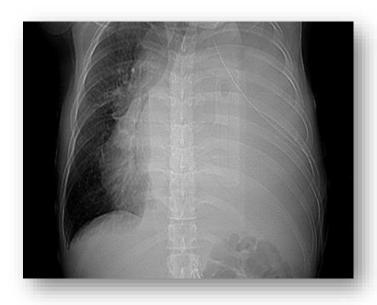


Update in Malignant Pleural Effusion Management



Kasia Czarnecka-Kujawa MD FRCPC MPH

Interventional Pulmonology
Division of Thoracic Surgery
Division of Respirology
University Health Network
Director RACE Program
Assistant Professor, University of Toronto



Disclosures

Olympus America





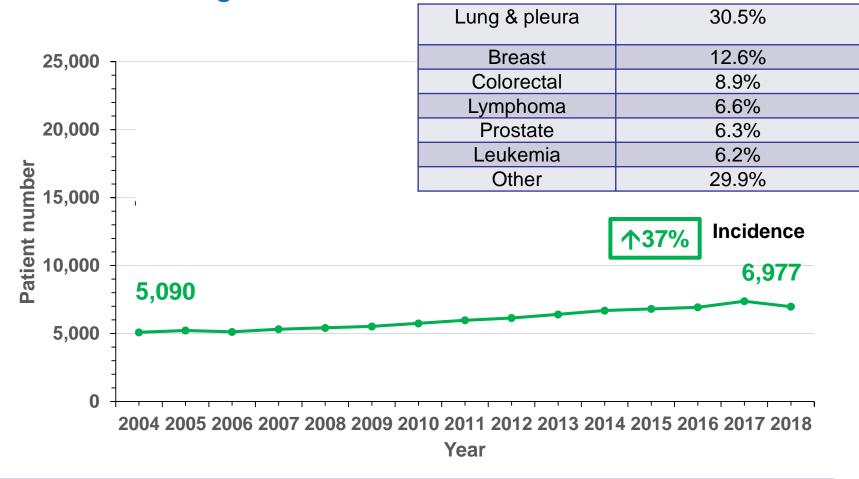
Overview

- MPE epidemiology
- Health care utilization and cost
- Update on definitive treatment options
- MPE quality gaps



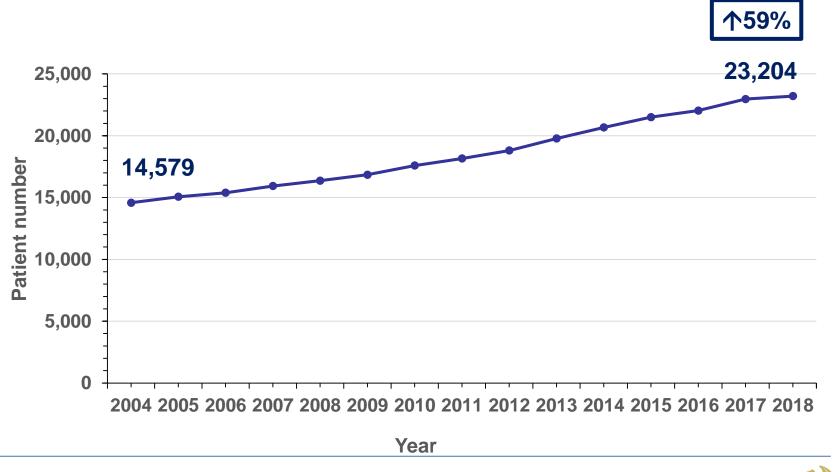


Incidence of Malignant Pleural Effusion in Ontario 2004-2018



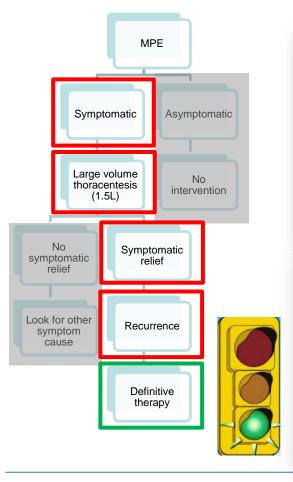


Prevalence of Malignant Pleural Effusion in Ontario 2004-2018





MPE – management guidelines



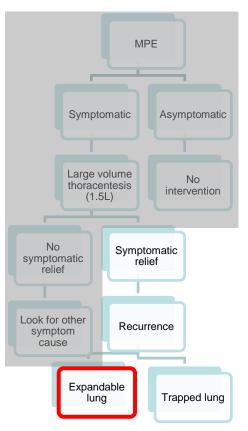




- > 50% effusions recur
- 58% recur rapidly (within 1 month)
- ? Plans for management at time of first drainage



MPE – management guidelines



MPE management options	Expandable lung
Thoracentesis	X
Tunneled pleural catheter	X
Pleurodesis	X
VATS	X
Chest tube	X
Tunneled pleural catheter	X
Pleuroperitoneal shunt	X
Decortication/pleurec tomy	X

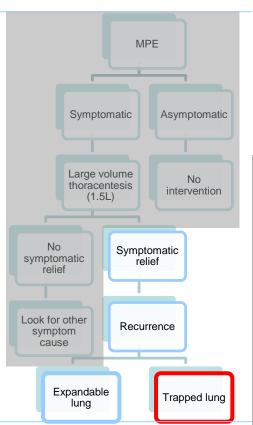




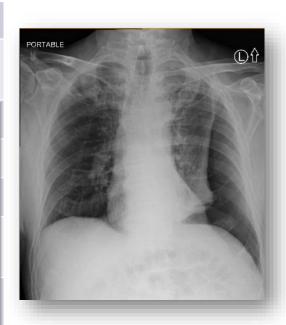
Am J Respir Crit Care Med. 2018;198:839–849.
Ost et al. CHEST. 2018;153:438-52.
Am J Respir Crit Care Med. 2018;(198):839–849.
Thorax. 2023;78:1143-56.
Eur Respir J. 2018.52: 1800349.
University Health Network



