

# **What we will be doing in 2015?**

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# In The Last 100 Years ...

- ▶ Photography > digital images (shared)
- ▶ Beginning of travel by cars, on ships > Travel to outer space
- ▶ Sound record medium (vinyl) > Music industry (merchandise based)
- ▶ Surgical procedures (apprentice style) > 0.3% to 0.9% of papers are on surgical RCTs
- ▶ Hysterectomies (clamps) – no change

# In 1915 ...

- The life expectancy was 47 years.
- Only one in 25 persons lived to age 60 years.



Gustav Klimt (1862 – 1918)

In 2015 ...

- People might live to 90 or 100 years
- Gynaecological Cancers become more common



# Uterine Cancer

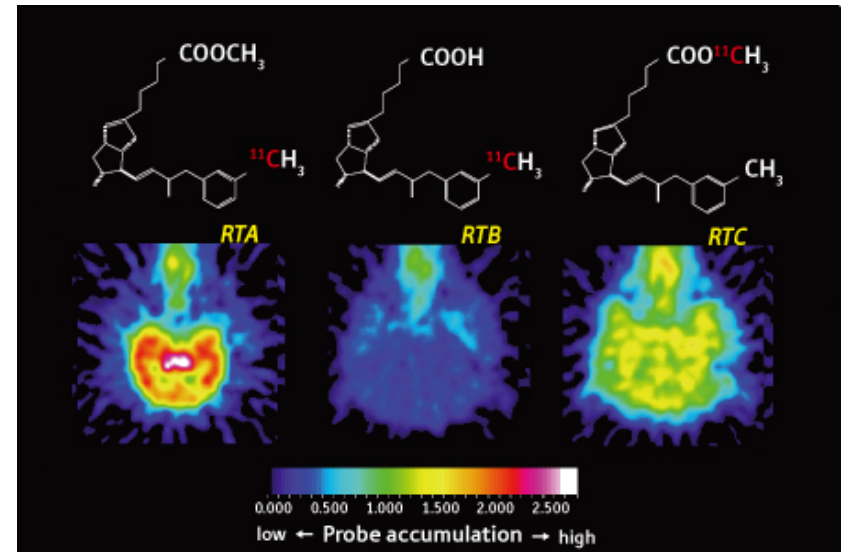
- Uterine cancer: + 25% in last 10 years
  - 8000 cases per annum
  - 10% in women <40 yrs age
- Body Mass Index
  - US Trial: 29
  - Dutch Trial: 29
  - Australian Trial: 34
- 20% of uterine cancers
  - AGGRESSIVE!



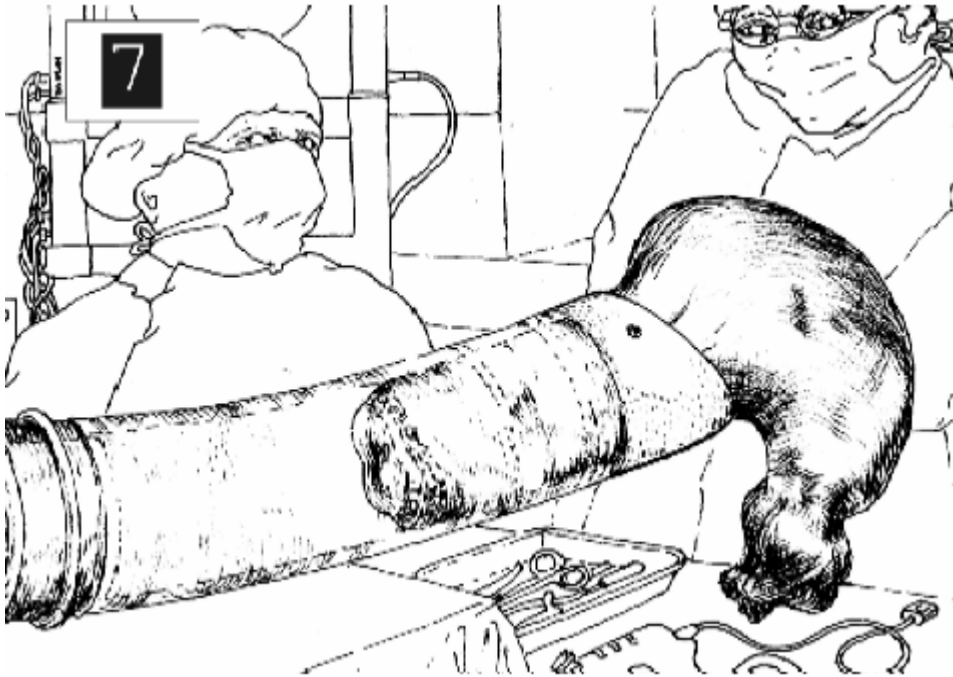
# Developments in Endometrial Cancer Prevention & Management

