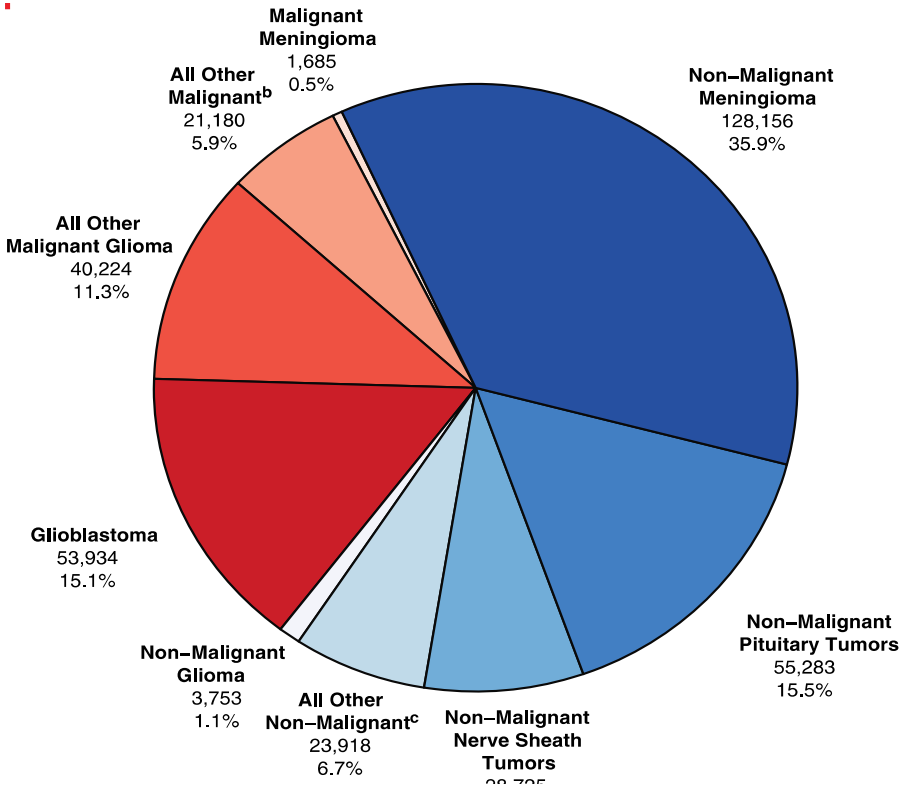
Brain tumours: disease burden

- Rare but affect all AGES, with varied pathological types (even more varied molecular subtypes)

- **2% of all cancers, n= 3,56,858**
- **Meningiomas: commonest tumour**
- **Malignant: 30%; Benign: 70%**
- **80% of gliomas: GBM**

- Childhood brain tumours: 2nd commonest cancers in children
- 2nd leading cause of cancer death in males and 5th in females aged 20-39