MPE – management guidelines



MPE management options	Expandable lung
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Study	LO	s	Additional procedures		Adverse events		QOL
	TPC	TP	TPC	TP	TPC	TP	
TIME2 Davies 2012	0 IQR 0-1	4 IQR 2-6	6%	22%	40%	13%	TPC > TP (6 mth
Fysh et al CHEST 2012	7 IQR 4-13	18 IQR 8-26	14%	32%	19%	45%	TPC >.TP
AMPLE Thomas. 2017	10 IQR 3-17	12 IQR 7-21	4%	22%	30%	18%	TPC=TP
Boshuizen 2017	0	5	16%	35%	19%	16%	TPC=TP





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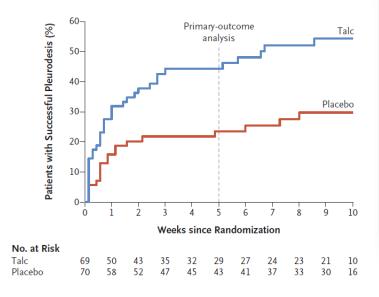
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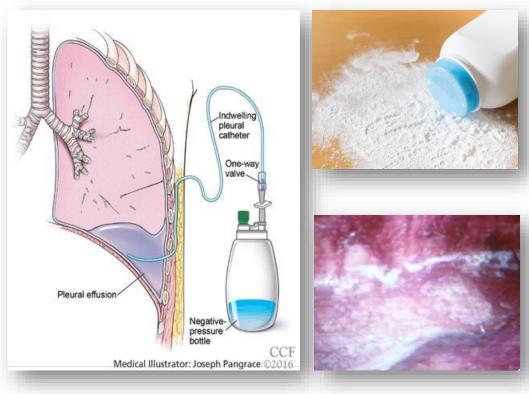




TPC + Talc in MPE management

- TPC + PLUS
- Pleurodesis at 70 days (max f/u time)
 - Talc: 51%
 - Placebo 27%
- > 50% patients excluded



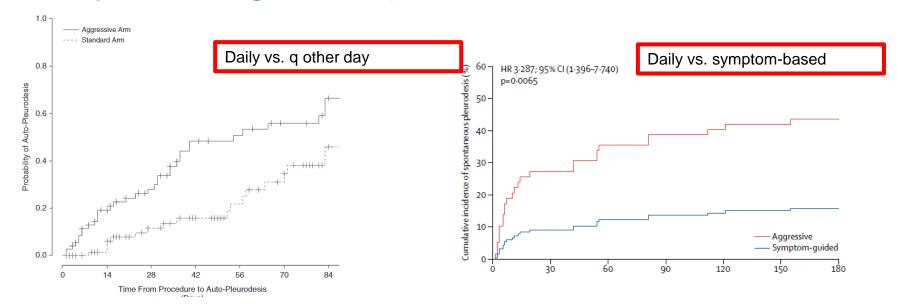




Toronto General Hospital

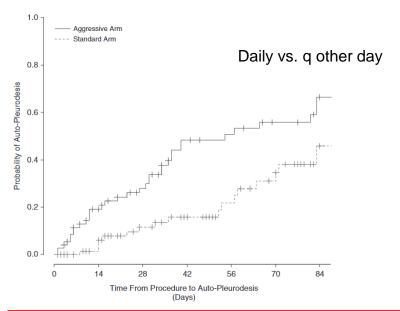


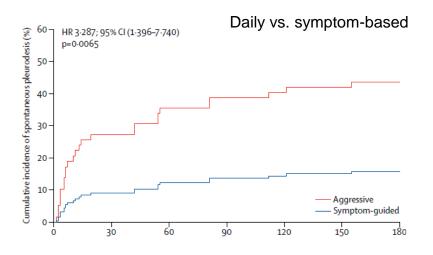
Daily drainage and pleurodesis rate





Daily drainage and pleurodesis rate





Pleurodesis rate: 47% vs. 24% Time to pleurodesis:

54 d 95% CI 34-83

90 d 95% CI 70 – non-estimable

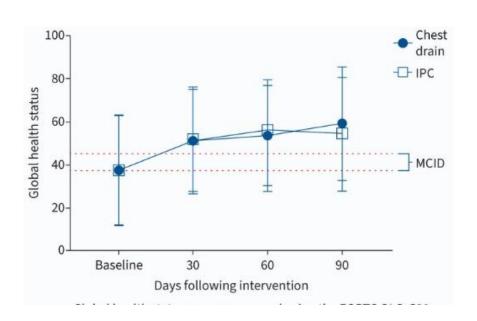
Pleurodesis rate
60d daily - 37% 6mth daily - 44%
prn - 11% prn - 16%

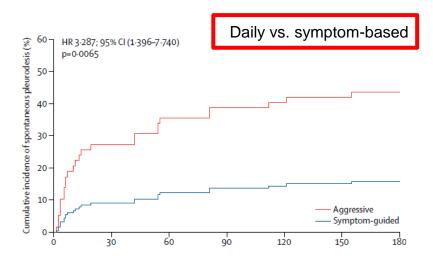


Symptom control

Pleurodesis: Tunneled pleural catheter vs. Chest drain

Global health status Chest drain = TPC





Dyspnea: Daily = prn

Pleurodesis rate 60d daily - 37% prn - 11%

6mth daily - 44% prn - 16%

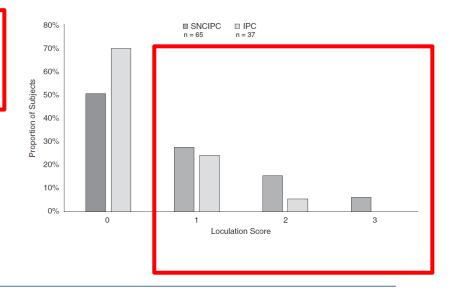


Silver nitrate-coated TPC?

