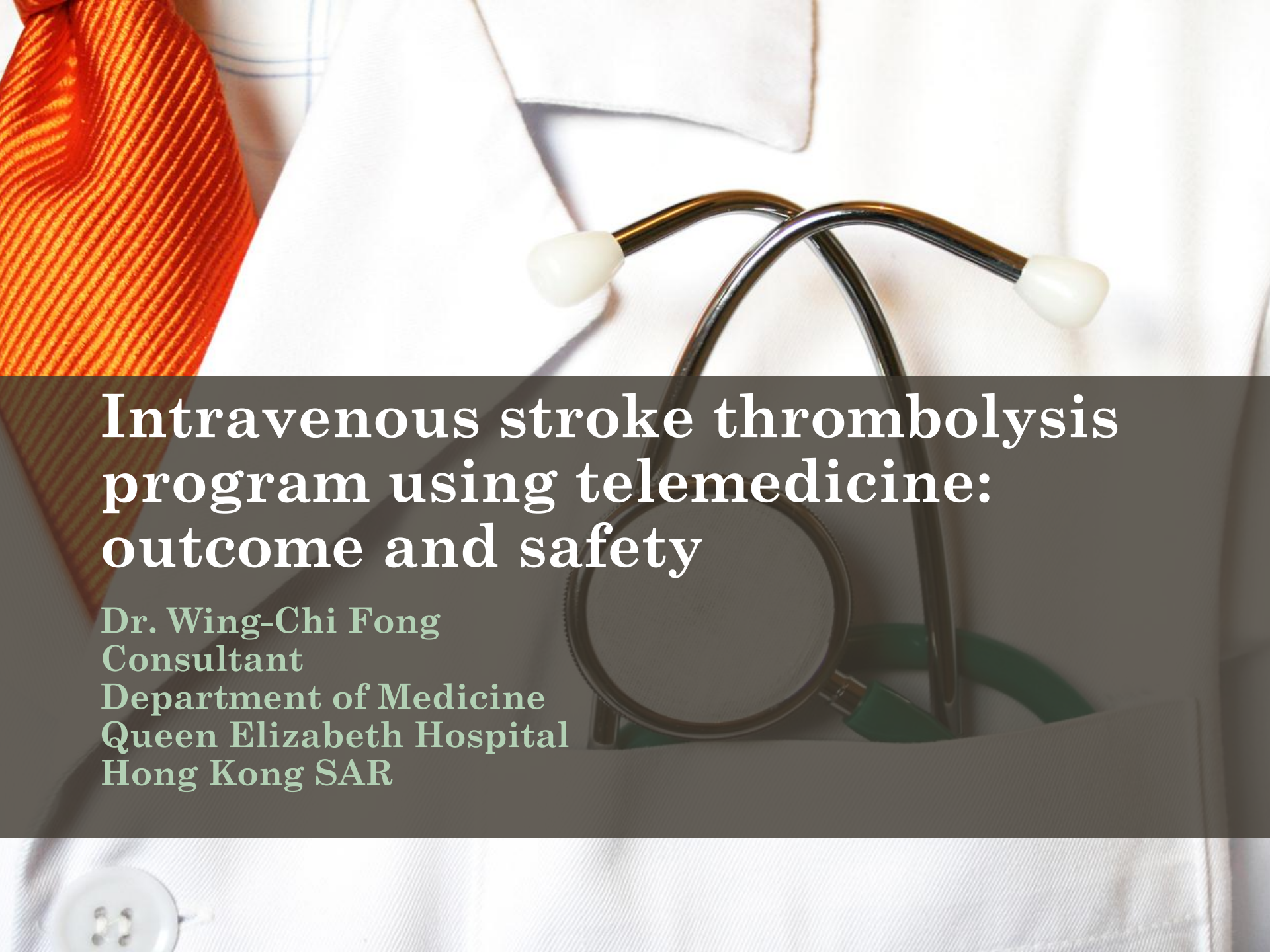

Intravenous stroke thrombolysis program using telemedicine: outcome and safety

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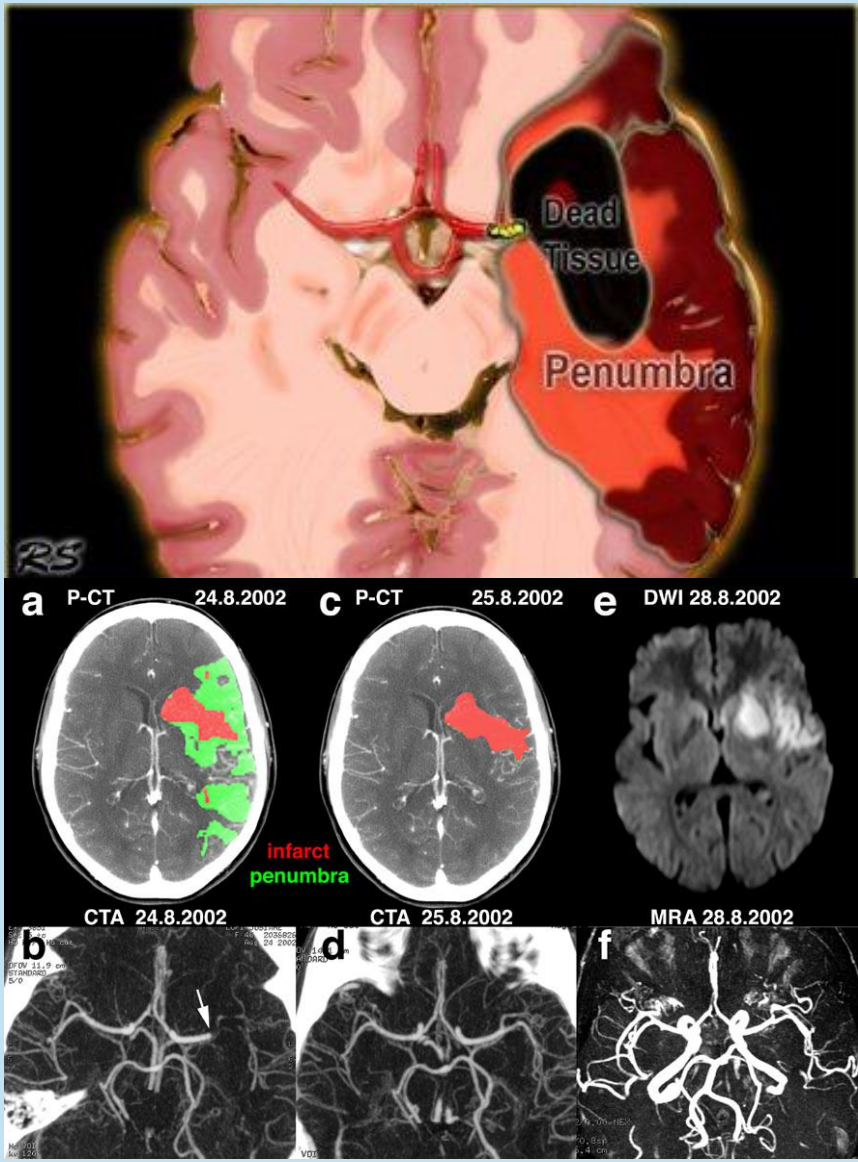
Background

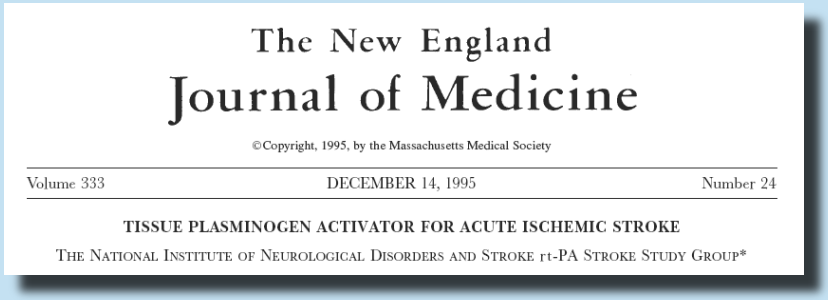
Mechanism of IV stroke thrombolysis

- Ischaemic stroke in hyperacute phase
  - Acute arterial occlusion led to irreversible infarct core with surrounding ischaemic tissues (ischaemic penumbra)
  - Tissue within ischaemic penumbra can be salvaged if blood supply can be restored within the therapeutic window from symptoms onset
- Infusion of fibrinolytic agent in hyperacute phase
  - Dissolve the blood clot and recanalize the vessel
  - Lead to recovery of the neurological impairment



Intravenous Thrombolysis

- ***NINDS t-PA Stroke Trial***
  - **Published in 1995**
  - ***Within 3 hrs* of stroke onset**
    - **58% within 90 min**
  - ***0.9 mg/kg* iv over 1 hr, *10%* of total dose as *bolus*, max 90mg**
  - **US FDA approved 1996**



