)	94

**People with a shorter lifespan have
been infected with a common virus**

cytomegalovirus



The Clinical importance of human herpesviruses

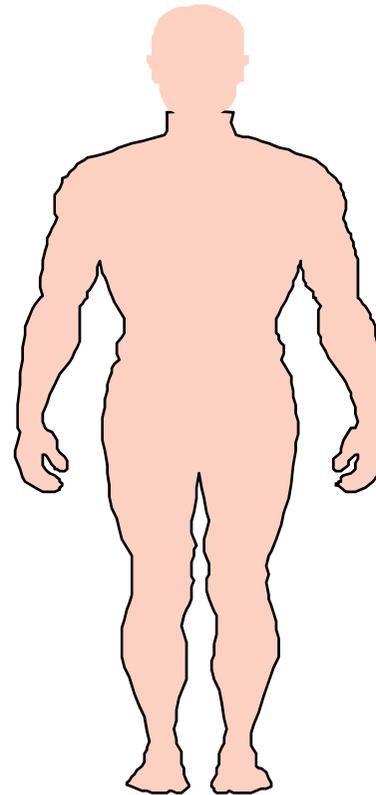
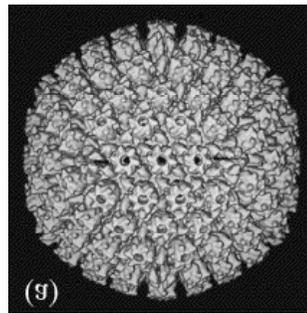


Family of eight viruses

Most of us are infected with several of them

They establish chronic infection

Virus and host must co-exist for 80+ years



Clinical significance in patients with weakened immune system is well established



- Organ transplantation**
- HIV infection**

Clinical significance in *immune competent* donors is becoming apparent

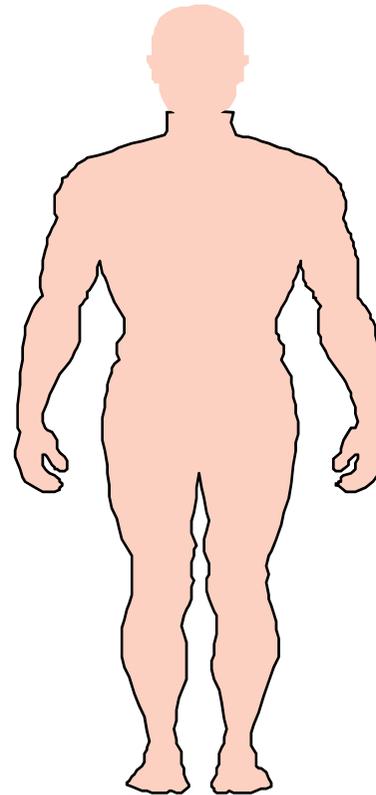
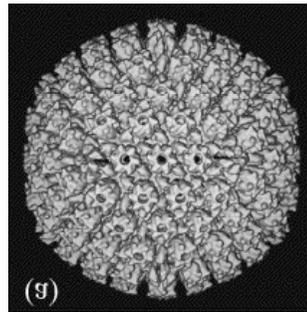


**-Multiple
sclerosis**

-SLE

**-Immune
senescence**

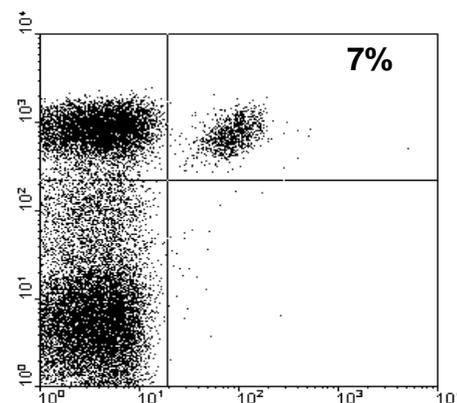
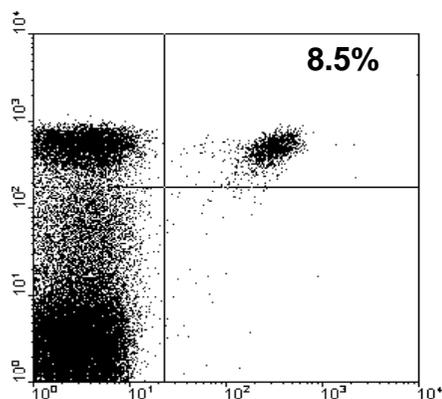
How do we control CMV ?