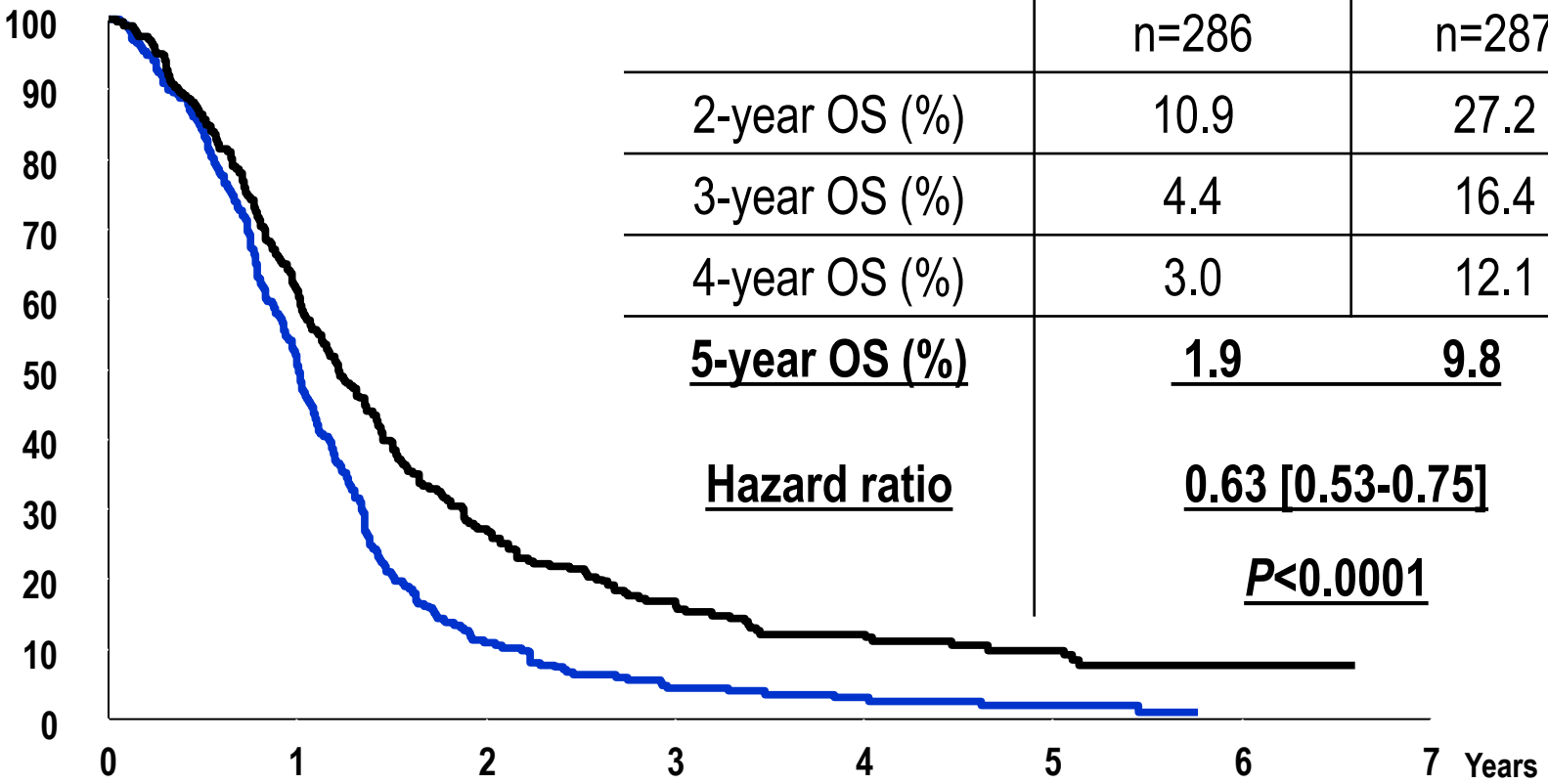


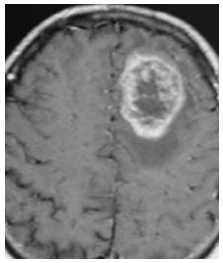
CBTRUS 2015

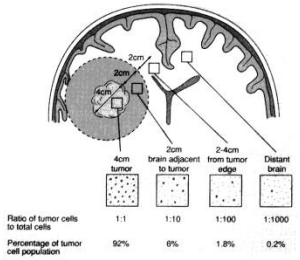
Glioblastoma

- One of the most challenging cancers anywhere in the body
- Remain locally invasive / recurrences hallmark
- Almost never metastasize, yet such dismal prognosis
- Local control in GBM should be = CURE

Treatment	RT n=286	RT+TMZ n=287
2-year OS (%)	10.9	27.2
3-year OS (%)	4.4	16.4
4-year OS (%)	3.0	12.1
5-year OS (%)	**1.9**	**9.8**
Hazard ratio	**0.63 [0.53-0.75]**	
	***P*<0.0001**	