## Molecular Imaging

- PET (FDG)
- Antigens and tracers currently in development



# Total Laparoscopic Hysterectomy



McCartney Tube

Tube -

- 1.Outlines the fornices – identification of bladder, uterine vessels
- 2.Maintains pneumoperitoneum
- 3.Assists with removal of specimens (uterus, lymph nodes, pelvic masses)

# Laparoscopic Hysterectomy

Little uptake (comp'd to other lapasc procedures)

- Technological limitations
- Combination of the procedure with vaginal repair
- Lack of RCTs
- Lack of measurement/audit
- Reimbursement (disincentives)

# Change is coming

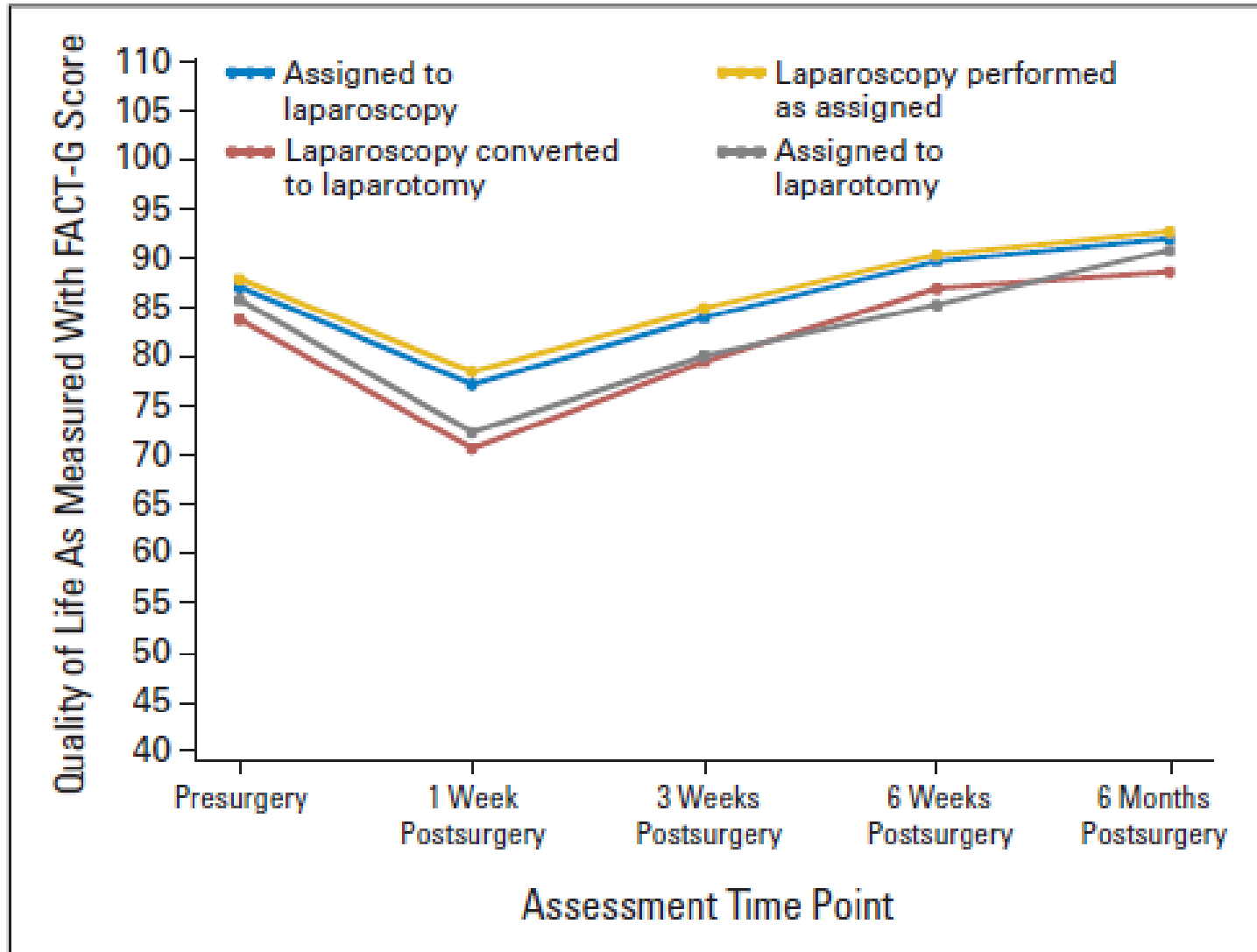
- Healthy ageing
- Exchange of information
- Equipment better
- Data from RCTs
- Audit