- 20 Centers UK, US
- MPE (predominantly lung and breast cancer)
- Primary outcome : pleurodesis at 30 days
- Followed for 3 mths

	SNTPC (n= 77)	TPC (n= 37)
Pleurodesis by 30 days n (%)	17 (22.1%)	12 (32.4%)
Rate difference 95%CI	- 0.10 (-0.300.09)	

Adverse events	SNTPC N (%)	TPC N (%)		
Effusion	19 (24.7%)	3 (8.1%)		
Loculated effusion	44 (49%)	11 (30%)		
Anemia	11 (14.3%)	4 (10.8%)		
Dyspnea	12 (15.6%)	4 (10.8%)		
Pneumonia	11 (14.3%)	4 (10.8%)		
Empyema	1 (1.3%)	1 (2.7%)		
Total	No difference			





Intrapleural chemotherapy?

Original Article

Intrapleural perfusion thermo-chemotherapy for pleural effusion caused by lung carcinoma under VATS

Runlei Hu¹, Hong Jiang¹, Hu Li¹, Dongshan Wei¹, Guoqing Wang¹, Shenglin Ma² **JTD. 2017**

- 54 patients with NSCLC
- VATS Intrapleural thermo/chemotherapy cisplatin 200mg/m² @ 43°C
- Apoptosis in all specimens
- 1y survival 74.1 % (median 21.7 mth)
- No adverse events

- Effusion control: >1 mth
- Complete response: 52/54
- Partial Response 2/54







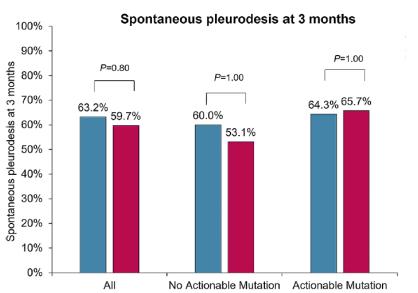


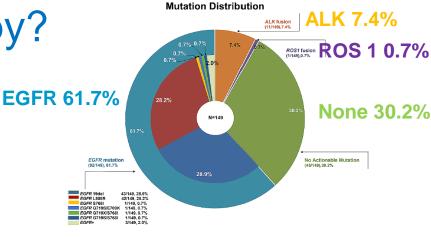


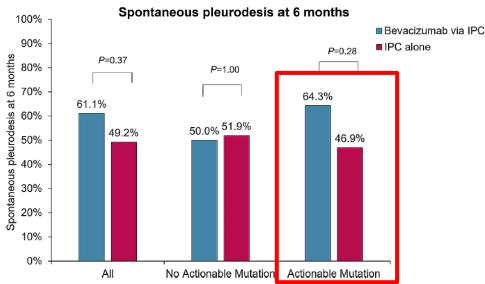
Intrapleural chemotherapy?

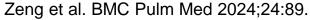
- Bevacizumab + TPC vs. TPC for MPE in NSCLC
- 149 patients, 69% with actionable mutations
- Intervention: TPC vs. TPC + bevacizumab
- No difference in adverse events

Pleurodesis: TPC = TPC+ bevacizumab









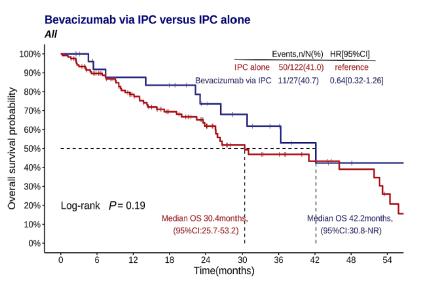


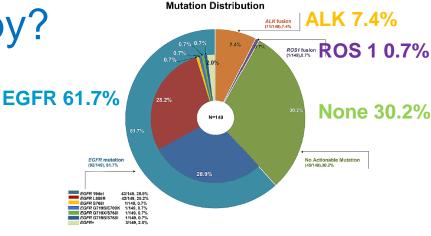


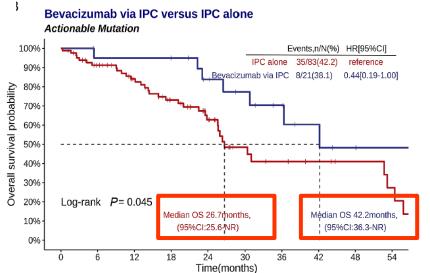
Intrapleural chemotherapy?

- Bevacizumab + TPC vs. TPC for MPE in NSCLC
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- No difference in adverse events

Survival: Bevacizumab + TPC vs. TPC







Zeng et al. BMC Pulm Med 2024;24:89.





MPE studies 2010-2025

IPC-Plus (2018)

Talc + TPC vs. TPC Pleurodesis at 35d and 75d Talc+ IPC > TPC

TIME1 (2015)

Plurodesis failure rate: 12F>24F (30% vs. 24%)

Pain lower with 12F

AMPLE (2017)

TPC vs talc pleurodesis TPC 2 days less in hospital

TIME3 (2018)

12 mth dyspnea and pleurodesis failure Urokinase = placebo

EPIToME (2019)

TPC+talc plurodesis rate 74% @ 20d (46% pts not suitable)

2010

TIME2 (2012)

Dyspnea @ 6 wk TPC=Chest tube LOS TPC<CT

ABAP (2017)

Daily better than 1 other day Pleurodesis rate:

47% vs. 24% Time to Pleurodesis: 54d vs. 90d

AMPLE-2 (2018)

Dyspnea: Daily = symptom-based drainage Pleurodesis: daily (37% @ 2mth, 44% @ 6 mth) > (11% @

2mth, 16% @ 6 mth)