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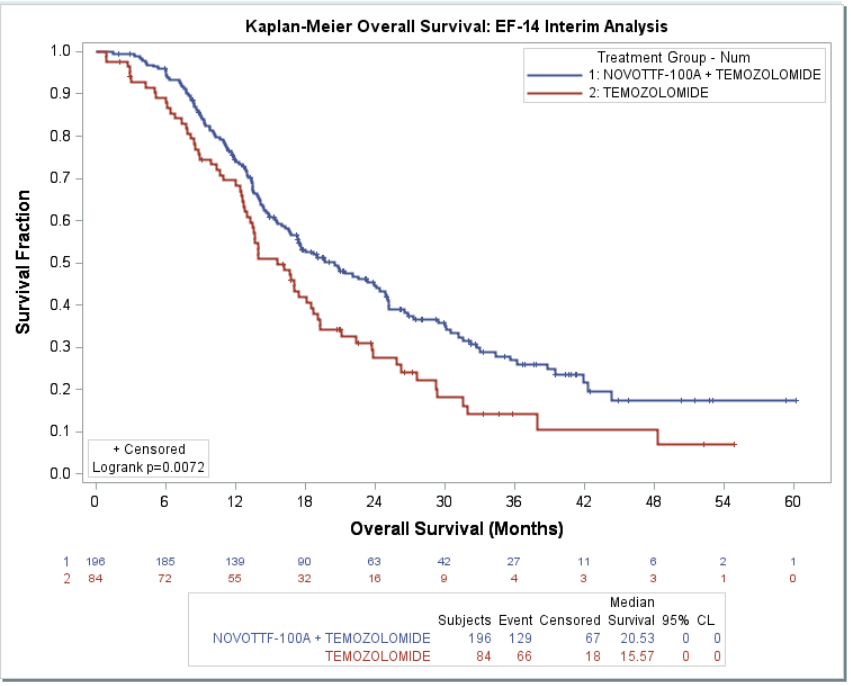
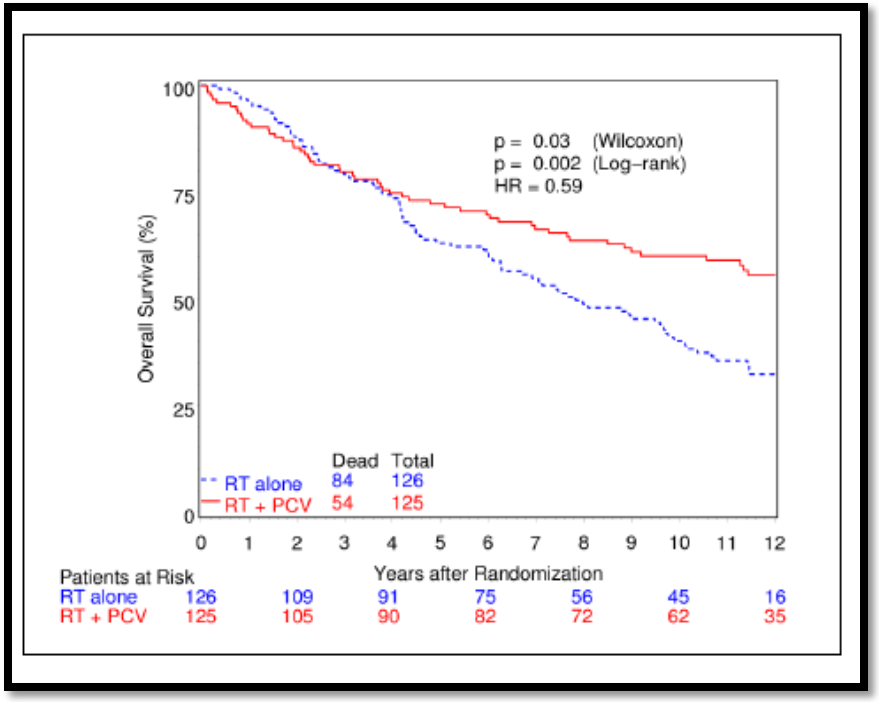
Stupp et al NEJM 2005
Stupp et al Lancet Oncol 2009

EF-14 trial



GBM

RTOG 9802 _ Overall Survival



High risk low grade gliomas

New WHO classification

Molecular features and the HR reduction for OS in the RT/PCV arm.

