AGENDA

- Definition of “drug misuse” and “doping”
- History of Performance-enhancement in sports
- Measures being taken to combat “doping”
- Categories of Drugs, how they work, other means of enhancing performance
- Testing Procedures and the Athlete’s Biological Passport (ABP)
- The extent of the problem today
- Avoiding detection
- Why do they do it?
Definition of Doping in Sport

The use of any artificial enhancements (substances, methods or procedures) to gain an unfair advantage over other competitors.

Substances and methods are banned for a reason.....

- It’s cheating and contrary to the spirit of sport
- It puts the athletes’ own health at risk
- It damages competition for athletes who play by the rules
- It threatens the integrity of clean athletes and the reputation of sport
Gladiator competitions and chariot races popular in Ancient Roman culture. In 100AD, Coliseum held 60,000 spectators.

Chariot racers fed their horses substances such as hydromel (an alcoholic beverage made from honey) to make them run faster.

Gladiators ingest hallucinogens and stimulants such as strychnine to stave off fatigue and injury and to improve the intensity of their fights.

Source: Ramlan Abdul Aziz, MD "History of Doping," Presented at the WADA Asia Education Symposium, Aug. 29, 2006
More recently, Rome Olympics 1960

Knud Jensen was a Danish cyclist whose death in 1960 during the 100km road race heralded the new age of Olympic doping.

At first it was thought he had suffered sunstroke, but when a second autopsy was conducted on Jensen it was discovered that his death was the result of doping/substance misuse (amphetamine)
British cyclist Tommy Simpson, named Sports Personality of the Year by the BBC in 1965, died during the 13th stage of the Tour de France on July 13, 1967.

The cyclist, whose motto was allegedly "if it takes ten to kill you, take nine and win", consumed a toxic cocktail of substances to combat the effects of an illness.

He continued to ride until his body shut down.

Simpson's death created added pressure for sporting agencies to take action against doping.
February 1968 – First Drug Testing at Olympic Games

The International Olympics Committee (IOC) instituted its first compulsory doping controls at the **Winter Olympic Games in Grenoble, France in 1968.**

And, again, at the **Summer Olympic Games in Mexico City** in the same year.
1988 Seoul Olympics - 100m Sprint

- The 100m final - One of the most infamous moments in the games.
- Ben Johnson won in a world-record time of 9.79sec.
- He had smashed the world record against the greatest ever field of sprinters.

Olympic Doping Control Centre found that Johnson's urine samples contained steroid (stanozolol)..... Stripped of his medal

Carl Lewis – 1988 9.92sec
Usain Bolt – 2009 9.58sec
But......

• Nothing really changed after 1988

• 6 of the 8 finalists in that 100m race would fail drugs tests (or be implicated in their use) during their careers

• Another 12 years would pass before the World Anti Doping Agency (WADA) was formed.
The world's leading cycling team Festina banned from the sport's most prestigious event (Tour de France) after its director admitted a "concerted" programme of giving riders performance enhancing drugs.

Director and the Team Doctor charged under a French anti-drugs law.

Team's masseur also charged after he was found carrying 400 bottles of a drug used to boost performance, syringes and other doping-related products and paraphernalia.
Athens Olympics 2004

- Considered the worst of all in terms of doping violations.
- At the time, there were 26 doping cases including catching six medallists (two gold winners).
- Since then, retrospective tests (up to Dec 2012) have increased cases to 31, including 11 medal winners and three gold medallists.
1999-2005 Lance Armstrong

- Seven times "winner" of Tour de France from 1999-2005, third place in 2009
- Allegedly tested positive back in 1999 when in 2004 an unofficial test was done on frozen urine. Exposed by former team members
- Client of the infamous Dr Michele Ferrari.
- 20 out of 21 podium finishers in the Tour de France from 1999-2005 directly tied to doping through admission, public investigations or blood tests

2012 - BANNED for life and stripped of all SEVEN Tour de France titles
Admitted doping to win all tours in a TV interview with Oprah Winfrey held on 17 January 2013
Dr Michele Ferrari

Italian physician and cycling coach

On 10 July 2012, the USA Anti-Doping Agency issued Ferrari with a lifetime sports ban for numerous anti-doping violations including:

• Possession
• Trafficking
• Administration and assisting doping
But..........