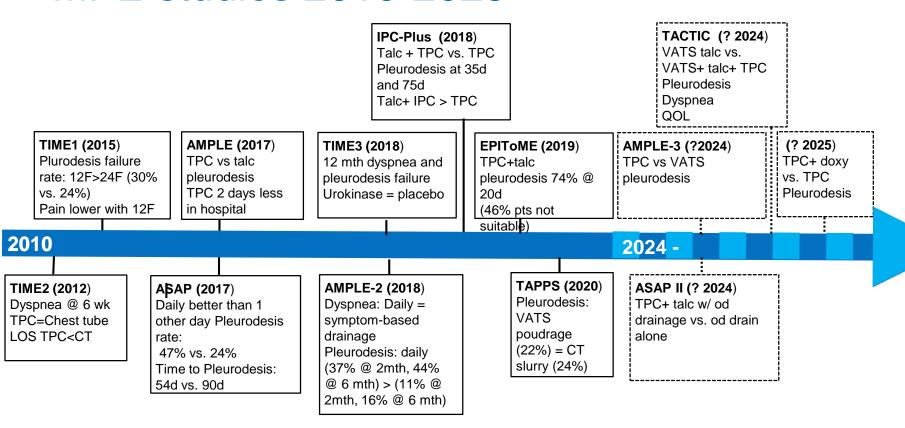
TAPPS (2020)

Pleurodesis: VATS poudrage (22%) = CT slurry (24%)