The New England
Journal of Medicine

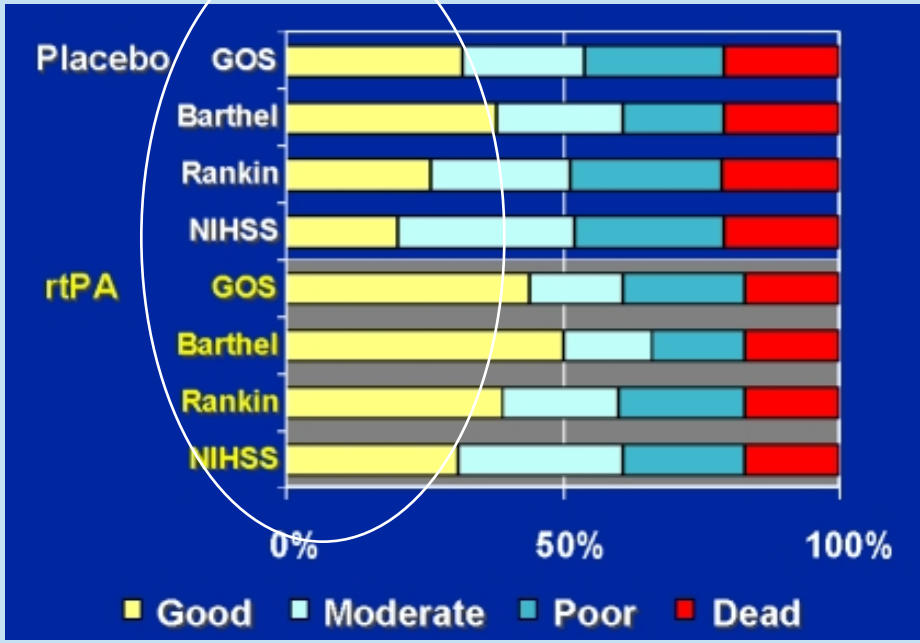
Volume 333 DECEMBER 14, 1995 Number 24

TISSUE PLASMINOGEN ACTIVATOR FOR ACUTE ISCHEMIC STROKE

THE NATIONAL INSTITUTE OF NEUROLOGICAL DISORDERS AND STROKE rt-PA STROKE STUDY GROUP*

Intravenous Thrombolysis

- More likely to have excellent functional outcome at 3 months (31% to 50% vs. 20 % to 38%, absolute difference 11 to 13%)
- Benefit maintained at 1 year
- Cost-effective
  - Discharge earlier to home
  - Less nursing home
  - Less extensive rehabilitation



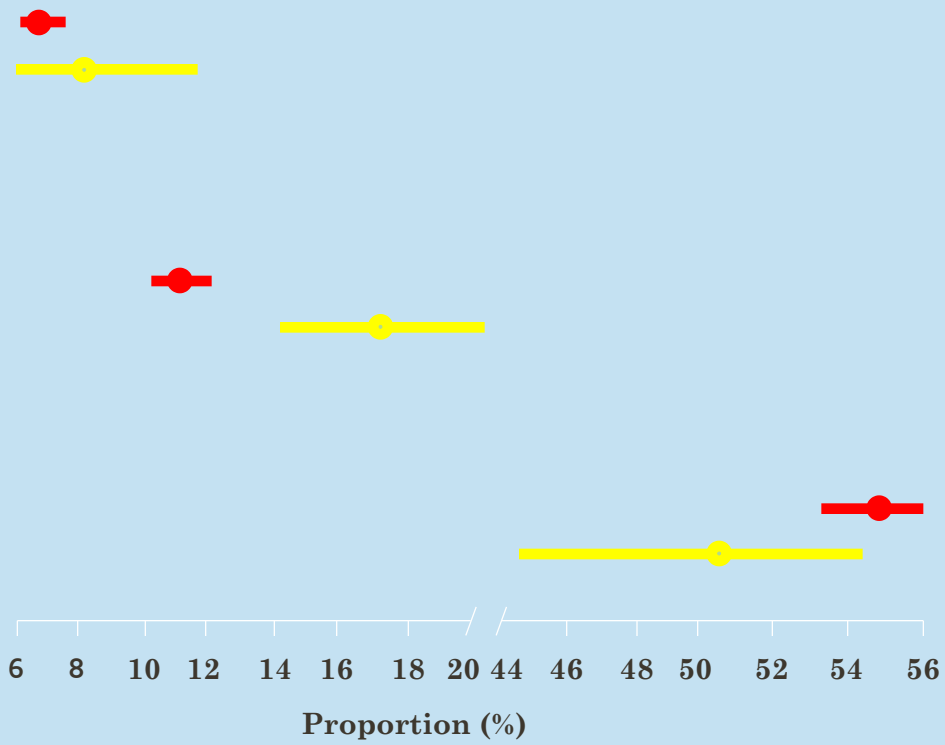
1. The NINDS rt-PA Sroke Study Group. N Engl J Med 1995;333:1581-7

2. Kwiatkowski TG et al. N Engl J Med 1999;340:1781-7

3. Fagan S et al. Neurology 1998;50:883-90

Outcomes of SITS-MOST compared to randomised controlled trials

	SITS-MOST (events/total; 95% CI)	Pooled RCTs* (events/total; 95% CI)
SICH per NINDS definition†	7.3% (468/6438; 6.7–7.9)	8.6% (40/465; 6.3–11.6)
Mortality within 3 months	11.3% (701/6218; 10.5–12.1)	17.3% (83/479; 14.1–21.1)
Independence (mRS 0–2) at 3 months	54.8% (3362/6136; 53.5–56.0)	50.1% (233/465; 44.5–54.7)

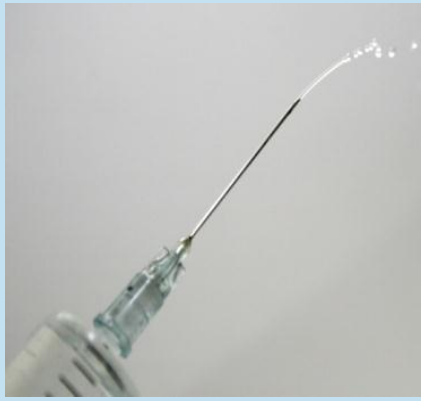


Proportions of patients with symptomatic intracerebral haemorrhage, including fatalities, and mortality and independence at 3 months in SITS-MOST and pooled randomised controlled trials
SICH=symptomatic intracerebral haemorrhage.
*Active arms. †NIHSS≥1 and any haemorrhage.

Wahlgren N et al. *Lancet* 2007; 369: 826.

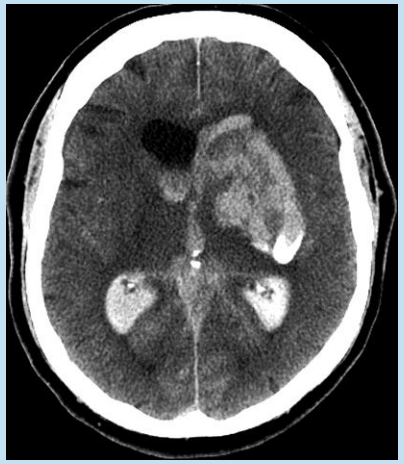
IV Thrombolysis in Acute Ischaemic Stroke

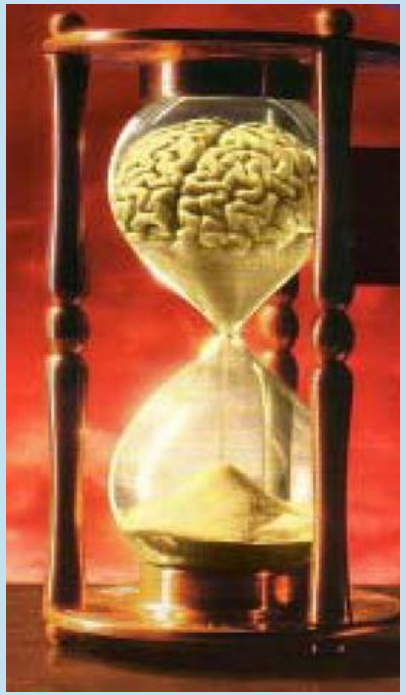
- **IV thrombolysis is evidence-based**
  - NINDS trial as landmark study
  - Meta-analysis of NINDS trial, ECASS I, ECASS II, ATLANTIS suggested the 4.5 hr treatment window
  - ECASS III confirmed the treatment efficacy up to 4.5 hr from symptom onset
  - IST III reinforce the efficacy in elderly patients
- **Effectiveness of IV thrombolysis is reproduced outside clinical trial setting**
  - STARS (USA, n=389, 97-98)
  - CASES (Canada, n=1135, 99-01)
  - SITS-MOST (Europe, n=6483, 02-06)
  - SITS-ISTR (International, n=23942, 02-08)