# Data from 3 RCTs

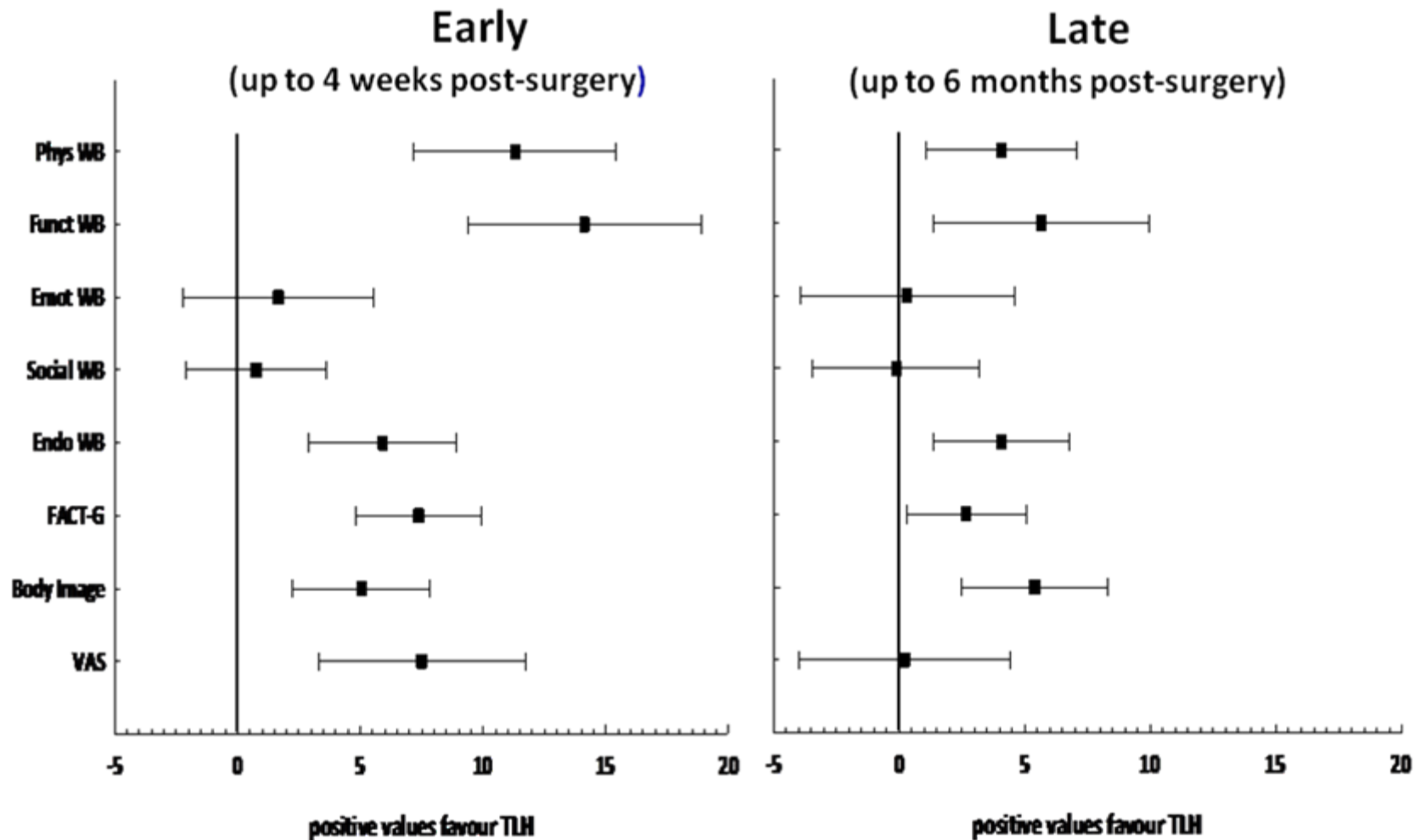
- US GOG Lap2
  - Kornblith et al., JCO 2009
  - Walker et al., JCO 2009
- Dutch Trial
  - Mourits et al., Lancet Oncol 2010
  - Mourits et al., Eur J Cancer 2011
- Australian LACE Trial
  - Janda et al., Lancet Oncol 2010
  - Obermair et al., ESGO 2011