By fighting it through our immune system

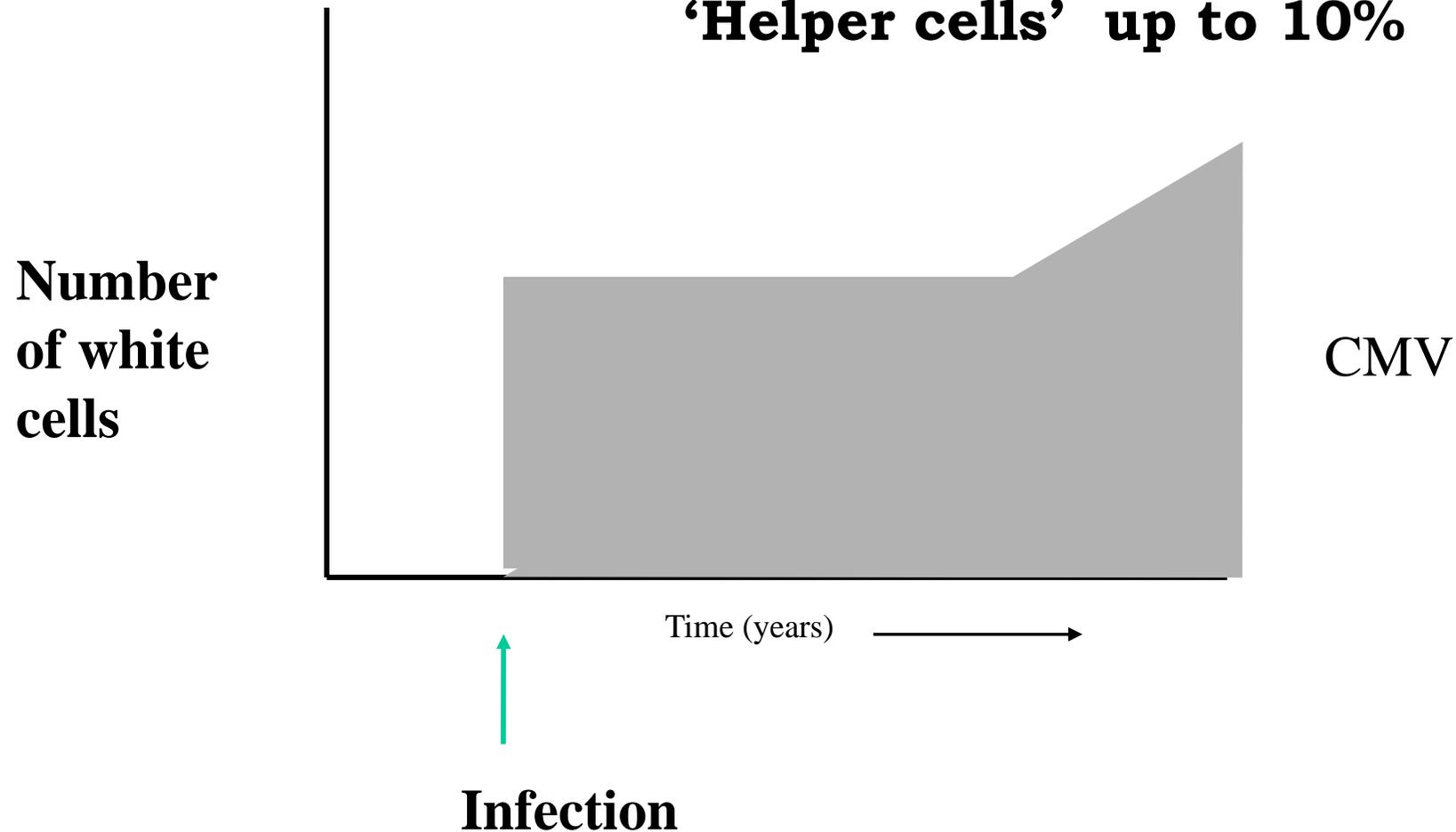
We can measure the immune response to CMV