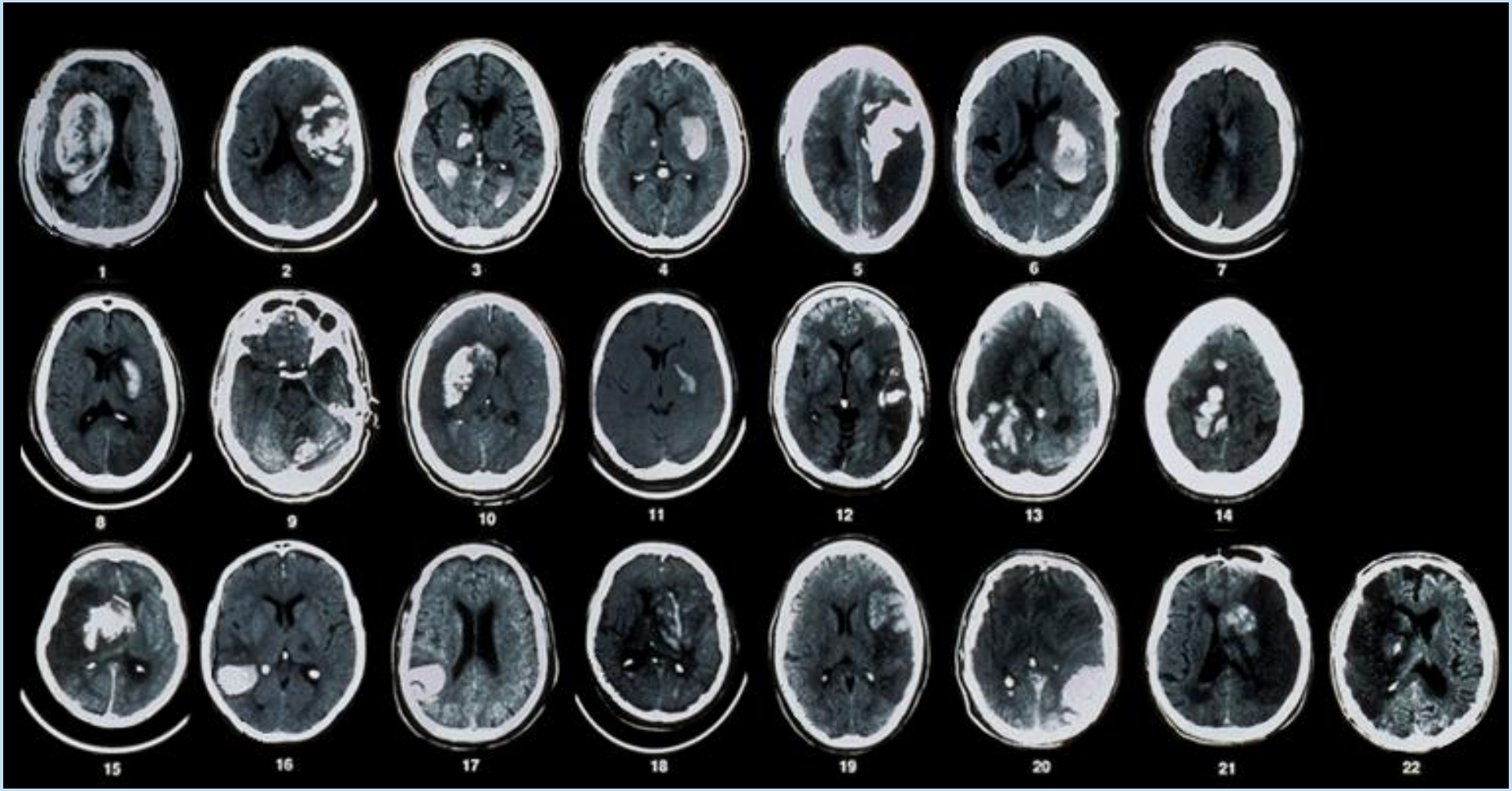
Difficulties of Stroke Thrombolysis

- Significant risk of ICH after thrombolysis
- Treatment response is time dependent
- No objective diagnostic investigation in early phase of ischaemic stroke