It is a sad reflection that the Spanish road rider, Fernando Escartin, appears to be the only rider not to be implicated in a cycling doping scandal during this era........

That was the extent of doping at that time.
What measures are being taken?
November 1999 – World Anti-Doping Agency

WADA - an independent foundation created, an initiative led by the International Olympic Committee (IOC).

Set up to **promote, coordinate and monitor** the fight against doping in sport.

WADA is responsible for the **World Anti-Doping Code**, adopted by more than 600 sports organisations.

UKAD – **UK Anti-Doping Agency** is responsible for ensuring sports bodies in the UK are compliant with the World Anti-Doping Code
Since 2004 World Anti-Doping Agency (WADA) has assumed responsibility for establishing and maintaining the list of prohibited substances and methods in sport

**i.e. the Prohibited List** *(copy available)*

New Items are being added all the time ......

*eg Xenon and Argon* (gases that induce hypoxia) were added to the Prohibited List, effective from 1 September 2014. (Russian athletes admit Xenon doping at Winter Olympics)
Prohibited Substances
(i) Main Categories of Prohibited Substances

- Stimulants
- Anabolic Agents
- Narcotic Analgesics
- Peptide Hormones
- Diuretics and other Masking Agents
STIMULANTS

**Effects:** Make athletes more alert and mask fatigue. Reduce pain, increase reaction speed and raise aggression

**Typical examples:** p-methylamphetamine, benzedrine, cocaine

**Medical Uses:** Narcolepsy, ADHD, nasal congestion

**Side effects:** Hypertension, heart & liver problems, addiction, psychosis, paranoia, increased injury as athletes continue to compete/train

**Misuse in Sport:**
Amphetamine and related substances are stimulants, often mimic the effect of adrenaline on the central nervous system. Athletes take them to feel more alert, more energetic and less fatigued
ANABOLIC STEROIDS

- **Effects:** Build muscle mass - Synthetic drugs (man-made), related to male sex hormones

- **Medical Use:** Clinically, prescribed to treat hormonal problems eg late onset of puberty, and some types of cancer or AIDS where patients have had significant muscle loss

- **Side Effects:** Can result in serious health problems: Hypertension, liver disease, heart problems, breast growth & testicular atrophy in men, body hair in women, acne, increased aggressive behaviour

- **Misuse in Sport:** Anabolic steroids are often used by body builders and athletes who want to build muscle and power to enhance performance.

- Also, use of anabolic steroids is a great problem in US high schools. In 2005, an estimated 660,000 students aged 14-17yrs have admitted to using them
GLUCOCORTICOSTEROIDS

• Closely related to hormones produced by the Adrenal glands

• **Typical examples:** Cortisone, Prednisone

• **Medical Uses:** Used to reduce pain, swelling, itching and inflammation associated with skin conditions eg bad insect bites. Used to treat various medical conditions such as severe allergic reactions, severe asthma, lupus and arthritis.

• **Side effects:** Hypertension, diabetes, increased risk of infection, cataracts, bone loss (osteoporosis), muscle weakness, fat deposits in chest, face, upper back and stomach, changes in appetite, weight gain, water retention and mood changes.

• **Misuse in sport:** All prohibited - Intravenous/intramuscular, rectal, oral
NARCOTIC ANALGESICS

**Effects:** Pain killers

**Typical examples:** Diamorphine (heroin), morphine, methadone, pethidine

**Medical Use:** Pain relief

**Side Effects:** Highly addictive and cause withdrawal symptoms when athlete ceases to use them. Constipation and low blood pressure are other side effects. Also, can lead to further injury/damage.

**Misuse in sport:** Athletes use them to mask pain from an injury or overtraining
PEPTIDE HORMONES : Erythropoietin (EPO)

Hormone produced by the kidney. Chemically, it’s a protein with an attached sugar (a glycoprotein).

Kidney cells that make erythropoietin are sensitive to low oxygen levels in the blood. These cells release erythropoietin when the oxygen level is too low.