Feature	Status	N	HR	95% CI	Status	N	HR	95% CI	P
1p/19q	Co-deleted	76	0.54	0.29, 1.01	Intact	224	0.82	0.61, 1.10	0.22
MGMT	Methylated	132	0.67	0.44, 1.01	Unmethylated	54	0.80	0.46, 1.42	0.6
IDH	Mutated	77	0.59	0.33, 1.07	Wild type	90	0.72	0.46, 1.11	0.58

International Society of Neuropathology-Haarlem Consensus Guidelines for Nervous System Tumor Classification and Grading

Molecular information	Histologic classification: Diffuse astrocytoma	Oligodendroglioma	"Oligoastrocytoma" or ambiguous histology
IDH-mut, 1p/19q-nondel, ATRX loss	*Diffuse astrocytoma, ATRX loss of expression*	*Diffuse glioma* (oligodendroglioma phenotype), 1p/19q non-deleted, ATRX loss of expression*	*Diffuse astrocytoma, ATRX loss of expression*
IDH-mut, 1p/19q-codel, ATRX intact	*Diffuse glioma (astrocytoma phenotype), 1p/19q-codeleted*	*Oligodendroglioma, 1p/19q-codeleted*	*Oligodendroglioma, 1p/19q-codeleted*
IDH wild type	*Diffuse astrocytoma, IDH wild type**	*Diffuse glioma* (oligodendroglioma phenotype), IDH wild type**	*Diffuse astrocytoma, IDH wild type**
Testing not performed	*Diffuse astrocytoma, NOS*	*Oligodendroglioma, NOS*	*"Diffuse glioma, NOS"*

Current focus on Immunotherapy

Vaccine type	Phase	N	Experimental design	PFS (mo)	OS (mo)	References
Tumor lysate vaccine	I	12	Autologous DC loaded with tumor lysate	15.5	23.4	NCT00068510, [27]
Tumor lysate vaccine	II		Resiquimod, poly-ICLC	Ongoing	Ongoing	NCT01204684
DCVax-Brain	III		2/3 vaccine, 1/3 placebo with option of crossover at disease progression	Ongoing	Ongoing	NCT00045968
Tumor lysate vaccine	II		Vaccine + standard therapy versus standard therapy alone	Ongoing	Ongoing	NCT01213407
Tumor lysate vaccine	II	10	DCs treated with PGE2 and TNF-α, cervical lymph node injection	9.5	28	NCT00323115, [35]
IMA950 multipeptide vaccine	I		11 tumor associated peptides (TUMAPs) + GM-CSF, cyclophosphamide, imiquimod	Ongoing	Ongoing	NCT01403285
Cancer stem cell vaccine, ICT-107	I	21	Six synthetic peptides associated with CSCs loaded onto autologous DCs	16.9	38.4	[50]
Cancer stem cell vaccine, ICT-107	II		Autologous DCs pulsed with immunogenic peptides from tumor antigens versus placebo	Ongoing	Ongoing	NCT01280552
Cancer stem cell vaccine	II		Autologous DCs loaded with stem cell-like antigens from irradiated GBM versus placebo	Ongoing	Ongoing	NCT01567202
CMV vaccine (Pep-CMV)	I		Intradermal Pep-CMV following chemoradiation	Ongoing	Ongoing	NCT01854099
Alpha type I DC peptide vaccine	I/II	22	Four peptides loaded onto alpha type I DCs + poly-ICLC, included GBM and anaplastic glioma	4 in GBM 13 in anaplastic glioma		NCT00766753, [61, 62]
HSPPC-96	I	12	Autologous tumor derived HSPPC-96 administered intradermally		47 weeks in immune responders 16 weeks in nonresponder	[67]
HSPPC-96	II		Autologous tumor derived HSPPC-96 administered intradermally	Ongoing	Ongoing	NCT00905060, NCT00293423
HSPPC-96	II		Vaccine + bevacizumab versus bevacizumab alone	Ongoing	Ongoing	NCT01814813
Irradiated glioma cells with GM-K562	I		Admixture of lethally irradiate glioma cells with GM-CSF producing K562 injected intradermally	Ongoing	Ongoing	NCT00694330