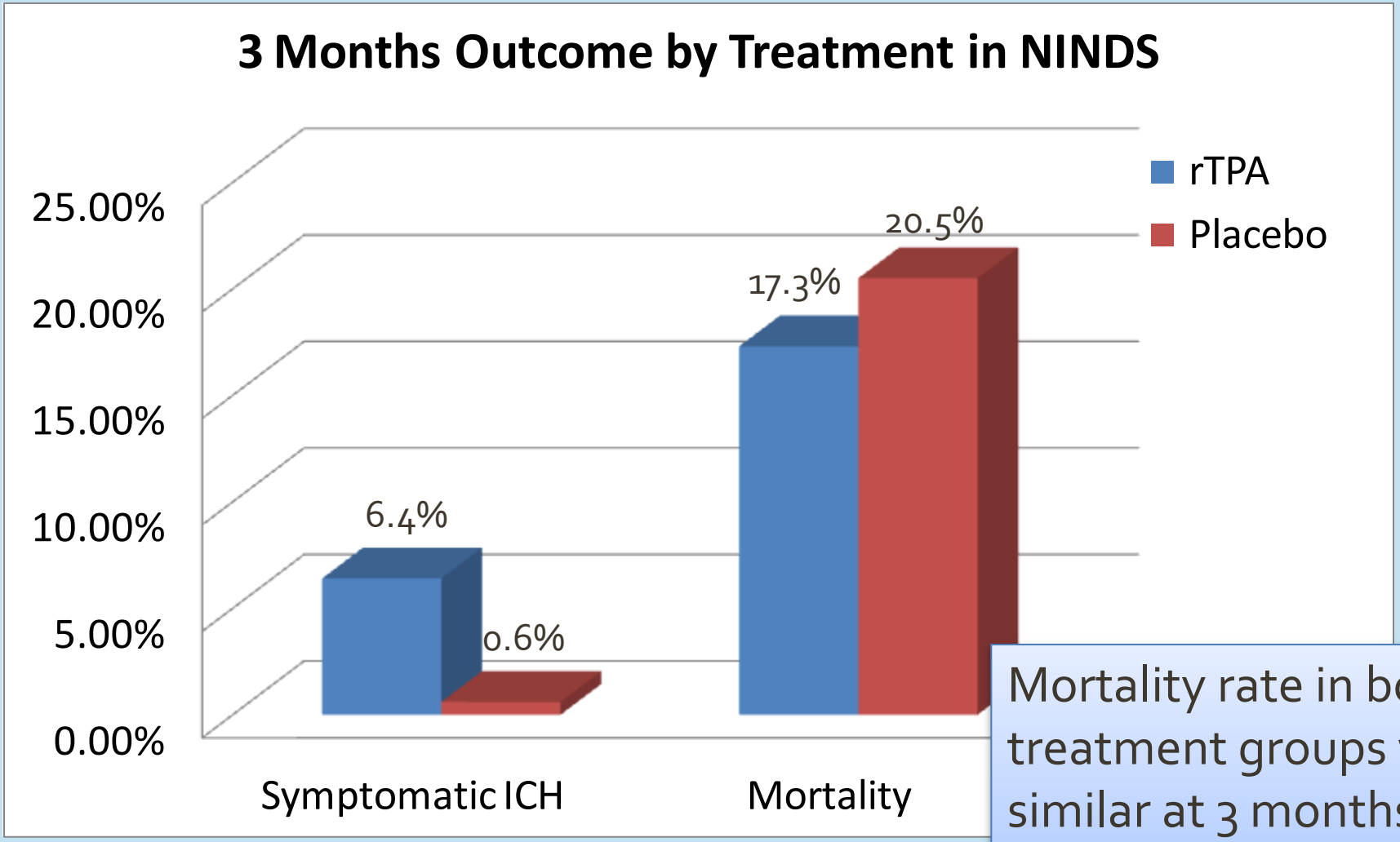


Intracranial Hemorrhage after IV Stroke Thrombolysis



NEJM 1995;333:1581-1587

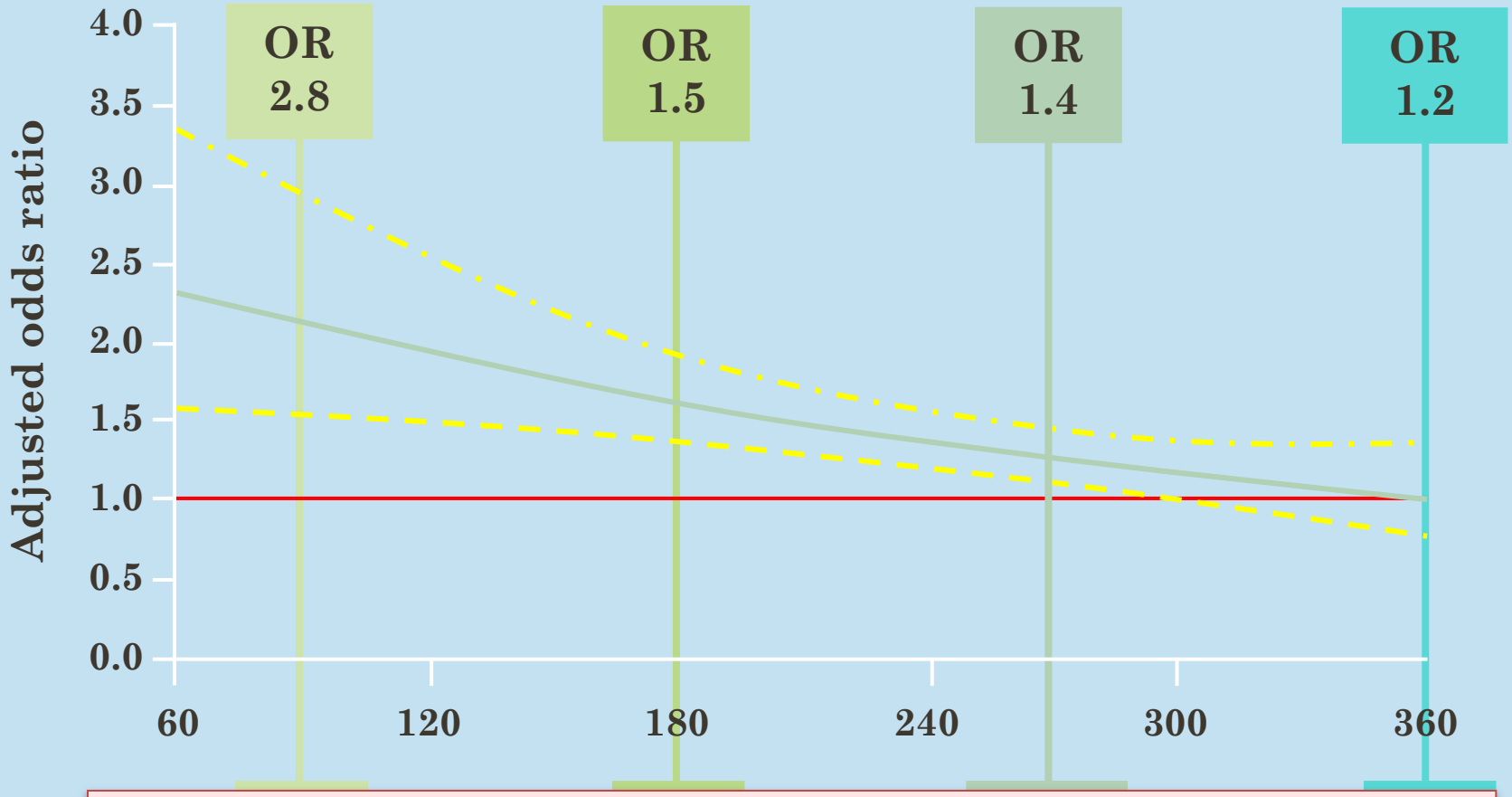
Safety Concern – Intracranial Hemorrhage



Mortality rate in both treatment groups was similar at 3 months & at 1 year

NEJM 1995;333:1581-1587

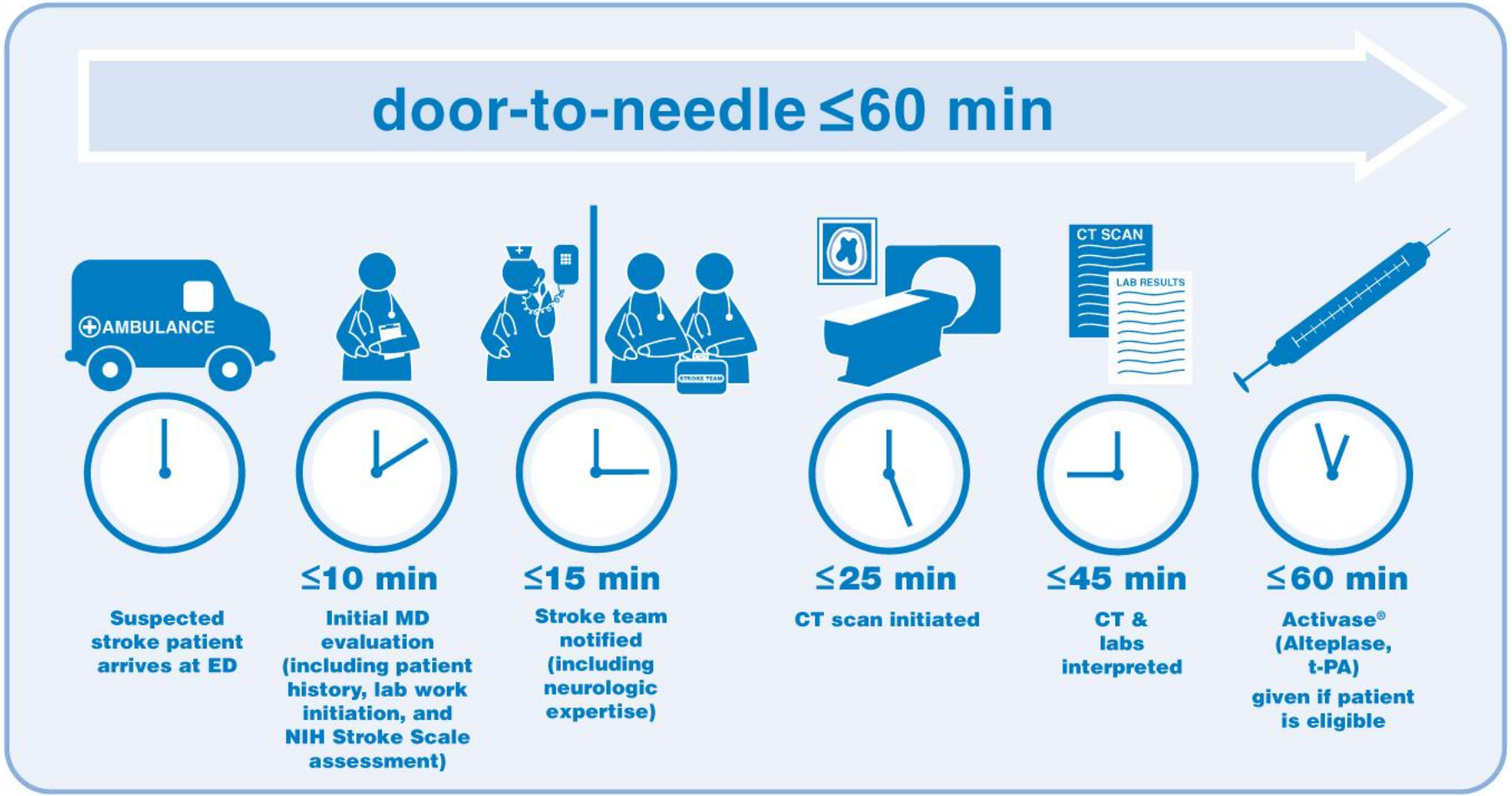
Treatment Efficacy is Time Dependent



Treatment response is time dependent!
Earlier the treatment,
Better chance for favourable outcome!

NIH-recommended Emergency Department response times

The "golden hour" for evaluating and treating acute stroke

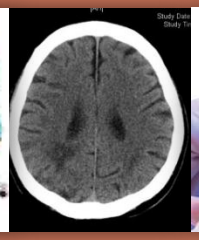


Reference: NINDS/NIH Web site: stroke proceedings.

Service Requirement

- Coordinated rapid response
- Neurology expertise needed to select the patient according to clinical and CT criteria