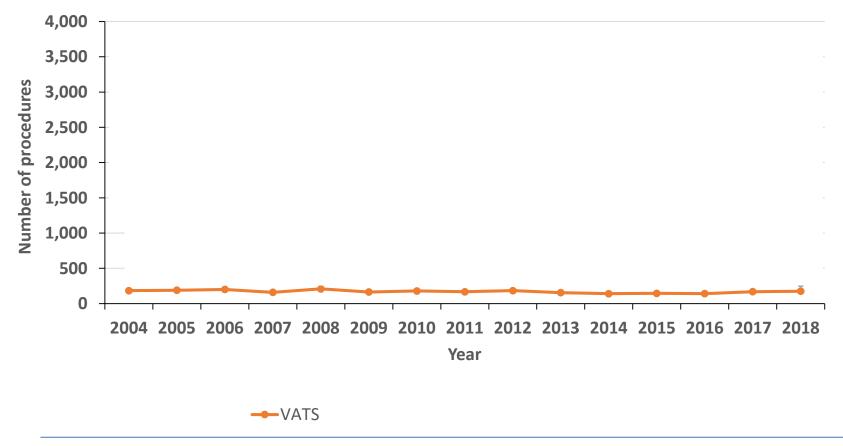


MPE studies 2010-2025

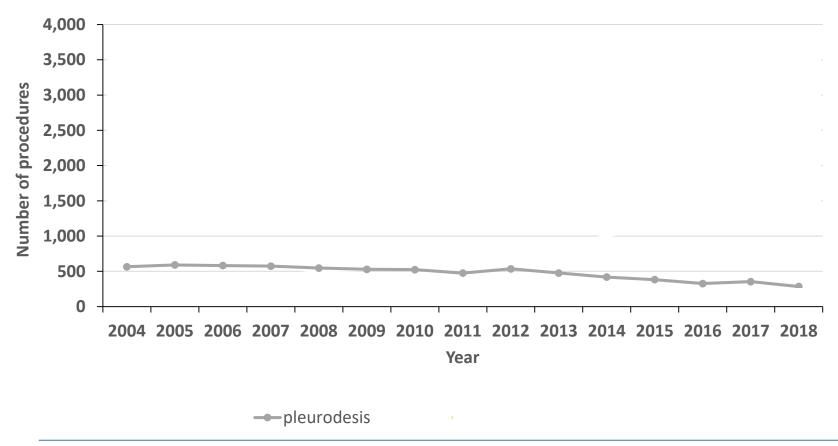






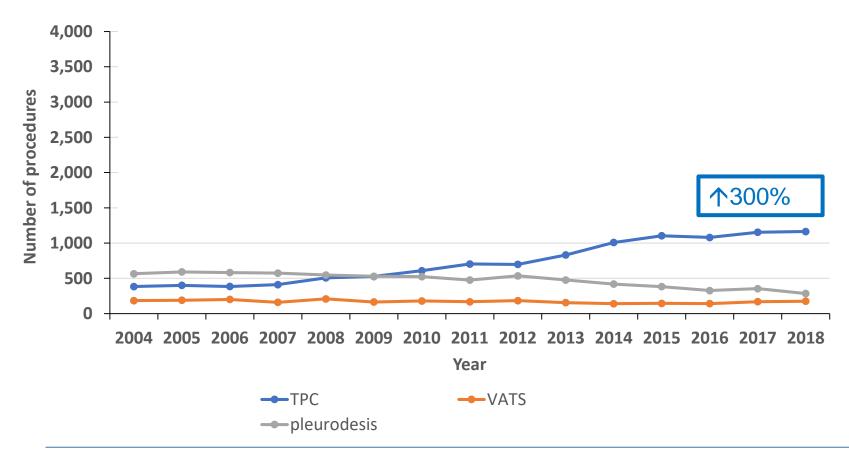






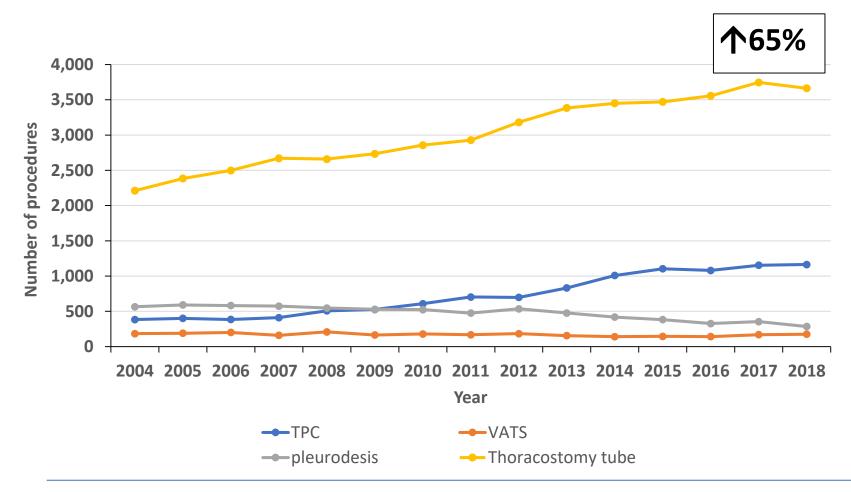
















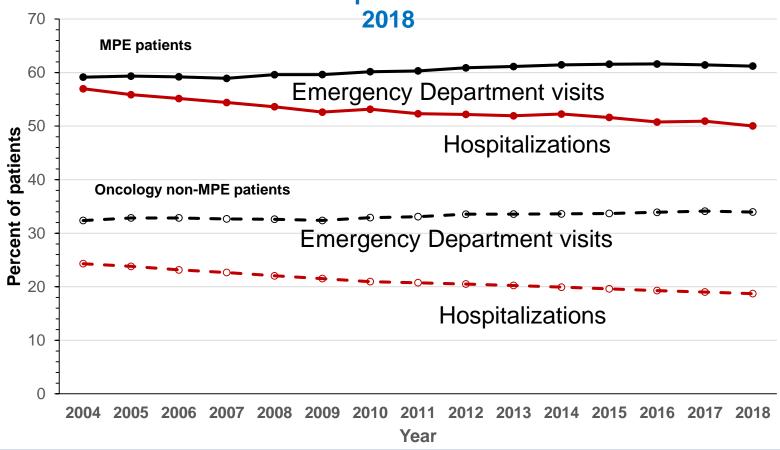
Inpatient days/procedures in MPE patients

Pleural procedure used for MPE recurrence	No (%)	Total inpatient days Median (IQR)	Additional pleural procedures
Thoracentesis	10,019 (77)	31 (15-67)	17
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Chest tube pleurodesis	1,779 (14)	34 (18-68)	1

Ost et al. CHEST. 2018;153(2):438-52.



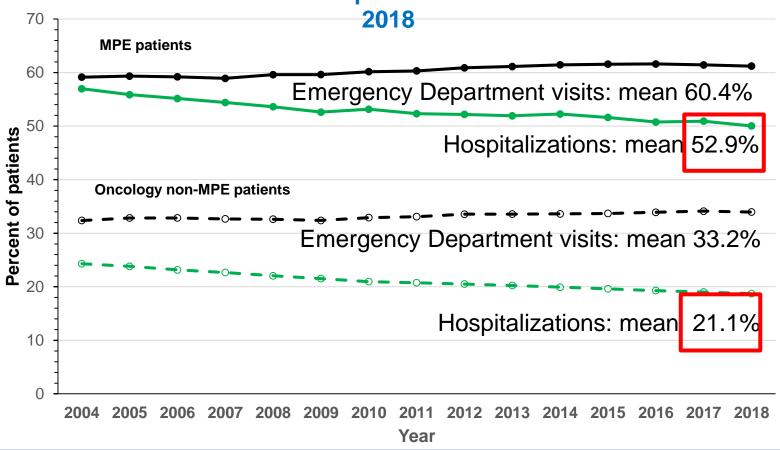
Percent of MPE and non-MPE oncology patients in Ontario who had ≥ 1 hospitalization or ED visit in 2004-







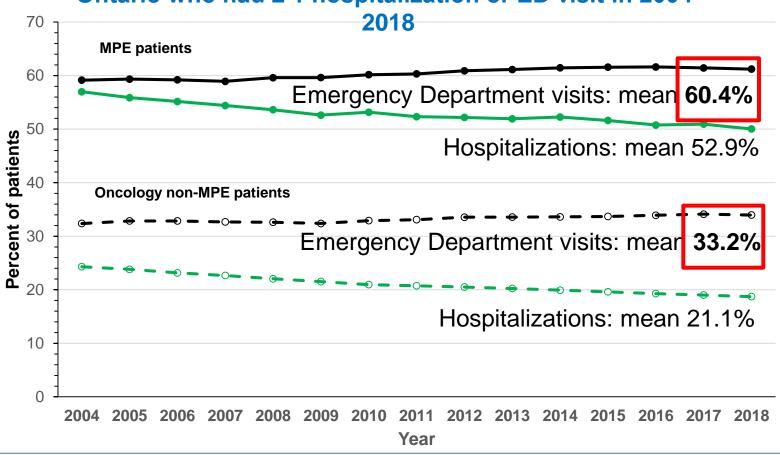
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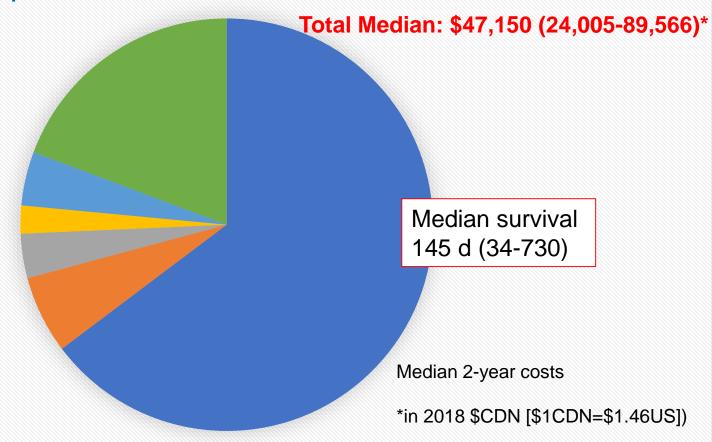