- Take blood
- Count the number of cells that are fighting CMV

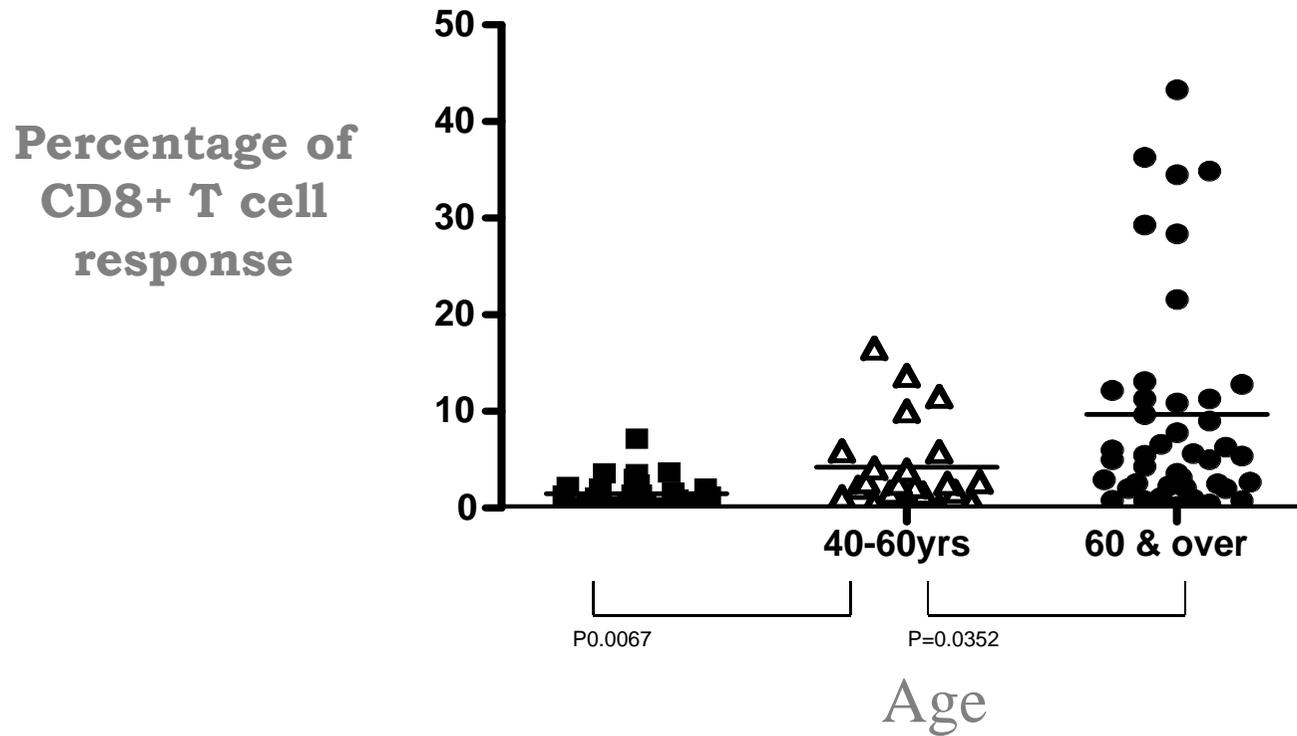


The immune response to CMV is massive

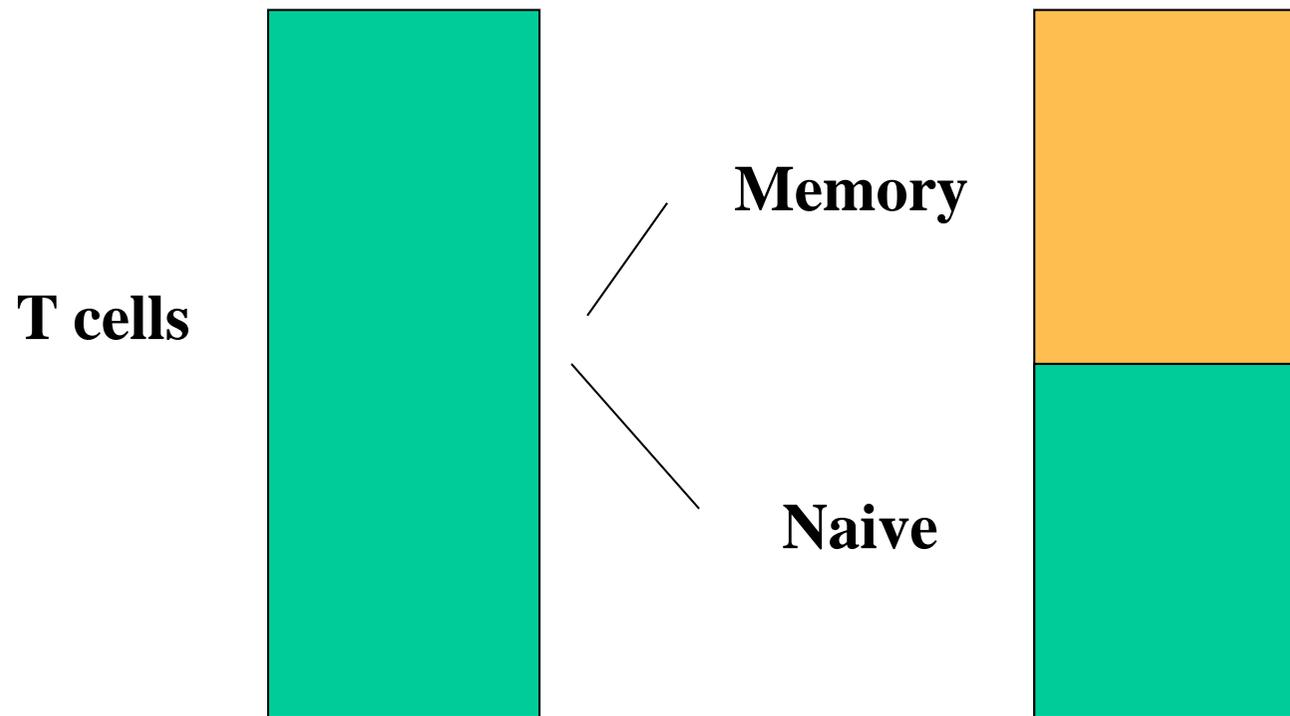