# LAP2 – QoL



# LACE QoL – Recovery from surgery

(Patients with TAH had better QoL at baseline)



VAS: single item visual analogue scale

# LACE: CA125 & extrauterine spread

**Table 2: Multivariable logistic regression models predicting extra-uterine spread**

	All patients (n=657)		P-value
	Odds ratio	95% CI	
CA-125	1.016	1.008-1.024	<0.001
Grade of differentiation			0.06
	1	1.000	
	2	1.423 0.904-2.242	0.13
	3	2.153 1.063-4.359	0.03

At CA125 cut-off 30 U/ml:

14.9 % of patients identified – 36.7% had extrauterine disease

Sensitivity 31.0%; Specificity 88.5%;

PPV 36.7% and NPV 85.7%.

# LACE: Surgical Adverse Events

- 753 of 760 patients followed for 6/12 analyzed
- 404 TLH, 349 TAH
- Node dissection: 371 pts (49.2%)
- Conversions: 28 pts (3.8%) [5 pts from TAH to TLH]
- Operating time: 132 (40.7) vs. 107 (33.6) mins
- Drop in Hb: 17.0 (10.4) vs. 19.3 (10.8)
- LOS: 2 (1-33) vs. 5 (2-48)
- Death < 30 days: none

# Intraoperative Complications

	TLH (n=404) n(%)	TAH (n=349) n(%)	p value
Any	30 (7.4%)	16 (4.6%)	0.105
Bowel injury	7 (1.7%)	6 (1.7%)	
Vaginal injury	12 (3.0%)	-	
Vascular injury	4 (1.0%)	5 (1.4%)	
Bladder injury	6 (1.5%)	1 (0.3%)	
Blood transfusion	3 (0.7%)	4 (1.1%)	
Ureter injury	-	2 (0.6%)	
Nerve injury	1 (0.2%)	-	

# Postoperative Complications

	TLH (n=404) n(%)	TAH (n=349) n(%)	p value
CTC Grade 2	174 (43.1%)	194 (55.6%)	0.006
CTC Grade 3	52 (12.9%)	65 (18.6%)	0.030
Serious Adverse Events	33(8.2%)	50 (14.3%)	0.007
Wound infection more likely with TAH			

# Prediction of surgical AEs

- Preventable?
  - 70% of complications are preventable (Harvard Medical Practice Study; 1991)
  - >37% of complications are preventable (UK, Canada, AUS, NZ; 1995 – 2004)
- Costs:
  - USA: \$ 30 billion/yr.
  - AUS: \$ 1-2 billion/yr.
- Are surgical complications predictable?