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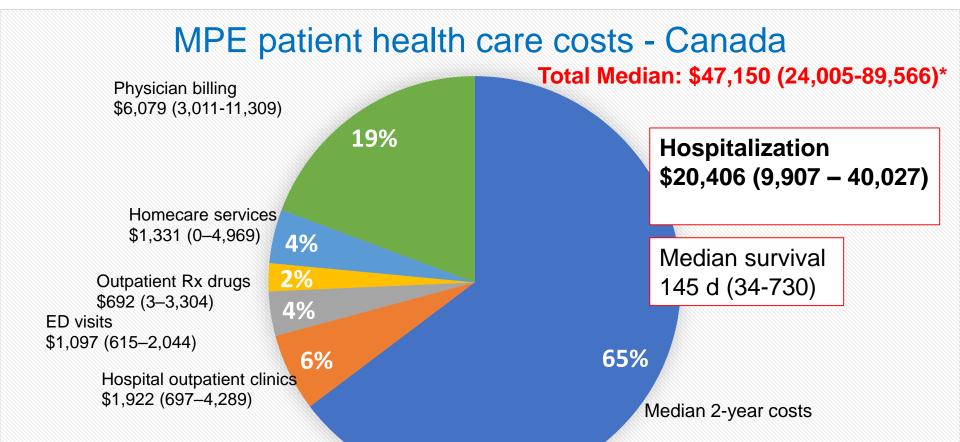


MPE patient health care costs - Canada











*in 2018 \$CDN [\$1CDN=\$1.46US])



Management of MPE?







Patients managed with TPC need ongoing outpatient support

- TPC complications
 - Blockage ~ 10%
 - 3-5% bleeding post TPA
 - Infection 1.9-25%
 - (empyema) 1-8%
 - Cellulitis 0.4-4%
 - Pneumothorax up to 4%
 - Tract metastasis < 1%
- Catheter removal/trouble-shooting
 - Malfunction ~ 8-10%
 - 45% pleurodesis rate

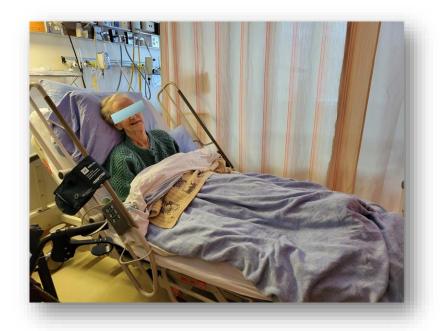




Talc pleurodesis?

	Pleurodesis
Symptom improvement	Yes
Pleurodesis success rate	60-90% (? 50% TPC)
Drainage duration	days
Complications	< 1%
Ambulatory	No/(Yes? TPC)
Need for outpatient care	No/(Yes? TPC)
Need for further interventions	Likely

MPE hospitalization: Avg LOS 5.5 - 16 days



Czarnecka-Kujawa et al. ACCP. 2023.
Alwakeel et al. JOBIP. 2023.
Taghizadeh et al. 2017. CHEST..

Toronto General Hospital
University Health Network
Ost et al 2018. CHEST.



Pleurodesis? Tunnelled catheter? Or?...



- Disease progression
 - Parenchymal
 - airway obstruction
 - Lymphangitic carcinomatosis
- Treatment complications
 - Pneumonitis
 - Fibrosis
- Other
 - Pneumonia
 - Venous thromboembolism
 - AECOPD/asthma/ILD
 - Tamponade
 - Ascites
 - Anemia
 - Arrhythmia

MPE hospitalization: Avg LOS 5.5 - 16 days



Czarnecka-Kujawa et al. ACCP. 2023.
Alwakeel et al. JOBIP. 2023.
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Toronto General Hospîtal
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Ost et al 2018. CHEST.



- Comprehensive assessment of the patient
 - Multidisciplinary pleural effusion management program





- Comprehensive assessment of the patient
 - Multidisciplinary pleural effusion management program



	Pre-program, n = 69 (%)	Post-program, n = 75 (%)	р
Hospitalizations (n)	33 (48)	18 (24)	0.003



- Comprehensive assessment of the patient
 - Multidisciplinary pleural effusion management program



Outcome	Pre-program, n = 69 (%)	Post-program, n = 75 (%)	р
Hospitalizations (n)	33 (48)	18 (24)	0.003
Patients with chest drain and no pleurodesis (n)	23 (46)	10 (13)	<0.001



- Comprehensive assessment of the patient
 - Multidisciplinary pleural effusion management program



Outcome	Pre-program, n = 69 (%)	Post-program, n = 75 (%)	p	
Hospitalizations (n)	33 (48)	18 (24)	0.003	
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Days with chest tube n, $\overline{X} \pm SD$	1.6 ± 4.1	0.7± 2.5	0.007	



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Days with chest tube n, $\overline{X} \pm SD$	1.6 ± 4.1	0.7± 2.5	0.007
Initial presentation in ED	30 (44)	29 39)	0.56
ED visits n, $\overline{X} \pm SD$	0.7 ± 0.7	0.6 ± 0.7	0.41



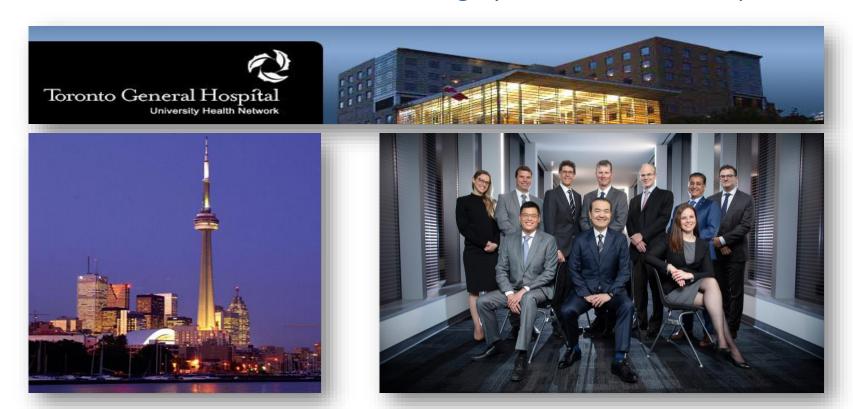
Summary

- Incidence and prevalence of malignant pleural effusion are rising.
- Malignant pleural effusion is associated with high health care utilization and cost.
- MPE management with TPC and talc result in equivalent QOL.
- Compared to talc pleurodesis via a chest tube, pleurodesis via TPC has lower pleurodesis rate.
- Intrapleural chemotherapy may be useful in MPE/NSCLC management.
- Multidisciplinary care of MPE patients may reduce MPE health care utilization and cost.