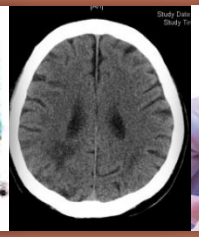


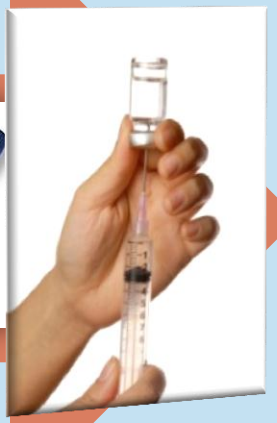



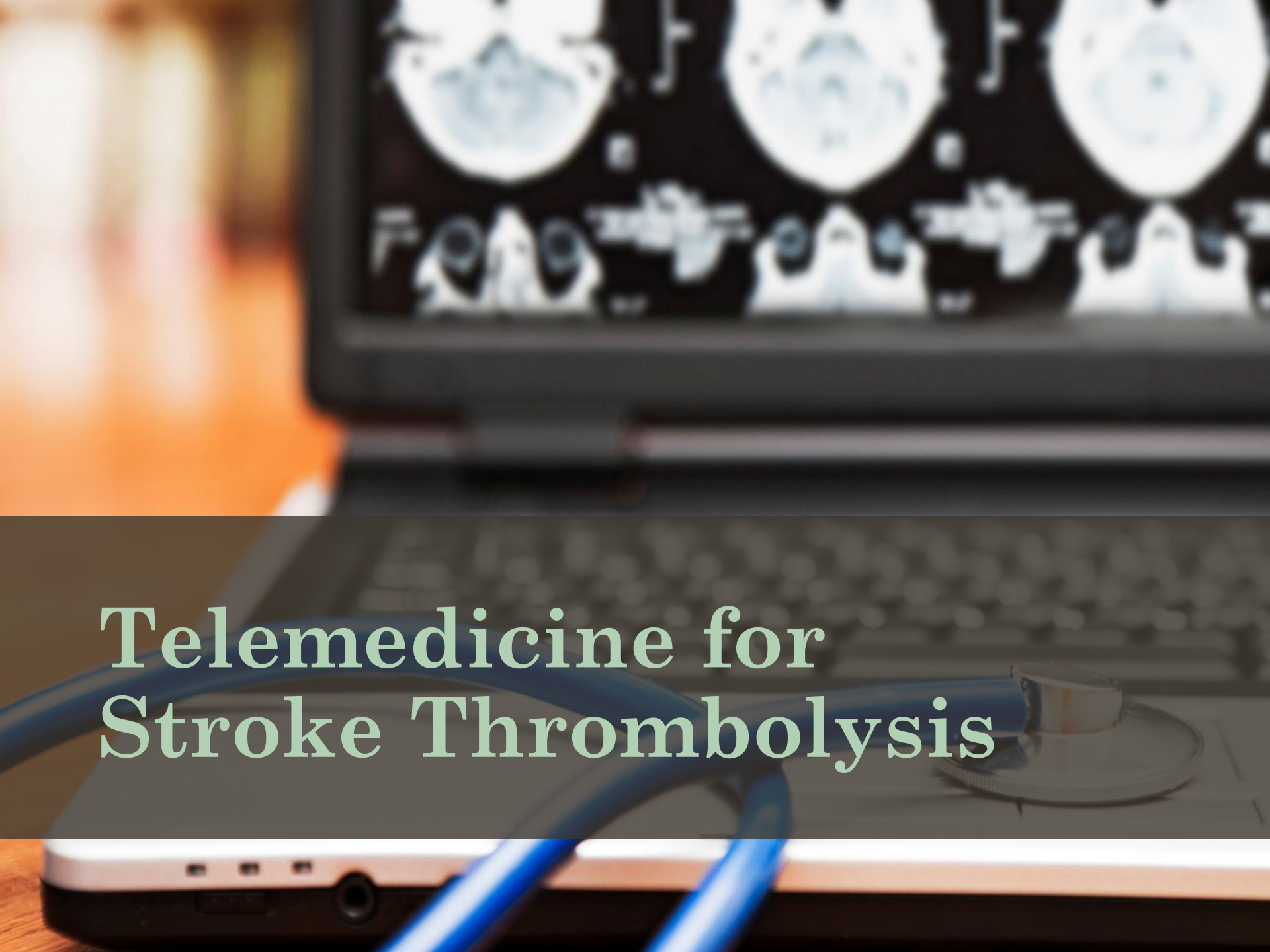
Low Utilization Rate

- Stroke thrombolysis is under-utilized
- Less than 5% of patients was treated
- It is related to:
  - Delayed presentation to A&E
  - Lack of neurologist expertise on site to support the stroke thrombolysis service







Telemedicine for Stroke Thrombolysis

Telestroke

- Application of telemedicine in stroke care
  - Remote evaluation of stroke patient by videoconferencing or telephone consultation
  - Remote review of neuroimaging
- Advantages
  - Overcome the lack of onsite stroke expertise
  - Increase stroke thrombolysis rate
  - Reduce the need of patient transfer
- Outcome similar as compared with treatment with neurologist on site

Telestroke-Guided Intravenous Tissue-type Plasminogen Activator Treatment Achieves a Similar Clinical Outcome as Thrombolysis at a Comprehensive Stroke Center

Stroke. 2011 Nov;42(11):3291-3

	Stroke Centre	Telestroke
Number	59	83
Age	71.9	71.9
Median NIHSS	10.5	12
Door to Needle time	67.8	89.9 ($p<0.05$)
Onset to Needle time	156.7	145.5
sICH (%)	5.1	1.2
mRS 0-1 (%)	22.0	34.9
mRS 0-2 (%)	37.5	42.1

Conclusion: Telestroke is a viable alternative to in-person evaluation

Two years of Finnish Telestroke
Thrombolysis at spokes equal to that at the hub

Neurology. 2011;76:11:1145-1152

	Onsite at HUCH	Finnish telestroke
Number	985	61
Age	67.7	70
Median NIHSS	10	10
Onset to Needle time	116	130
sICH (%)	9.4	6.7
mRS 0-1 (%)	36.8	29.4
mRS 0-2 (%)	58.1	49.1

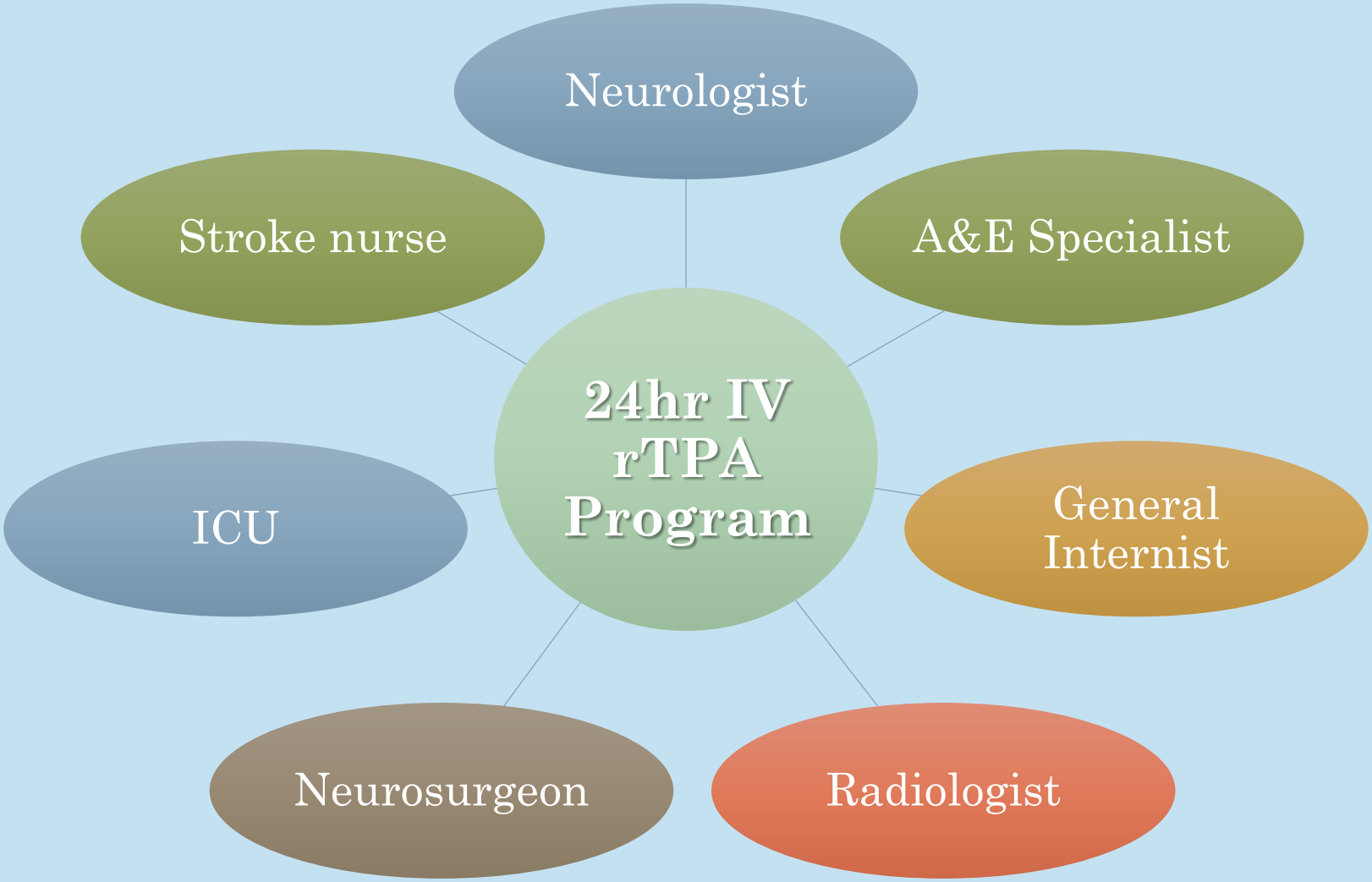
Conclusion: Outcome of stroke thrombolysis via Finnish Telestroke was very similar to on-site thrombolysis at HUCH.