# Risk factors: Univariate Analysis (LACE Trial)

## Risks

- **Treatment (TAH)**
- **BMI**
- Charlson Index\*
- Grade (on D&C)
- ECOG (baseline)
- Haemoglobin
- PLT count
- Liver function tests

## No Risks

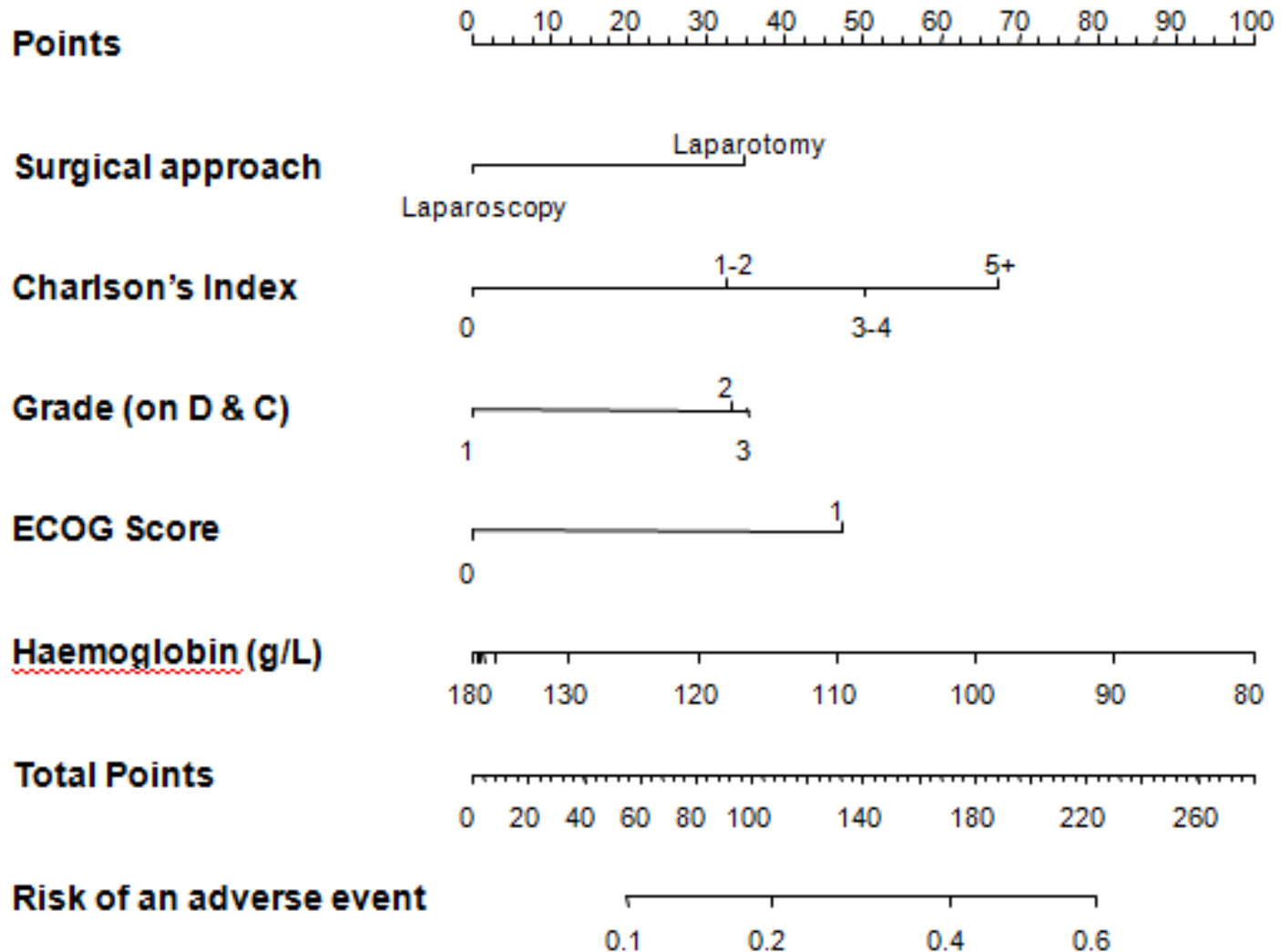
- Age
- Lymph node dissection
- Employment
- Income
- Marital status
- Education
- Private Health Insurance
- Country of birth