Erythropoietin's major functions are to:

a) Promote the development of red blood cells in bone marrow
b) Initiate the synthesis of haemoglobin, the molecule in RBC
c) Increase oxygen-carrying capacity of the blood
ERYTHROPOIETIN AND SPORT

- Used clinically to treat anaemia when its use and effects are carefully monitored.
- EPO is banned from sports because it is believed to enhance an athlete's performance and confer an unfair advantage.
- When misused in sport, it can have serious consequences e.g. thickens a person's blood and so increases risk of clots. These clots obstruct blood flow to tissue, leading to cell death. Clot in the heart - myocardial infarction; brain – stroke

Professional cyclist and seven-times Tour de France winner, LANCE ARMSTRONG systematically used EPO with a cocktail of other performance-enhancing drugs.
Human Growth Hormone (HGH)

- Produced by anterior pituitary gland. Until early 1980s, only available from human cadavers. Now, recombinant HGH, can be produced in the lab.

- **Medical Use:** Growth deficiencies

- **Misuse in Sport:** Very limited evidence that HGH improves performance, although the common perception is that it increases lean body mass, breaks down fat, aids muscle repair.

- **Side effects:** From animal studies, long-term use of human growth hormone can increase the risk of diabetes, retention of fluids, joint and muscle pain, hypertension, cardiomyopathy, osteoporosis, irregular menstruation, impotence and elevated HDL cholesterol.
Substances prohibited in specific sports: Beta Blockers

• Class of drugs that target the **beta receptors** in heart muscles, smooth muscle, airways, arteries and other tissues that make up the **sympathetic nervous system**.

• Beta blockers **interfere with the production of stress hormones** (adrenaline and noradrenaline) and their effects

• Thus, beta-blockers can reduce the heart rate and reduce the force at which the heart contracts.

• Athletes have been known to use Beta-blockers to **steady nerves, reduce anxiety and stop trembling**.

• This is of particular advantage in sports requiring a high degree of accuracy and a steady hand **eg archery, golf, shooting, billiards**
Substances prohibited in specific sports: Alcohol

Banned for:

- Air sports
- Archery
- Automobile
- Karate
- Power boating
- Motor cycling
Diuretics and other Masking Agents

This category includes substances having the potential of:

i. modifying a urine sample

ii. influencing the elimination of substances in urine and/or

iii. masking the presence of banned substances.

The WADA list prohibits three main types:

- **DIURETICS**
- **PROBENECIDS**
- **PLASMA EXPANDERS**
Diuretics and other Masking Agents

Medications that promote the elimination of urine from the body. Act on the kidneys. Potent diuretics result in a large water loss in only a few hours, and weight reduction of 1-2kg.

**Medical use:** Used to treat high blood pressure or an accumulation of fluids in tissue (oedema).

**Side effects:** Interfere with the balance of water/salts/minerals, resulting in an electrolyte imbalance. Can lead to an acute drop in BP, muscle cramps, heart failure, gastro-intestinal problems or kidney damage. Impotence can occur in men and menstrual disorders in women.

**Misuse in sports:** Don’t enhance performance but used to dilute the urine sample, making detection of doping substances more difficult. Also used to force rapid weight loss.

Probenecid

**Effects:** Acts to inhibit the renal excretion of a large number of substances.

**Medical use:** Used in the treatment of gout and related disorders.

**Side effects:** Can result in gastro-intestinal ailments and in allergic reactions.

**Misuse in sports:** Causes the body to retain substances (eg anabolic steroids) longer and to excrete them at a slower rate. It can consequently become more difficult to detect the substances in analysis.

Probenecid has been prohibited in- and out-of-competition since 1987.
Plasma Expanders

**Effects:** Increase the amount of fluid in plasma.

**Medical use:** Used therapeutically as blood thinners as well as to treat excessive blood loss and large-scale skin burns.

**Side effects:** Can provoke allergic reactions, dizziness, symptoms similar to asthma and even cardiopulmonary arrest.

**Misuse in sports:** Misused in an attempt to counteract the effects of EPO or other forms of blood manipulation.

Another misuse is in endurance sports to **compensate for the loss of fluids.**
Prohibited Methods
(ii) Prohibited Methods: Blood Doping/Transfusion

**Blood doping** - practice of boosting the number of red blood cells in the bloodstream in order to enhance performance. RBCs carry oxygen from the lungs to the muscles, a higher concentration in the blood can improve aerobic capacity (VO2 max) and endurance.