'Killer cells' up to 40% of total
'Helper cells' up to 10%



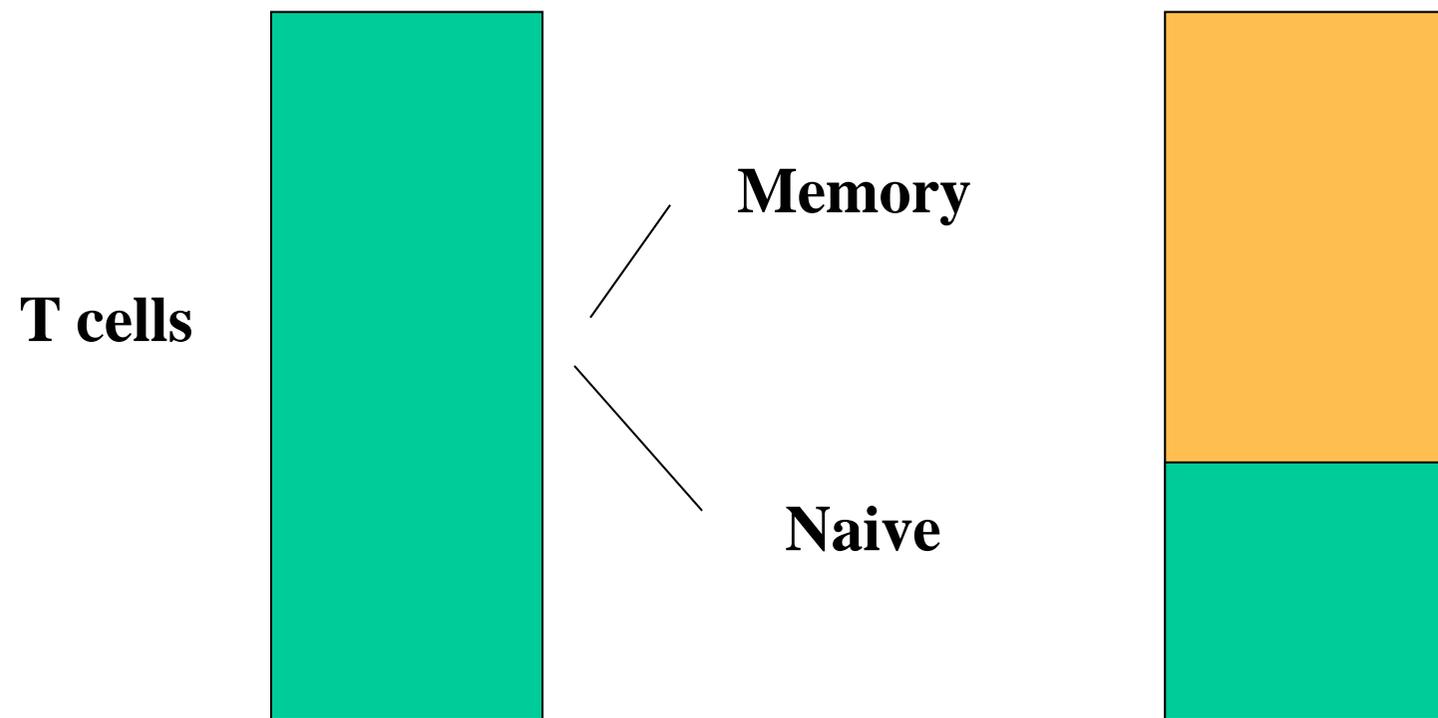
The immune response to CMV *increases with age*