Development of 24 hr IV Stroke Thrombolysis in Queen Elizabeth Hospital, Hong Kong

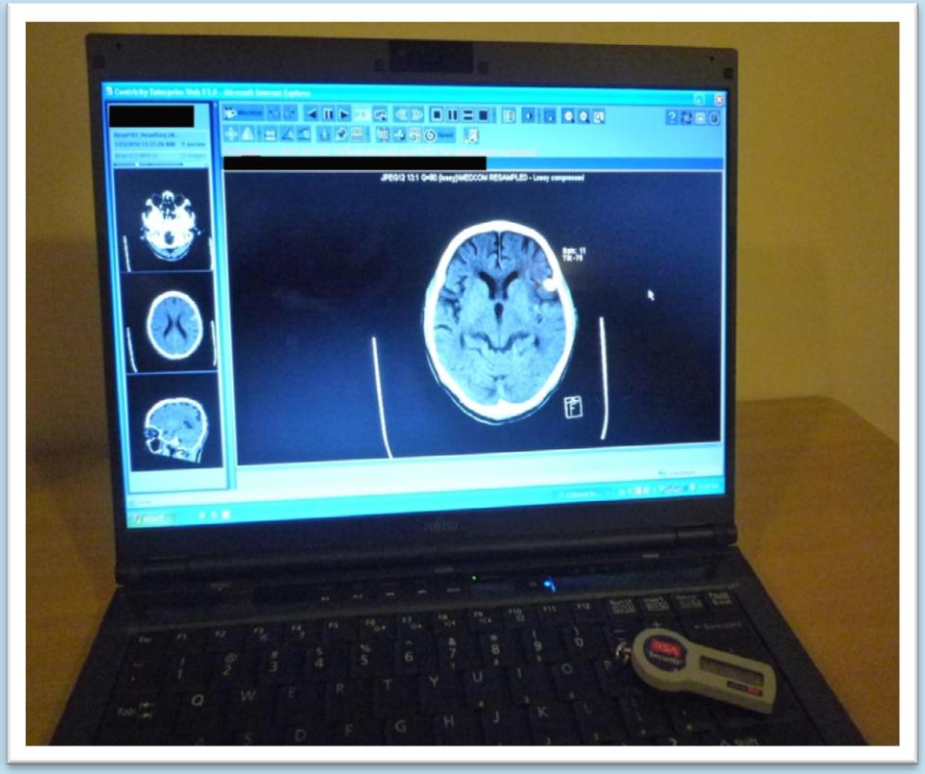
IV Stroke Thrombolysis Service in QEH

- Office-hour thrombolysis service started in 2005
  - 2 to 4 patients treated per year
  - Lack of awareness of the service
  - Under identification of eligible patients
- IT development within HA
  - Remote access of patient information (clinical notes, investigation and imaging)
  - Teleradiology is technically feasible
- 24 hour iv stroke thrombolysis service was implemented on Dec 2008, and it is the first 24-hour program in HA

Multi-disciplinary Team



Utilization of Teleradiology



Token for remote access of HA ePR and images	Remote access of CT images via computers outside HA system

24hr Services by Internists and Neurologists supported by Telemedicine

Office Hour Or Outside office hours with Neurologist on site

- Assessed and managed by neurologist

Outside office hours without neurologist on site

- Assessed and managed by onsite internist
- Telephone consultation to on call off site Neurologists who will review the CT scan via tele-radiology and make the decision to treat or not
- Informed consent process and treatment initiated by internist

Post Treatment Monitoring

- Admitted to Acute Stroke Unit or ICU for close monitoring

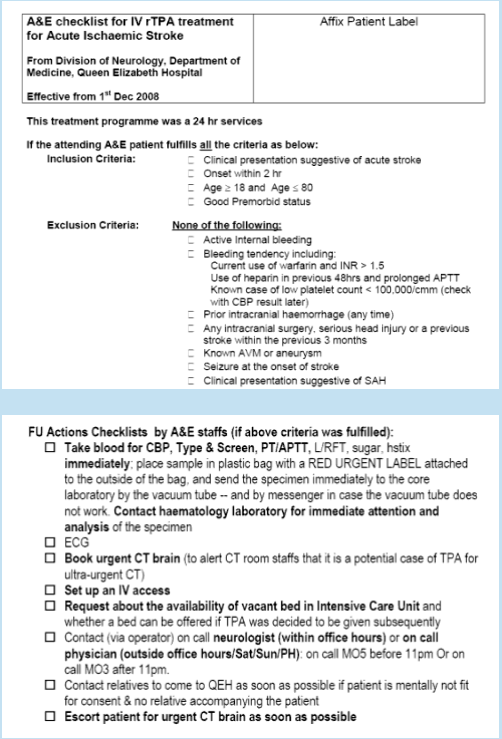
Key Role of Internal Medicine Specialist

- ✓ Assessment of potentially eligible patients: confirmation of diagnosis, onset time, assessment of stroke severity
- ✓ Check for any contraindication for iv thrombolysis
- ✓ Preliminary review of CT scan images
- ✓ Telephone consultation to on-call neurologist
- ✓ Clarify the risk/benefit of treatment to patients/relatives (Informed consent)

QEH Model of Tele-stroke

- Telephone-based consultation
  - Reconfirm onset time
  - Assess stroke severity & bleeding risk
  - Look for contraindication
  - Decision to treat or not
- Teleradiology
  - Remote review of CT image via internet access of the hospital image server
  - Guided by ASPECT score

Protocol-driven Management



A&E checklist for IV rTPA treatment for Acute Ischaemic Stroke | Affix Patient Label

From Division of Neurology, Department of Medicine, Queen Elizabeth Hospital

Effective from 1st Dec 2008

This treatment programme was a 24 hr services

If the attending A&E patient fulfills all the criteria as below:

Inclusion Criteria:
- ☐ Clinical presentation suggestive of acute stroke
- ☐ Onset within 2 hr
- ☐ Age ≥ 18 and Age ≤ 80
- ☐ Good Premorbid status

Exclusion Criteria: None of the following:
- ☐ Active Internal bleeding
- ☐ Bleeding tendency including:
  Current use of warfarin and INR > 1.5
  Use of heparin in previous 48hrs and prolonged APTT
  Known case of low platelet count < 100,000/cmm (check with CBP result later)
- ☐ Prior intracranial haemorrhage (any time)
- ☐ Any intracranial surgery, serious head injury or a previous stroke within the previous 3 months
- ☐ Known AVM or aneurysm
- ☐ Seizure at the onset of stroke
- ☐ Clinical presentation suggestive of SAH

FU Actions Checklists by A&E staffs (if above criteria was fulfilled):
- ☐ **Take blood for CBP, Type & Screen, PT/APTT,** L/RFT, sugar, hstix **immediately**: place sample in plastic bag with a RED URGENT LABEL attached to the outside of the bag, and send the specimen immediately to the core laboratory by the vacuum tube -- and by messenger in case the vacuum tube does not work. **Contact haematology laboratory for immediate attention and analysis** of the specimen
- ☐ ECG
- ☐ **Book urgent CT brain** (to alert CT room staffs that it is a potential case of TPA for ultra-urgent CT)
- ☐ **Set up an IV access**
- ☐ **Request about the availability of vacant bed in Intensive Care Unit** and whether a bed can be offered if TPA was decided to be given subsequently
- ☐ Contact (via operator) on call **neurologist (within office hours)** or **on call physician (outside office hours/Sat/Sun/PH)**: on call MO5 before 11pm Or on call MO3 after 11pm.
- ☐ Contact relatives to come to QEH as soon as possible if patient is mentally not fit for consent & no relative accompanying the patient
- ☐ **Escort patient for urgent CT brain as soon as possible**

Assessment Form: IV rTPA treatment for Acute Ischaemic Stroke

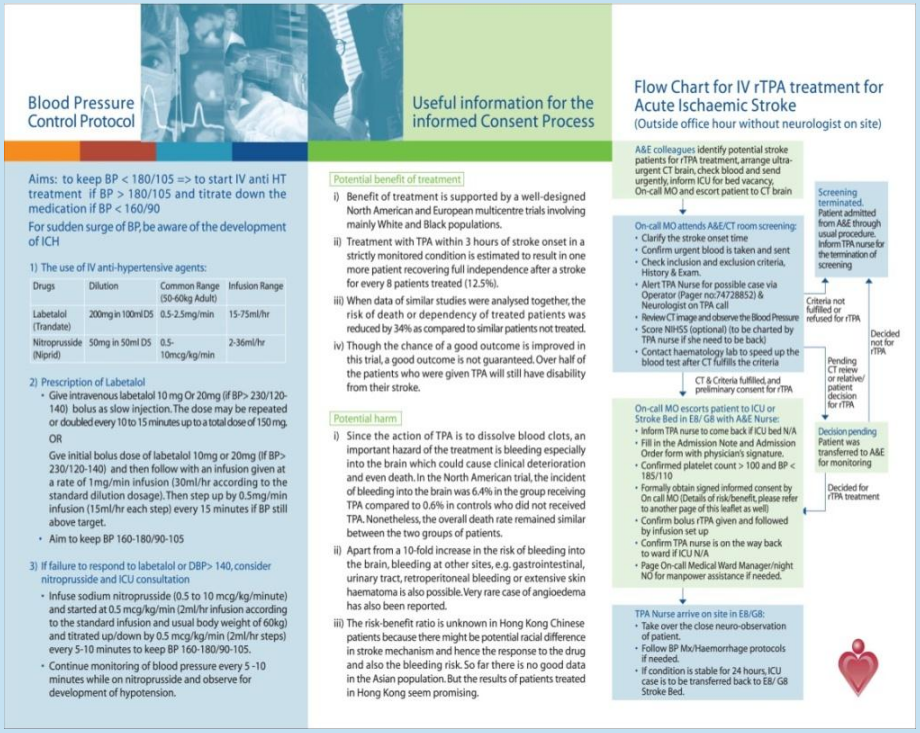
Name:
Sex/ Age:
ID no:
Ward/ Bed:
Hospital No:
Or Affix Patient's label

Department of Medicine
Queen Elizabeth Hospital

6. **CT scan brain Result (page neurologist on TPA call):** None of the following:
   - ○ Intracranial haemorrhage or subarachnoid haemorrhage
   - ○ Early changes suggestive of > 1/3 MCA territory infarct
   - ○ Other significant intracranial pathology e.g. tumour