Cancer Cell
Article

Genome Sequencing of SHH Medulloblastoma Predicts Genotype-Related Response to Smoothened Inhibition

Cancer Cell
Article

Hotspot Mutations in *H3F3A* and *IDH1* Define Distinct Epigenetic and Biological Subgroups of Glioblastoma

nature genetics

Recurrent somatic alterations of *FGFR1* and *NTRK2* in pilocytic astrocytoma

doi:10.1038/nature13296

Novel somatic and germline mutations in intracranial germ cell tumours

doi:10.1038/nature11284

Dissecting the genomic complexity underlying medulloblastoma

Cancer Cell
Article

Delineation of Two Clinically and Molecularly Distinct Subgroups of Posterior Fossa Ependymoma

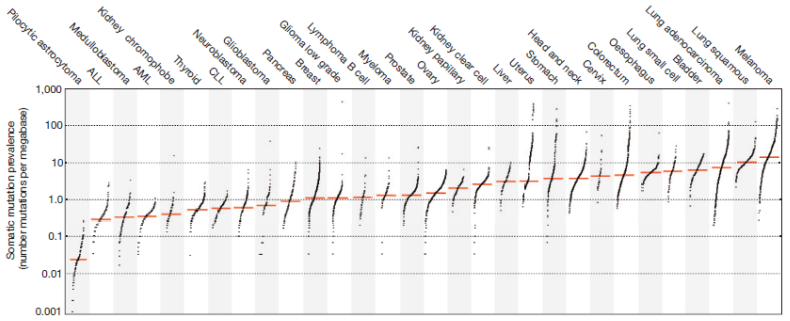
nature genetics

Recurrent somatic mutations in *ACVR1* in pediatric midline high-grade astrocytoma

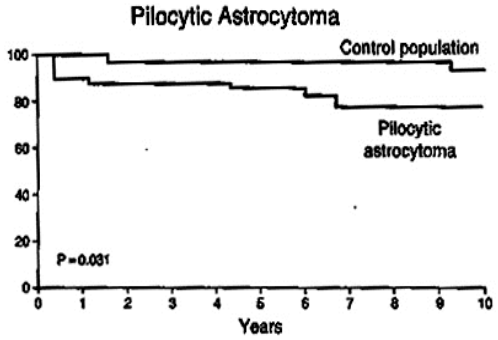
ARTICLE

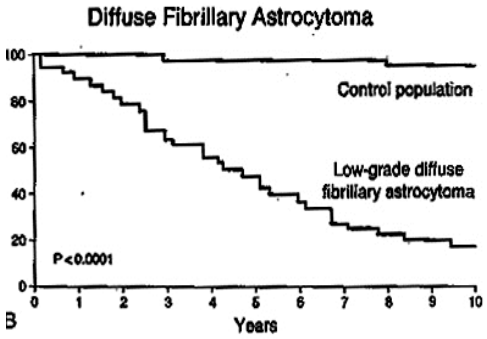
doi:10.1038/nature12477

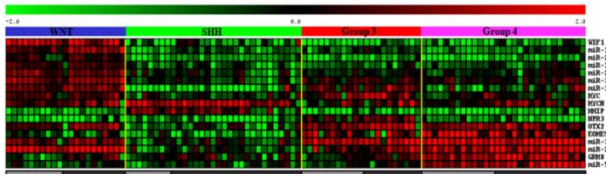
Signatures of mutational processes in human cancer