Blood contains a mixture of 'memory' and 'new' immune cells



CMV infection alters the proportion of *memory* and *naïve* T cells in peripheral blood



**So does CMV infection affect
human health ?**

- Immune function in the elderly
- Vascular disease

Can we do anything about it ?

- Vaccination
 - Not yet
- Anti-viral drugs
 - Maybe

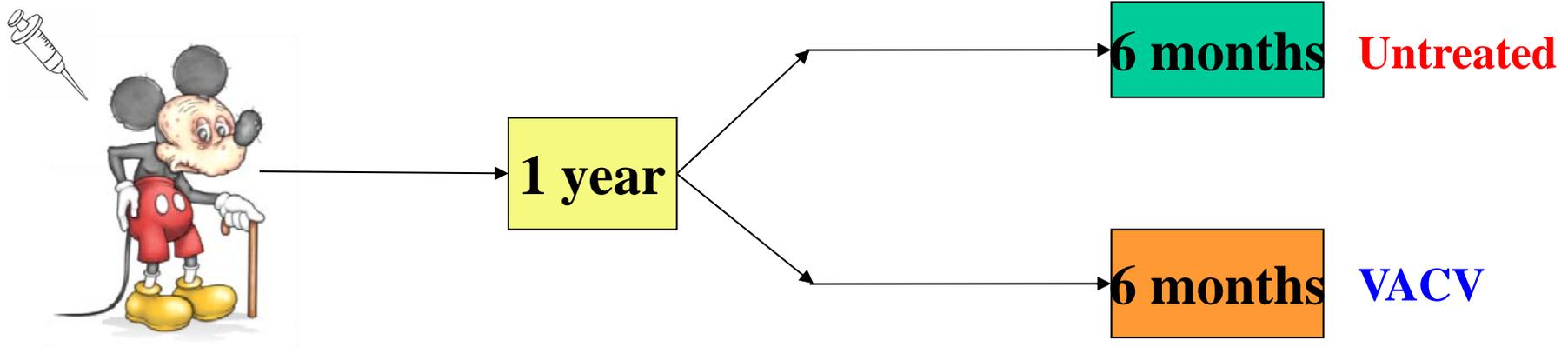
The potential role of anti-viral medication

- Anti-viral drugs which reduce antigen load have the potential to thereby reduce the CMV-specific immune response

Anti-viral drugs

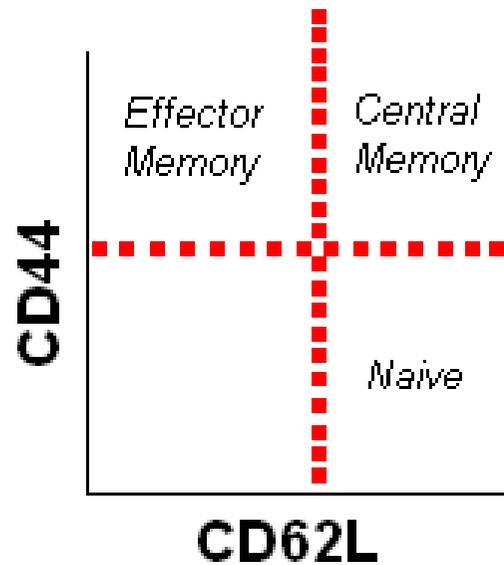
- Common anti-viral drugs do have some activity against CMV
- Low doses of these *do* suppress the CMV-specific immune response
 - PATENT APPLIED FOR