Division of Thoracic Surgery, Toronto General Hospital



Thank you













Kasia Czarnecka-Kujawa
Division of Thoracic Surgery
Division of Respirology
Toronto General Hospital
University Health Network

Thank you







Advantages and disadvantages of most common MPE management options

	TPC
Symptom improvement	Yes
Pleurodesis success rate	Up to 45%
Drainage duration	4 weeks - > 4y
Complications	5-25%
Ambulatory	Yes
Need for outpatient care	Yes
Need for further interventions	Less likely





Factors to consider while offering definitive management of MPE

Patient factors/wishes

- 86F with MPE and expandable lung, on chemo
 - Slow re-accumulation
 - Mild cognitive impairment
 - Wheelchair bound
 - Delirium with narcotics

Option offered: TPC

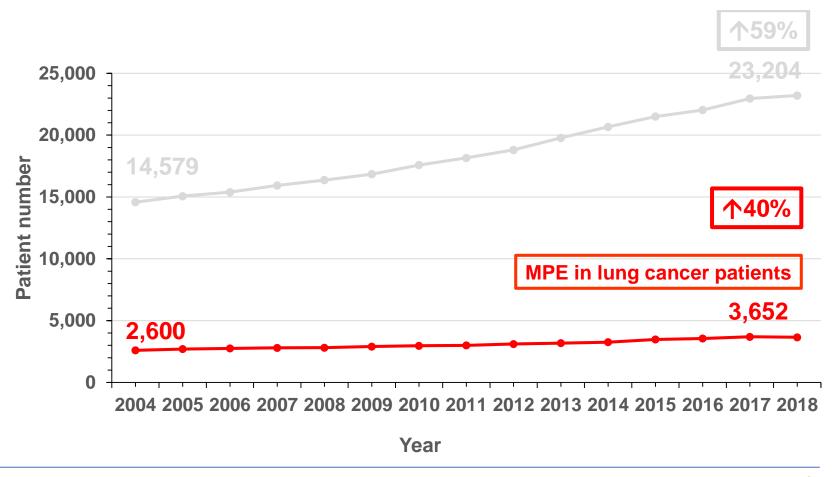
- 55F MPE, trapped lung
 - Large MPE
 - Weekly thoracentesis
 - Improvement of dyspnea with drainage
 - Issue: not comfortable with TPC AND with CCAC visits at home

 Option offered: continue with thoracentesis until ready to commit



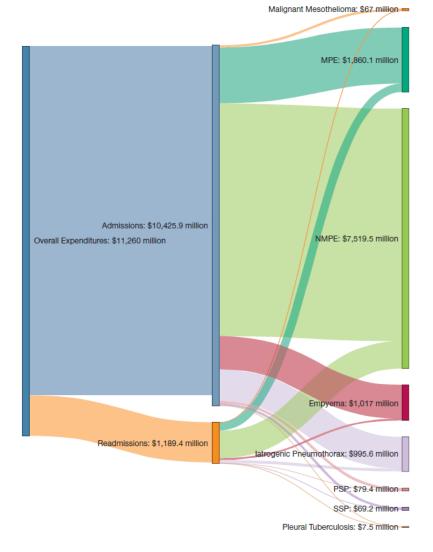


Prevalence of Malignant Pleural Effusion in Ontario 2004-2018













MPE vs. para-malignant effusion

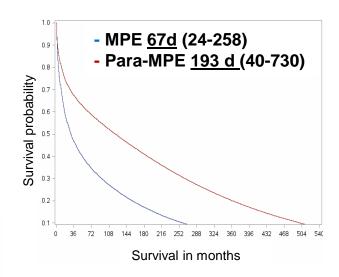
• MPE

 Effusion directly related to malignancy

· Para-malignant effusion

- Tumor effect on pleural space
 - Bronchial obstruction
 - VTE
 - SCV syndrome
 - Post-radiation (trapped lung, lymphatic injury)







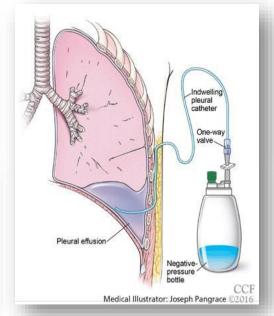


Definitive MPE management













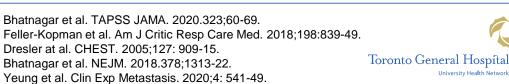
Tunneled pleural catheter

Pleurodesis

Xia et al.PLoS ONE, 2014

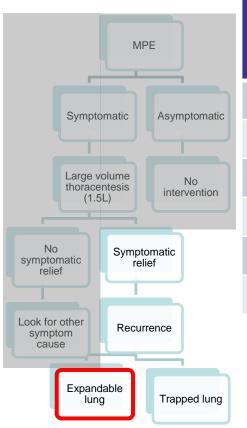
- Talc > other agents
- Slurry = poudrage
- VATS = chest tube

Pleurodesis via Tunneled pleural catheter





MPE management



MPE management options	Expandable lung
Thoracentesis	✓
TPC	\checkmark
Pleurodesis	✓
VATS	✓
Chest tube	✓
TPC	✓