\*Charlson M et al: J Chron Dis 1987

# Risk Factors: Multivariate Models

	<b>OR</b>	<b>95% CI</b>		<b>P-value</b>	
		Lower	Upper limit		
Treatment Allocation TAH vs. TLH	1.734	1.174	2.561	0.006	
Age	0.981	0.959	1.003	0.096	
Charlson Index score	1.213	1.066	1.380	0.003	
Grade (D&C)				0.027	
	1	Ref	-	-	
	2 vs 1	1.678	1.105	2.549	0.015
	3 vs 1	1.862	0.904	3.837	0.092
ECOG (baseline)	2.162	1.302	3.592	0.003	
Hb (baseline)	0.983	0.969	0.998	0.023	

# Nomogram – Risk Calculator



## Calculator to predict the risk of an adverse event

in the surgical management of apparent early stage endometrial cancer patients

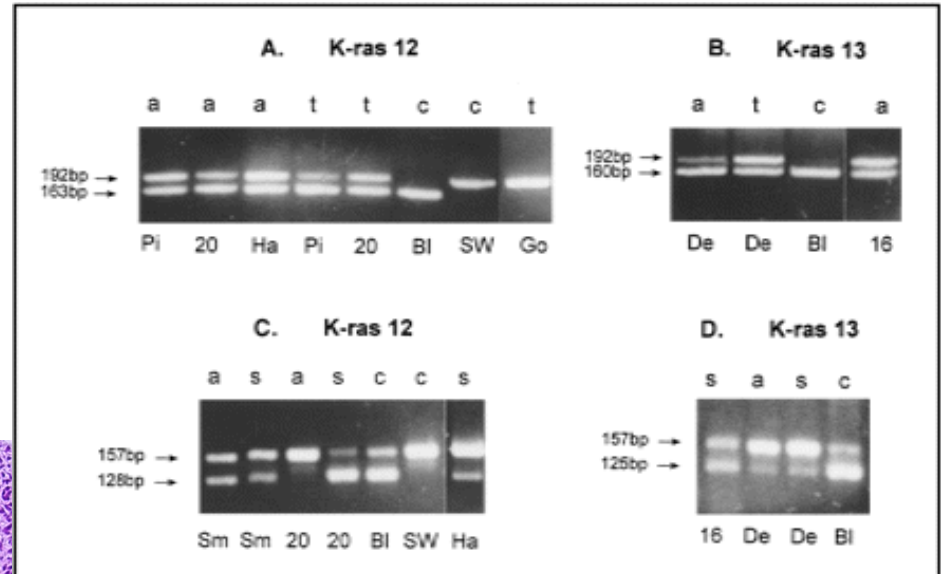
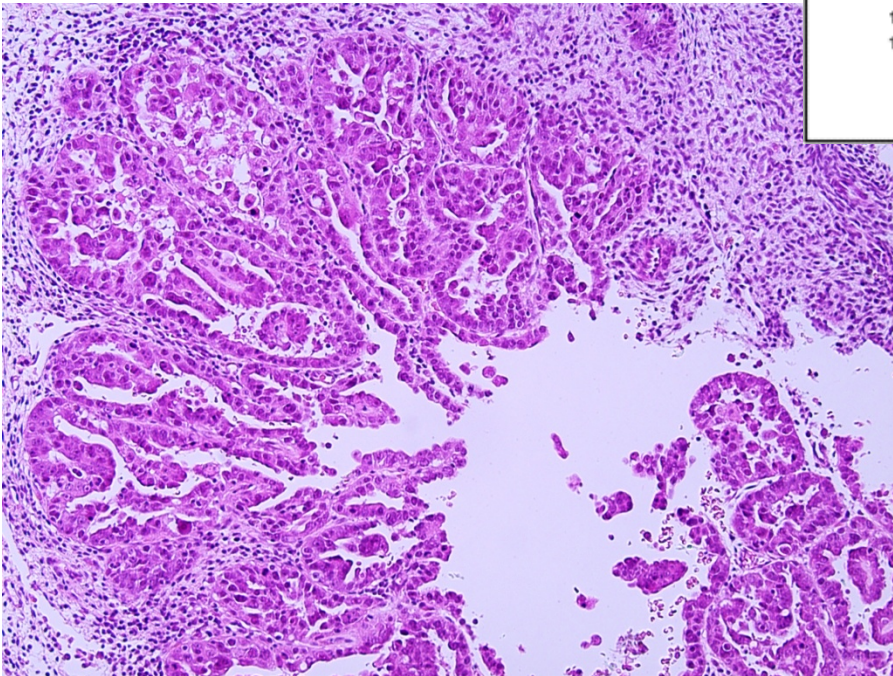
Laparoscopy or laparotomy	TLH	?
Charlson's score	0	?
Grade (on D & C)	2	?
ECOG score	1	?
Haemoglobin (g/L)	110	?