**Blood transfusion** - an effective means of increasing RBCs. Popular in the 1970s among elite endurance athletes. Method declined in the 1980s with the introduction of *exogenous erythropoietin* (produced by recombinant DNA technology in cell culture).

2001 - Introduction of a test to detect *exogenous erythropoietin*

2004 - Test to detect **allogeneic blood transfusion** (ie genetically different blood due to different antigens)

This forced cheating athletes to re-infuse fully immunologically compatible blood.

**Athlete's Biological Passport is now a powerful deterrent**
Other Methods: Gene Doping

The following are prohibited because of their potential to enhance performance in sport:

• The transfer of nucleic acids or nucleic acid sequences;
• The use of normal or genetically modified cells;
• The use of agents that directly or indirectly affect functions known to influence performance by altering gene expression
Testing in Sport
Testing Procedures - Urine

- Whereabouts and Notification
- Reporting in
- Selecting a specimen vessel
- Sample collection
- Selecting sample collection equipment
- Dividing and sealing the sample
- Testing suitability of sample
- Declaration and signature
- Transfer to an Accredited Laboratory
Testing Procedures - Urine

- **Whereabouts and Notification**
  - Reporting in
  - Selecting a specimen vessel
  - Sample collection
  - Selecting sample collection equipment
  - Dividing and sealing the sample
  - Testing suitability of sample
  - Declaration and signature
  - Transfer to an Accredited Laboratory

In or out of competition:
Athlete provides an advance schedule of their whereabouts
Receive notice of test by Drug Centre Official (DCO)
Must attend regardless of any prior commitments
Testing Procedures - Urine

- Whereabouts and Notification
- **Reporting in**
- Selecting a specimen vessel
- Sample collection
- Selecting sample collection equipment
- Dividing and sealing the sample
- Testing suitability of sample
- Declaration and signature
- Transfer to an Accredited Laboratory

On receipt of notification, athlete must report for test immediately.
Sealed drinks are provided
Athletes taking their own drinks do so at own risk
Must avoid excessive rehydration
Testing Procedures - Urine

- Whereabouts and Notification
- Reporting in
- Selecting a specimen vessel
- Sample collection
- Selecting sample collection equipment
- Dividing and sealing the sample
- Testing suitability of sample
- Declaration and signature
- Transfer to an Accredited Laboratory

Athlete selects own sealed vessel for collecting specimen and checks seal is intact

Vessel is kept in sight of DCO and athlete at all times

DCO observes the athlete providing the sample, with sufficient clothing removed to ensure visibility of flow

If DCO has any concerns, another sample can be requested
Testing Procedures - Urine

- Whereabouts and Notification
- Reporting in
- Selecting a specimen vessel
- Sample collection
- Selecting sample collection equipment
- Dividing and sealing the sample
- Testing suitability of sample
- Declaration and signature
- Transfer to an Accredited Laboratory

Athlete selects own sealed bottles, includes Sample A and Sample B, Checks that bottles haven’t been tampered with

Athlete divides sample between the two bottles
Testing Procedures - Urine

- Whereabouts and Notification
- Reporting in
- Selecting a specimen vessel
- Sample collection
- Selecting sample collection equipment
- Dividing and sealing the sample
- **Testing suitability of sample**
- Declaration and signature
- Transfer to an Accredited Laboratory

DCO will check the **specific gravity** of the remaining sample. If it falls outside the permitted range, DCO will record this on form, and request additional samples until one is produced that meets the required range.
Testing Procedures - Urine

- Whereabouts and Notification
- Reporting in
- Selecting a specimen vessel
- Sample collection
- Selecting sample collection equipment
- Dividing and sealing the sample
- Testing suitability of sample
- Declaration and signature
- Transfer to an Accredited Laboratory

Athlete invited to declare:
- Any substances/medications during the past 7 days
- Details of any Therapeutic Use Exemptions (TUEs)
- Include any comments on collection procedures

All of the above may be helpful in explaining any adverse analytical finding (AAF)

Bottles placed in security sealed transit bag, sent to WADA accredited lab for analysis with secure chain of custody
Accredited Laboratories: Drug Control Centre, Kings College, London