Administration of valaciclovir to elderly mice with CMV infection

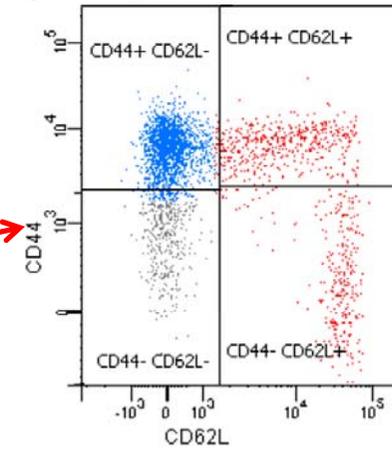


Valacyclovir in drinking water

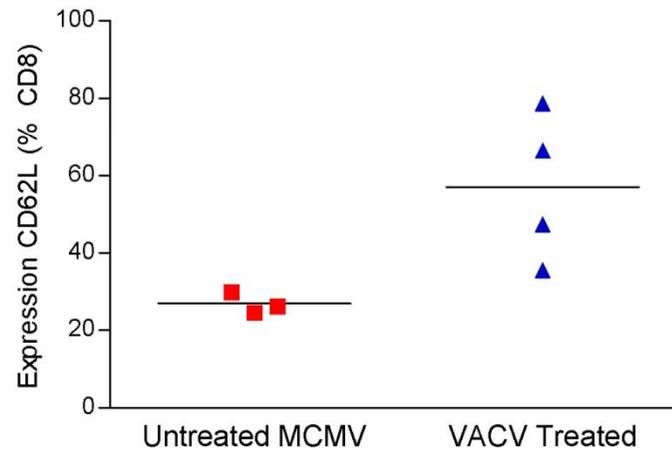
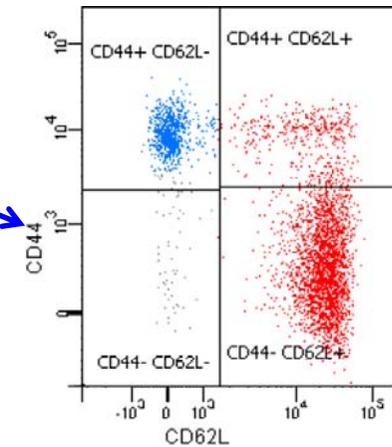
Valaciclovir 'rejuvenates' the immune system



Untreated



VACV treated



Does this help the mice ?

- Increased protection against influenza infection
- Better immune response and less clinical complications

So what do we do in humans?

There has been no assessment of how these drugs may suppress the CMV-specific immune response

Medical Research Council Grant (£750,000)

1. 'Dose finding' with anti-viral drugs
 - Escalating dose in 50 elderly subjects
2. Randomized trial of drug prior to annual influenza vaccination

Collaboration with

- Professor Richard McManus

The Market

- In 2000, there were 600 million people aged 60 and over but this number is predicted to rise to 1.2 billion by 2025 and 2 billion by 2050 (WHO report 2007)