   Films (mandatory) reviewed by: Name: _____ (Radiologist or Neurology team member)
7. **Final Destination:**
   - ○ Patient/relative agree for TPA -- Inform and transfer to ICU or E8/G8 escorted by Neurologist/On call MO and A&E nurse +/- stroke nurse.
   - ○ Contraindication present and/or patient/relative refuse TPA – If E8/ G8 stroke bed available, admit to E8/G8 ASU bed accordingly.
   - ○ Contraindication present and/or patient/relative refuse TPA – If E8/G8 bed not available, admit to medical admission ward as usual practice

IV Fluid & O_2	☐ NS Q8h ☐ NS Q6h ☐ NS Q4h ☐ Others: ☐ O_2 ___ L/min
Therapeutics	• Ask for voiding and check bladder, if unable to void, insert foley catheter before IV rTPA infusion. • Set IV access (if not yet done): ▪ For TPA infusion, followed by IV fluid ▪ If initial BP on high side, set up 2nd IV access (potential for IV antiHT Rx) • Administer IV rTPA as follow: (confirm informed consent and blood is taken) ▪ Total dose = BW ____ Kg X 0.9mg/kg = _____ mg (max 90mg) ▪ IV bolus = 10% of total dose _____ mg ▪ Then infuse remaining 90% over 1 hr = _____mg (See Dosing Table according to Body Weight) • Stop rTPA infusion for all potential life-threatening haemorrhage, including suspected intracranial haemorrhage. • If BP > 180/105mmHg for 2 two readings 5 – 10 minutes apart, follow Blood Pressure Control Protocol. • Avoid foley insertion for at least 30 minutes after infusion • Avoid Ryle tube insertion for at least 24 hours unless definitely indicated • If venepuncture is required, apply direct pressure to puncture site for 20 minutes. • No anticoagulant (heparin, warfarin, low molecular weight heparin) or antiplatelet medication (aspirin, plavix, persantin) for 24 hours • Arrange ultra-urgent CT whenever intracranial haemorrhage is suspected • Prepare to give 5 unit FFP and platelet conc if ICH or other potential life-threatening haemorrhage is suspected.
Start time: ____:____ **Finish time:** ____:____	



Blood Pressure Control Protocol

Aims: to keep BP < 180/105 => to start IV anti HT treatment if BP > 180/105 and titrate down the medication if BP < 160/90

For sudden surge of BP, be aware of the development of ICH

1) The use of IV anti-hypertensive agents:

Drugs	Dilution	Common Range (50-60kg Adult)	Infusion Range
Labetalol (Trandate)	200mg in 100ml D5	0.5-2.5mg/min	15-75ml/hr
Nitroprusside (Niprid)	50mg in 50ml D5	0.5-10mcg/kg/min	2-36ml/hr

2) Prescription of Labetalol
- Give intravenous labetalol 10 mg Or 20mg (if BP> 230/120-140) bolus as slow injection. The dose may be repeated or doubled every 10 to 15 minutes up to a total dose of 150 mg.

  OR

  Give initial bolus dose of labetalol 10mg or 20mg (if BP> 230/120-140) and then follow with an infusion given at a rate of 1mg/min infusion (30ml/hr according to the standard dilution dosage). Then step up by 0.5mg/min infusion (15ml/hr each step) every 15 minutes if BP still above target.
- Aim to keep BP 160-180/90-105

3) If failure to respond to labetalol or DBP> 140, consider nitroprusside and ICU consultation
- Infuse sodium nitroprusside (0.5 to 10 mcg/kg/minute) and started at 0.5 mcg/kg/min (2ml/hr infusion according to the standard infusion and usual body weight of 60kg) and titrated up/down by 0.5 mcg/kg/min (2ml/hr steps) every 5-10 minutes to keep BP 160-180/90-105.
- Continue monitoring of blood pressure every 5 -10 minutes while on nitroprusside and observe for development of hypotension.

Useful information for the informed Consent Process

Potential benefit of treatment

i) Benefit of treatment is supported by a well-designed North American and European multicentre trials involving mainly White and Black populations.

ii) Treatment with TPA within 3 hours of stroke onset in a strictly monitored condition is estimated to result in one more patient recovering full independence after a stroke for every 8 patients treated (12.5%).

iii) When data of similar studies were analysed together, the risk of death or dependency of treated patients was reduced by 34% as compared to similar patients not treated.

iv) Though the chance of a good outcome is improved in this trial, a good outcome is not guaranteed. Over half of the patients who were given TPA will still have disability from their stroke.

Potential harm

i) Since the action of TPA is to dissolve blood clots, an important hazard of the treatment is bleeding especially into the brain which could cause clinical deterioration and even death. In the North American trial, the incident of bleeding into the brain was 6.4% in the group receiving TPA compared to 0.6% in controls who did not received TPA. Nonetheless, the overall death rate remained similar between the two groups of patients.

ii) Apart from a 10-fold increase in the risk of bleeding into the brain, bleeding at other sites, e.g. gastrointestinal, urinary tract, retroperitoneal bleeding or extensive skin haematoma is also possible. Very rare case of angioedema has also been reported.

iii) The risk-benefit ratio is unknown in Hong Kong Chinese patients because there might be potential racial difference in stroke mechanism and hence the response to the drug and also the bleeding risk. So far there is no good data in the Asian population. But the results of patients treated in Hong Kong seem promising.

Flow Chart for IV rTPA treatment for Acute Ischaemic Stroke
(Outside office hour without neurologist on site)

A&E colleagues identify potential stroke patients for rTPA treatment, arrange ultra-urgent CT brain, check blood and send urgently, inform ICU for bed vacancy, On-call MO and escort patient to CT brain

On-call MO attends A&E/CT room screening:
- Clarify the stroke onset time
- Confirm urgent blood is taken and sent
- Check inclusion and exclusion criteria, History & Exam.
- Alert TPA Nurse for possible case via Operator (Pager no:74728852) & Neurologist on TPA call
- Review CT image and observe the Blood Pressure
- Score NIHSS (optional) (to be charted by TPA nurse if she need to be back)
- Contact haematology lab to speed up the blood test after CT fulfills the criteria

Screening terminated. Patient admitted from A&E through usual procedure. Inform TPA nurse for the termination of screening

Criteria not fulfilled or refused for rTPA

Decided not for rTPA

Pending CT relew or relative/ patient decision for rTPA

CT & Criteria fulfilled, and preliminary consent for rTPA

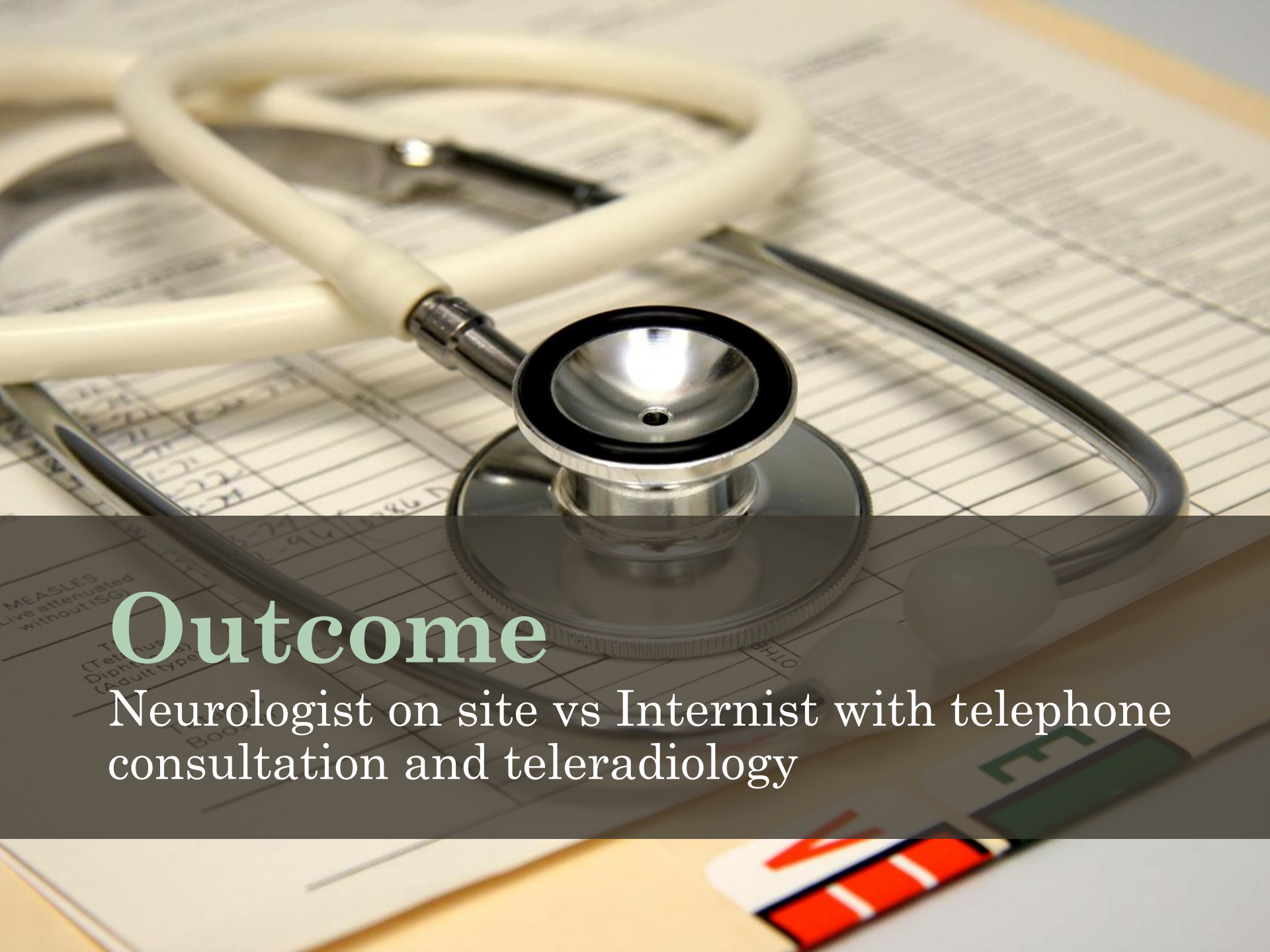
On-call MO escorts patient to ICU or Stroke Bed in E8/ G8 with A&E Nurse:
- Inform TPA nurse to come back if ICU bed N/A
- Fill in the Admission Note and Admission Order form with physician's signature.
- Confirmed platelet count > 100 and BP < 185/110
- Formally obtain signed informed consent by On call MO (Details of risk/benefit, please refer to another page of this leaflet as well)
- Confirm bolus rTPA given and followed by infusion set up
- Confirm TPA nurse is on the way back to ward if ICU N/A
- Page On-call Medical Ward Manager/night NO for manpower assistance if needed.