- Only **35 accredited** anti-doping laboratories in the world.
- DCC at KINGS COLLEGE is the only UK-based lab.
- Set up in **1978** and was the first human sports drug-testing laboratory to be established outside of an Olympic Games.
- Ran the anti-doping facility for **2012 Olympics/Paralympics**
- Analyses samples from athletes, and carries out research into the **metabolism and detection of substances** in the human body.
- Carried out more than **8,000 tests across 70 sports last year.**
Analytical methods

- In humans, tests carried out on blood and urine samples in first instance (in horses, hair is used)
- Many different analytical methods are used
Chromatography

- Process of separating chemical substances into its constituents.
- Mixture is dissolved in a fluid (*mobile phase*), which carries it through a structure holding another material (*stationary phase*). The various constituents of the mixture travel at different speeds, causing them to separate *ie different partitioning behaviour*.
- Various techniques: Gas, thin-layer, liquid, paper etc
- Simplicity, sensitivity, and effectiveness means *gas chromatography* is one of the most important tools in chemistry. Widely used for quantitative and qualitative analysis of mixtures.
The fundamental principle of the Athlete Biological Passport (ABP) is to monitor selected biological variables (biomarkers) over time. It relies on longitudinal monitoring of specific measures within the individual. The ABP aims to reveal the effects of doping rather than the doping substance or method itself. WDA’s ABP operating guidelines came into effect on 1st December 2009. The first module (2009) focuses on haematological (blood) measures, and the second module (2014) focuses on steroidal (urine) markers.
1. Haematological Module collects data on the Markers of blood doping.

2. Aims to identify the Use of Prohibited Substances and/or Prohibited Methods.

3. This approach aims to uncover:
   - The enhancement of oxygen transport or delivery
   - Use of Erythropoiesis-Stimulating Agents (ESAs) eg peptide hormones, growth factors, related substances and mimetics, and
   - Any form of blood transfusion or manipulation, including homologous blood transfusion (HBT).
The ABP haematological markers

- HCT: Haematocrit and HGB: Haemoglobin
- RBC: Red blood cell (erythrocyte) count
- RET%: Reticulocytes percentage and RET#: Reticulocyte count
- MCV: Mean corpuscular volume and MCH: Mean corpuscular haemoglobin
- MCHC: Mean corpuscular haemoglobin concentration
- RDW-SD: Red cell distribution width (standard deviation)
- IRF: Immature reticulocyte fraction
Haematocrit (HCT)

Athletes' haematocrit levels are measured as part of tests for **BLOOD DOPING** or **ERYTHROPOIETIN** use.

The HCT level in a blood sample is compared with the long-term level for that athlete (to allow for individual variations), and against an absolute permitted range within the population.

Anabolic androgenic **STEROID** use can also increase the amount of RBCs and, therefore, impact the haematocrit, in particular the compounds **BOLDENONE** and **OXYMETHOLONE**

If a patient is **DEHYDRATED** the haematocrit may be elevated.
HGB: Haemoglobin (Hb)
RBC: Red blood cell (erythrocyte) count

**HGB / Hb**
Oxygen-carrying molecule in red blood cells, typically:
- Male: 13.0-18.0 g/dL in adult males
- Female: 11.5-16.5 g/dL (non-pregnant) females.

**RBC count**, typically:
- Male: 4.7-6.1 million cells per microlitre (cells/mcL)
- Female: 4.2-5.4 million cells/mcL
An Example of HGB Profiling for an Individual Athlete

Blue line – shows 14 test results for the athlete for the HGB biomarker

Red lines - represent the personal limits/expected range of values for that individual athlete
Count and Percentage of Reticulocytes

Considered within the ABP Haematological Module:

- **Reticulocytes** are *immature RBC*, typically about **1% of red cells** in the human body.

- Develop and mature in the red bone marrow and then **circulate for about a day** in the bloodstream before developing into mature red blood cells.

- Like mature red blood cells, reticulocytes have no nucleus.

- Called reticulocytes because of a **mesh-like network of ribosomal RNA**, visible under microscope with certain stains eg new methylene blue.