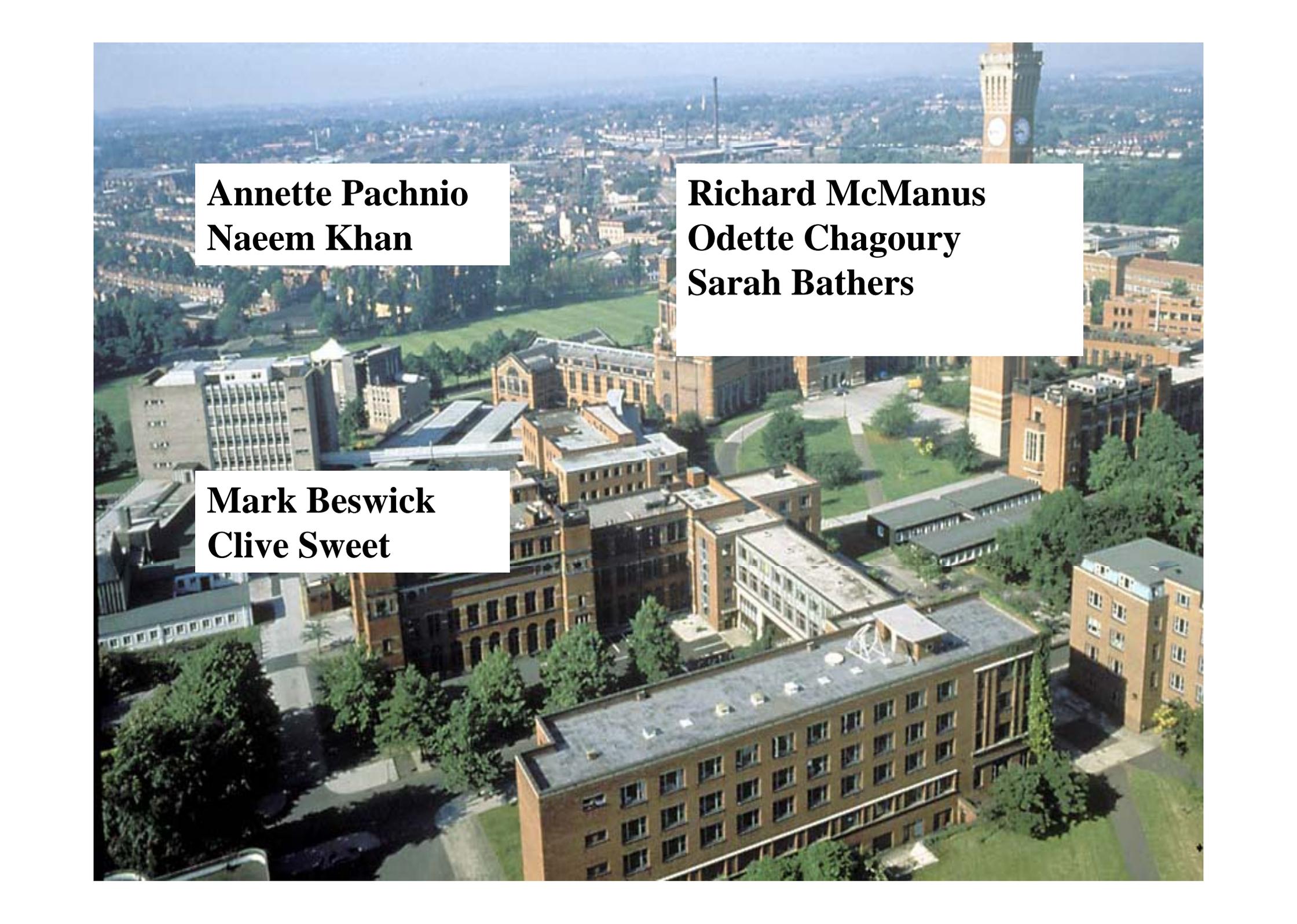
Potential

- Potential large market
- Leading position
- Many other ideas in CMV
 - Could have drug in clinical trials in 2 – 3 years
 - Could have reagents to sell immediately

What have we learnt ?

- Difficult to develop new health concepts
- Enthusiasm sometimes overreached reality
- Difficult to engage Pharma



An aerial photograph of a university campus. In the foreground, there are several large, multi-story brick buildings with many windows. A prominent clock tower stands on the right side of the image. The campus is surrounded by green lawns and trees. In the background, a cityscape is visible under a clear sky.

Annette Pachnio
Naeem Khan

Richard McManus
Odette Chagoury
Sarah Bathers

Mark Beswick
Clive Sweet

So many different lengths of time. Brian Patten

How long is a man's life, finally?

Is it a thousand days, or only one?

One week, or few centuries?

How long does a man's death last?

And what do we mean when we say, 'gone forever'?

Adrift in such preoccupations, we seek clarification.

We can go to the philosophers,

But they will grow tired of our questions.

We can go to the priests and the rabbis

But they might be too busy with administrations.

So, how long does a man live, finally?

And how much does he live while he lives?

We fret, and ask so many questions -Then when it comes to us

The answer is so simple

**A man lives for as long as we carry him inside us,
For as long as we carry the harvest of his dreams,
For as long as we ourselves live,
Holding memories in common, a man lives.
His lover will carry his man's scent, his touch:
His children will carry the weight of his love.
One friend will carry his argument,
Another will hum his favourite tunes,
Another will still share his terrors**

.

**And the days will pass with baffled faces,
Then the weeks, then the months,
Then there will be a day when no question is asked
And the knots of grief will loosen in the stomach,
And the puffed faces will calm.
And on that day he will not have ceased,
But will have ceased to be separated by death.
How long does a man live, finally?**

A man lives so many different lengths of time.