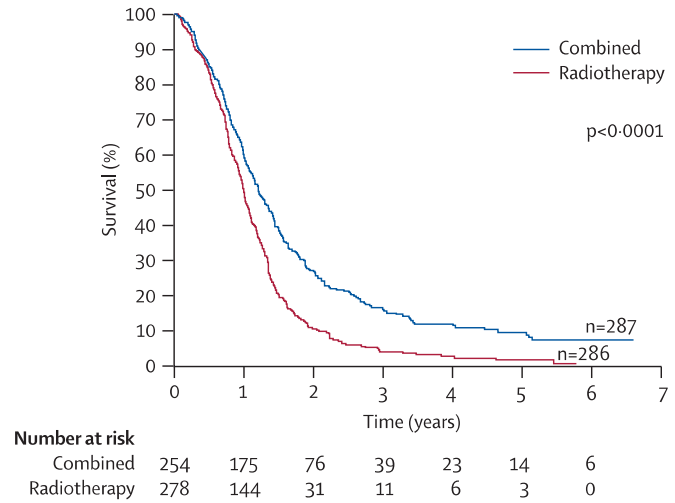


Survivals and survivorship





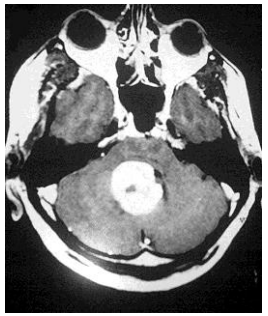


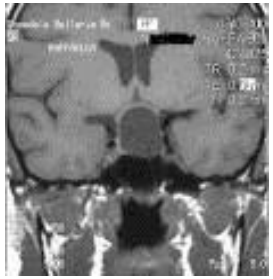


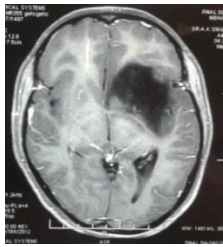
GBM

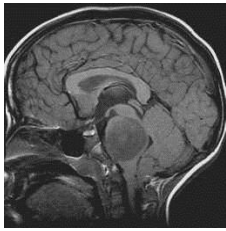
- Benign brain tumours: 10 yr OS: 80-90%
- Childhood brain tumours: 10 ys OS: 70%
- Low grade gliomas: 5-10 yr OS: 50-60%
- High grade gliomas: 2 yr OS: 25-40%

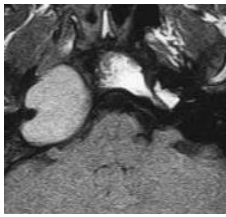
Neuro Oncology status in Asia











Neuro-oncology group at TMH

Total number of primary CNS tumours in 2014: **1595;** GBM=250

Paediatric brain tumours in the year 2014: **253**

Age group	Number of patients	Percentage
0-3	31	14%
4-8	74	33%
9-14	76	34%
15-18	39	17%

Medulloblastoma	**n = 40**	
Histological subtype	**Number**	**Percentage**
Classical	21	52.5%
Nodular /Desmoplastic	9	22.5%
Anaplastic/ large cell	10	25%

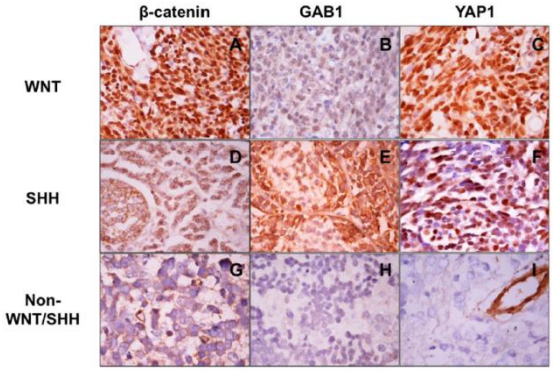
- All patients prospectively recruited in the molecular profiling study
- Also a prospective radiogenomics study ongoing

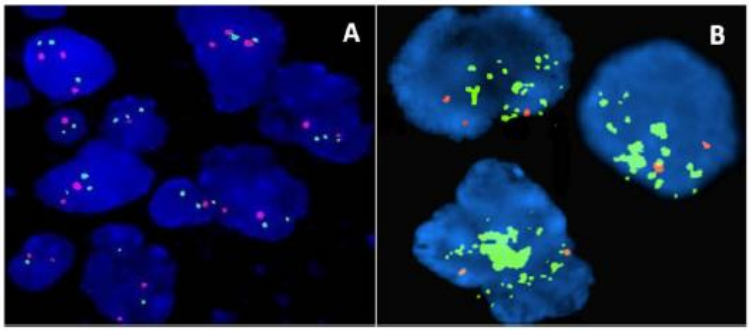
Brain Pathology ISSN 1015-6305

RESEARCH ARTICLE

Integrating Molecular Subclassification of Medulloblastomas into Routine Clinical Practice: A Simplified Approach