- **High levels of reticulocytes can indicate doping with EPO or Stimulating Agents**.
Athlete Biological Passport – The steroidal module

- Steroidal Module monitors selected *urinary* steroid concentrations
- Unique steroidal variables such as *testosterone*
- Useful technique in spotting athlete abuse of Anabolic Androgenic Steroids.
Testing for Anabolic Steroids

• Urine (hair eg horses)
• Gas chromatography-high-resolution mass spectrometry (GC-HRMS)
• Gas chromatography-tandem mass spectrometry (GC-MS/MS).
What’s the picture now?
<table>
<thead>
<tr>
<th>Sport</th>
<th>Samples</th>
<th>AAF</th>
<th>%</th>
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<td>Table Tennis</td>
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Source: UKAD Olympic data
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<td>Badminton</td>
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2010 Findings

The remaining sports
HIGH ALTITUDE TRAINING

• Exposure to high altitude causes the body to acclimatise to the lower level of oxygen available in the atmosphere.

• Many of the changes that occur with acclimatisation - EPO stimulates red blood cell production and improves the delivery of oxygen to the muscles.

• It is believed that more oxygen will lead to better performance in aerobic sports.

• Up to a point, the more blood cells you have, the more oxygen you can deliver to your muscles. A number of other changes happen during acclimatisation which may help athletic performance, including:
  - an increase in the number of small blood vessels,
  - an increase in buffering capacity (ability to manage the build up of waste lactic acid)
  - changes in the microscopic structure and function of the muscles themselves.
Negative aspects of Acclimatisation to High Altitude

• Too many blood cells makes the blood thicker and can make blood flow sluggish.
• Heart works harder to pump blood round the body, and can actually decrease the amount of oxygen getting to where it is needed.
• At very high altitudes (>5000m), weight loss is unavoidable (body ‘burns’ muscle in order to provide energy. Further problems are encountered: loss of appetite, inhibition of muscle repair processes and excessive work of breathing.
• Risk that the body’s immune system will become weakened, leading to an increased risk of infections.
• Possible adverse changes in the chemical make-up of the muscles.
• Training intensity is reduced as altitude which may reduce performance.
• Altitude sickness - can dramatically reduce the capacity to be active at altitude.
• **Live High and Train Low**
Athletes’ previous attempts to avoid detection

- Avoid the testers
- Change whereabouts information at very late notice
- Stay in remote locations
- Drop out of races when testers are on site
- Saline injections to restore blood concentrations to more normal levels
- Use substances /techniques that are difficult to detect
- Injection Sites: into veins rather than under skin
- Claim therapeutic use/backdate prescriptions
A cruder means of avoiding detection - The Whizzinator

- $139 available to purchase online
- Dried synthetic urine
- Heat pads
- Syringe and distilled water
- Prosthetic penis - a variety of ethnically-sensitive skins shades available
- Female versions available
Other legitimate ways of enhancing performance

Access to:

- Scientific athletic training, and specialised exercise schedules
- Physiotherapy and other therapies
- Sports Injury treatment Centres and specialist medical equipment
- Use of altitude chambers
- Special diets and dietary supplements.
- Specialist equipment/clothing
But why do athletes risk everything?

• “Everyone does it, we have ways to make sure you never get caught”?

• Pressure from Team/fellow athletes?

• Fear of failure?

• Given up everything to become professional athlete – may have no other skills/training/education?

• Injury and hardship.... Needs money to pay for travel, subsistence, coaching, physios

• Drive for success and celebrity; Appeal of lucrative Sponsorship deals?
Typical Values of Sponsorships/Endorsement Deals

- **GOLF: Rory McIlroy** – Nike - Estimated Value: $250 million (10 years)

- **TENNIS: Roger Federer** – Nike, Wilson, Lacroix, Rolex, Gillette, Jura, Mercedes, Credit Suisse, Lindt ... Estimated Value $71m/year

- **NBA: Derrick Rose** – Adidas - Estimated Value: $260 million

- **FOOTBALL: David Beckham** – Adidas - Estimated Value: $160 million (Lifetime)

- **BOXING: George Foreman** - Salton, Inc. - Estimated Value: $137.5 million

- **HEPTATHALON: Jessica Ennis** - Jaguar, Olay, Adidas, Powerade, BA, Aviva, Omega, BP Income £1m (2012)

- **CYCLING: Lance Armstrong** - Earned c$17.5m from sponsors in 2005 (the year he retired after his 7th Tour “victory”. Estimated net worth at $125m, most coming from sponsors.)