Decision pending Patient was transferred to A&E for monitoring

Decided for rTPA treatment

TPA Nurse arrive on site in E8/G8:
- Take over the close neuro-observation of patient.
- Follow BP Mx/Haemorrhage protocols if needed.
- If condition is stable for 24 hours, ICU case is to be transferred back to E8/ G8 Stroke Bed.

- **Protocol driven with checklist, assessment form, standard treatment order form, patient information sheet & management protocol**
- **To speed up the screening process**
- **To standardize the management**



Outcome

Neurologist on site vs Internist with telephone consultation and teleradiology

Baseline Characteristics

	On site (N=102)	Telemedicine (N=50)	p value
Age (median)	70.5	65.0	0.234
HT	54.9%	62.0%	0.406
DM	25.5%	18.0%	0.303
AF	24.5%	24.0%	0.945
Baseline NIHSS	12	12.5	0.843
ASPECT score	10	10	0.882

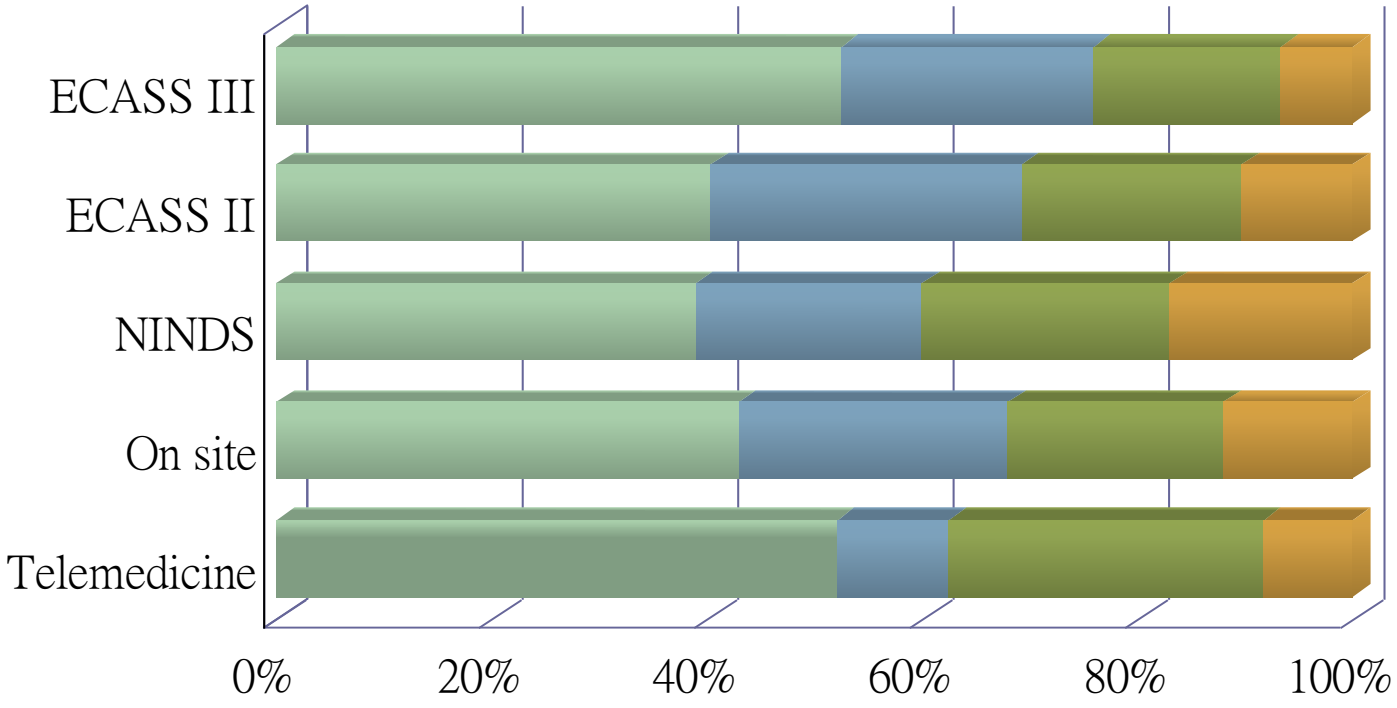
Logistics (Onsite vs. Telemedicine)

Median (in minutes)	On site (N=102)	Telemedicine (N=50)	p value
Onset to Door time	54	43.5	0.015
Door to CT time	26	30	0.291
CT time to Needle time	40.5	67	<0.001
Door to Needle time	71	96.5	<0.01
Onset to Needle time	133	147.5	0.012

Outcome (Onsite vs. Telemedicine)

	On site (N=102)	Telemedicine (N=50)	p value
Symptomatic ICH	4.9%	4.0%	1.0
mRS 0-1 (3 months)	43.0%	52.1%	0.299
mRS 0-2 (3 months)	54.0%	58.3%	0.620
Mortality (3 months)	11.9%	8.2%	0.583

Three Month Functional Outcome



Based on 148 patients data

	Window	NIHSS median
ECASS III	**3 – 4.5**	**9**
ECASS II	**0 – 6**	**11**
NINDS	**0 – 3**	**14**
QEH on site /telemedicine	**0 – 3**	**12/ 12.5**

***mRS (Modified Rankin Scale): functional scale from 0 (full recovery) to 6 (death)**

Telestroke

Queen Elizabeth Hospital Hong Kong

- Managed by internists on site
- Telephone consultation + teleradiology
- Longer door to needle time
- Safety (sICH) and three month functional outcome is comparable to cases managed by neurologist on site

Feasibility and Safety of Remote Radiology Interpretation with telephone consultation for acute stroke in Thailand

Neurol India. 2010 Sep-Oct;58(5):740-2.

- Managed by internal medicine resident on-duty
- Telephone consultation + teleradiology
- 100 patients treated with iv thrombolysis
- NIHSS: 15, Door to needle time: 54 minute
- SICH: 2%, 3-month mRS 0-1: 42%

Comparison of Telestroke Cohorts

	TEMPiS	Zaidi	MGH	Finland	QEH	Thailand
Number	106	83	181	61	50	100
Age	68	71.9	71.5	70	65	NA
Median NIHSS	13	12	13	10	12.5	15
Door to Needle time	76	89.9	NA	NA	96.5	54
Onset to Needle time	141	145.5	140	130	147.5	160
sICH (%)	8.5	1.2	3.9	6.7	4.0	2.0
mRS 0-1 (%)	NA	34.9	31	29.4	52.1	42
mRS 0-2 (%)	NA	42.1	NA	49.1	58.3	NA

Conclusion

- **Telestroke increases accessibility to a 24/7 stroke thrombolysis service**
- **Role of internists is critical**
- **With internist' support, telestroke model in QEH had achieved similar safety and outcome data as compared to direct management by neurologists**
- **24-hr IV stroke thrombolysis program in QEH is effective and safe. And outcome is comparable with oversea cohorts.**

Stroke Thrombolysis Team

Acknowledgment

- ***All Internal Medicine Specialists*** **involving in the screening & management of stroke patients with potentials for thrombolytic therapy**
- ***All A&E physicians*** **who had triggered the stroke thrombolysis call**
- ***All Radiologists*** **who provided timely neuroimaging**
- ***All Nursing staffs*** **who had provide nursing care and monitoring of those patients**


Thank You