Kavneet Kaur[1]*; Aanchal Kakkar[1]*; Anupam Kumar[1]; Supriya Mallick[2]; Pramod K. Julka[2]; Deepak Gupta[3]; Ashish Suri[3]; Vaishali Suri[1]; Mehar C. Sharma[1]; Chitra Sarkar[1]



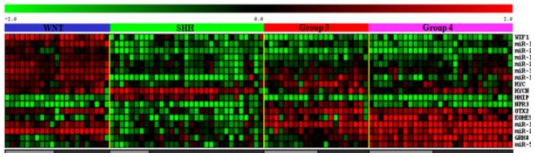


Neuro-Oncology
doi:10.1093/neuonc/not123

NEURO-ONCOLOG

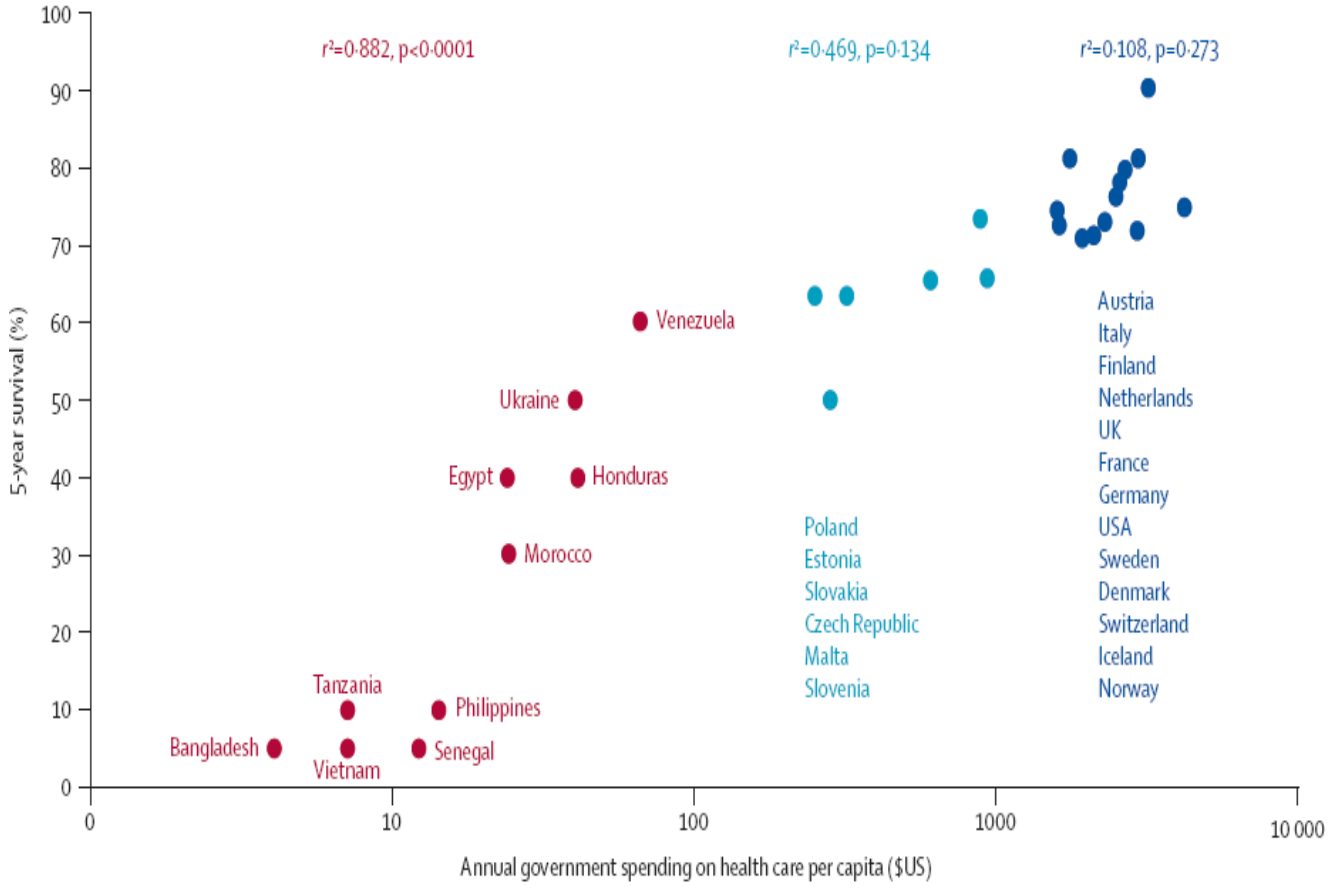
Real-time PCR assay based on the differentia expression of microRNAs and protein-coding genes for molecular classification of formalin fixed paraffin embedded medulloblastomas