**25.3%**

Laparoscopy or laparotomy	TAH	?
Charlson's score	0	?
Grade (on D & C)	2	?
ECOG score	1	?
Haemoglobin (g/L)	110	?

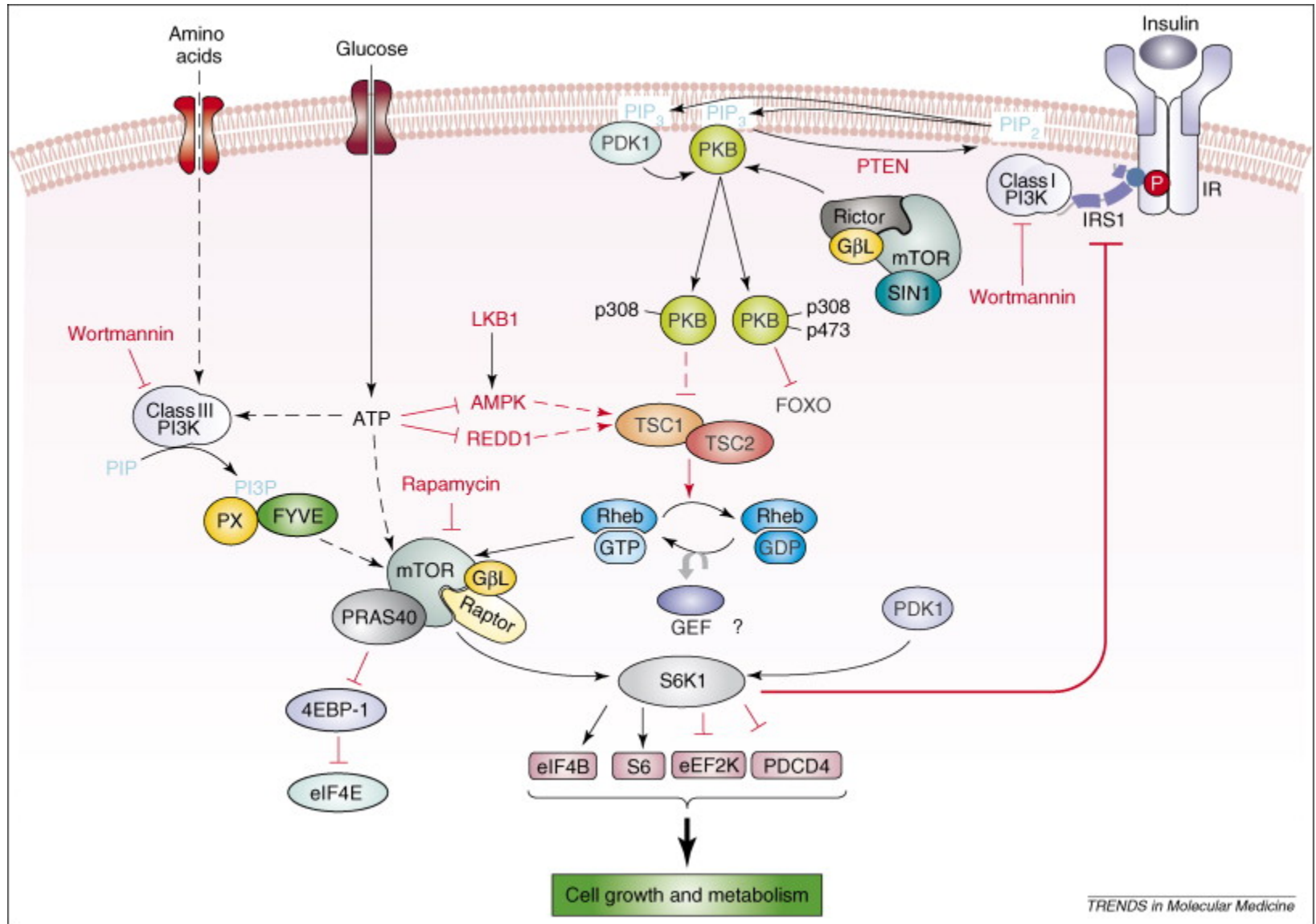
**36.6%**

# Molecular Diagnosis



Will H.E. Stains survive ?

# Targeted - Molecular - Treatments



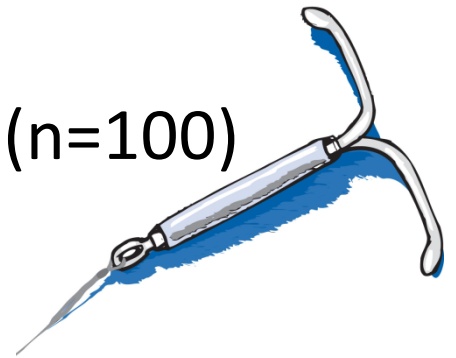
# Medical Treatment of Endometrial Ca

## 1. Prostate Cancer treated by weight loss

- Glisson score lowered

## 2. Proposed Trial:

- Mirena  $\pm$  Metformin  $\pm$  Weight loss (n=100)
- Endpoints:
  - Complete pathological response
  - Molecular markers (PTEN, Ghrelin, GHS-R, GPX3, p53)
- Powered to detect an increase in the complete pathological response rate from 50% to 70%.



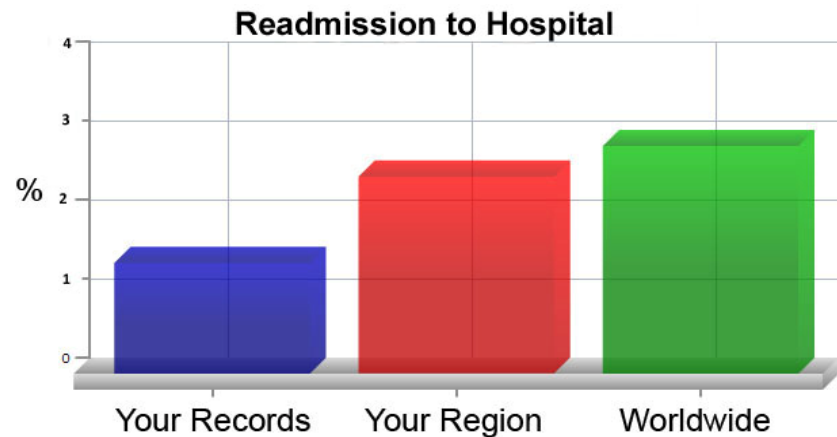
# Women at risk

- Breast cancer patients
  - 150% increased risk of uterine cancer
  - Causes??? (Tamoxifen; genetic; shared risk factors)
- Carriers of Lynch Syndrome
  - Identify women
    - 18% of patients diagnosed with endometrial ca < 50 years age
  - Prevention: IUD?
  - Networking of information: colorectal & gynaecology
  - Screening: kras?

# Overcome Resistance to Accountability

Health enjoys exemption from accountability.

- What outcomes do we achieve from treatment?
- Cost of our efforts
  - Financial cost
  - Grief & Pain
- Proactive approach?



Surgicalperformance.com

# What will we be doing in 2015 ?

- Only laparoscopic surgical procedures
  - Laparotomies referred to gyn oncologists
- Eating less – exercising more – living healthier
- Trialling new medical treatments for endometrial cancer
- Active research group focussed on molecular management of uterine cancer
- Accountability either self-administered clinicians or handed down by government.