Ratika Kunder, Rakesh Jalali, Epari Sridhar, Aliasgar Moiyadi, Naina Goel, Atul Goel, Tejpal Gupta, Rahul Krishnatry, Sadhana Kannan, Purna Kurkure, Chandrashekhar Deopujari, Prakash Shetty, Naresh Biyani, Andrey Korshunov, Stefan M. Pfister, Paul A. Northcott, and Neelam Vishwanath Shirsat



Diversity in cancer care

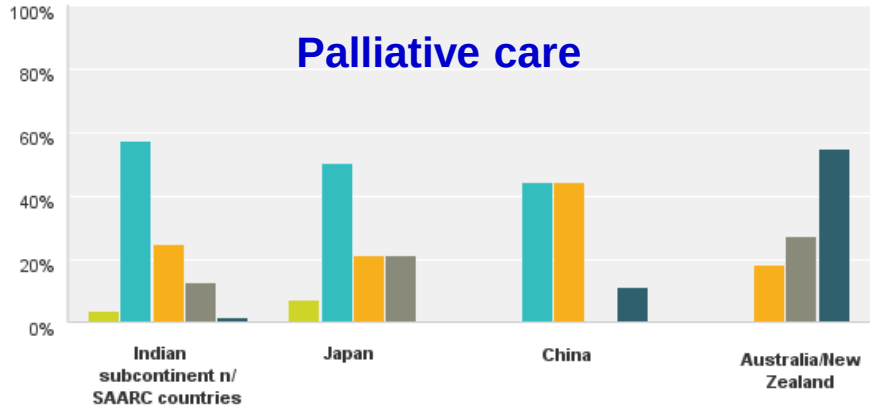
Lancet Oncology 2008

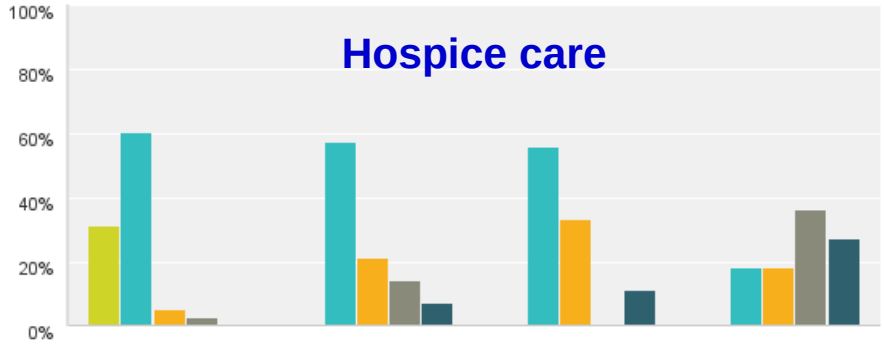


Culturally & linguistically diverse brain tumour patients have significantly lower rates of recruitment, accrual & retention in clinical trials Lwin 2015

International patterns of palliative care in neuro-oncology: a survey of physician members of the Asian Society for Neuro-Oncology, the European Association of Neuro-Oncology, and the Society for Neuro-Oncology

Tobias Walbert, Vinay K. Puduvalli, Martin J.B. Taphoorn, Andrew R. Taylor, and Rakesh Jalali





Patient referral to pall care

- Only 8% at the time of diagnosis
- 11% at recurrence
- Majority when symptoms aggravate