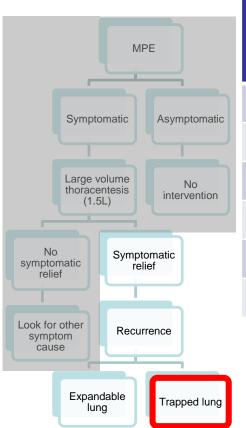




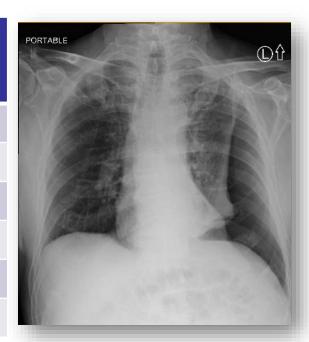
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MPE management



Trapped lung
✓
\checkmark

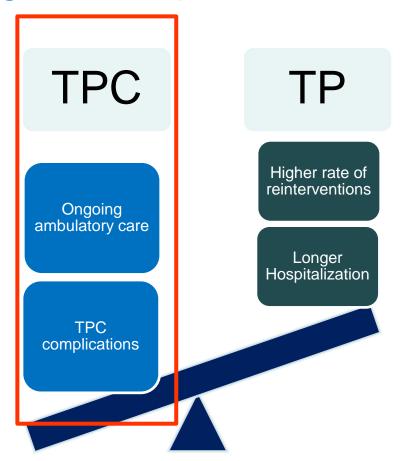


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Choosing MPE management option

? Patients with survival < 6 mths



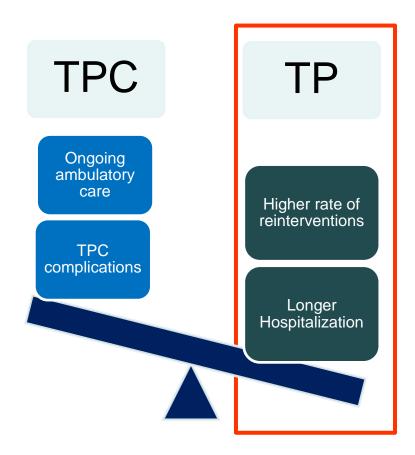




Choosing MPE management option

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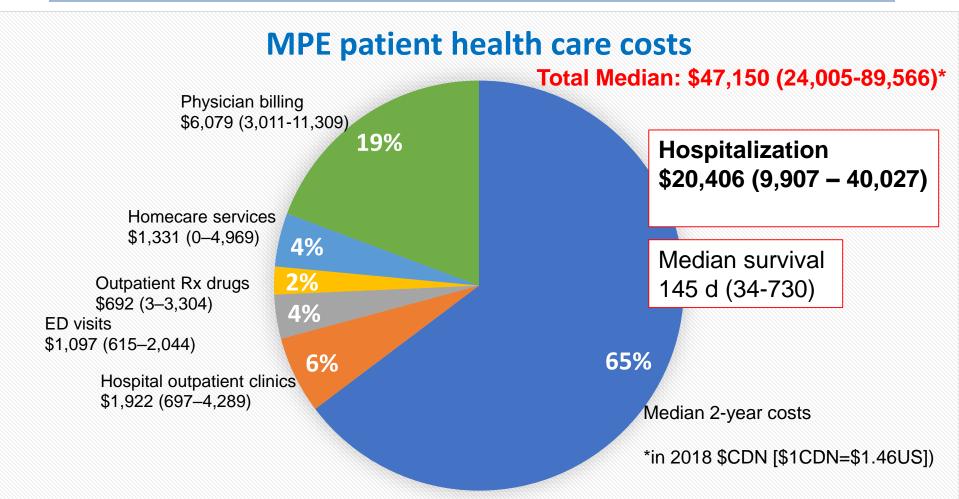
















Inpatient days/procedures in MPE population

Pleural procedure used for MPE recurrence	No (%)	Total inpatient days Median (IQR)	Additional pleural procedures
Thoracentesis	10,019 (77)	31 (15-67)	17*
TPC	496 (4)	23 (12-52)	<1
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Factors to consider while offering definitive

management of MPE

- Comprehensive assessment of patient symptoms
- Patient factors/wishes/expected survival
- Local resources
- 86F with MPE and expandable lung, on chemo
 - Slow re-accumulation
 - Mild cognitive impairment
 - Wheelchair bound
 - Delirium with narcotics

Option offered: TPC









- MPE management by a dedicated program:
- ↓ hospitalization

RACE (Rapid Assessment of Complex Pleural Effusions) Program Toronto General Hospital





Ambulatory MPE management outcomes

	Number	Perce	ent with Outco	ome ——	% Combined
Outcome	of Studies	Combined Results	Single Study Minimum	Single Study Maximum	% Combined participants with outcome
Bleeding	6	0.4 (4/903)	0 (0/295)	0,9 (1/109)	
Infection, unspecified	3	2.0 (7/346)	1.7 (5/295)	5.9 (1/17)	
Cellulitis	10	3.4 (32/935)	1,3 (1/77)	25 (3/12)	
Empyema	13	2.8 (33/1168)	0 (0/12)	16,7 (2/12)	
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					0 20 40 60 80

Meter et al. J Gen Int Med. 2011; 1: 70-6.



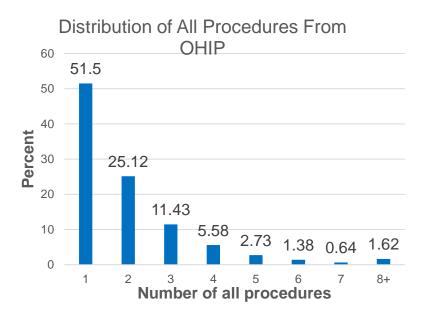


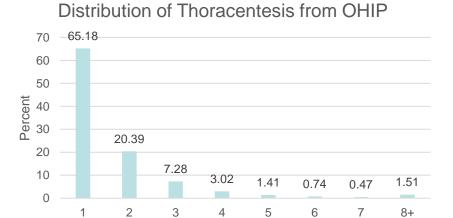
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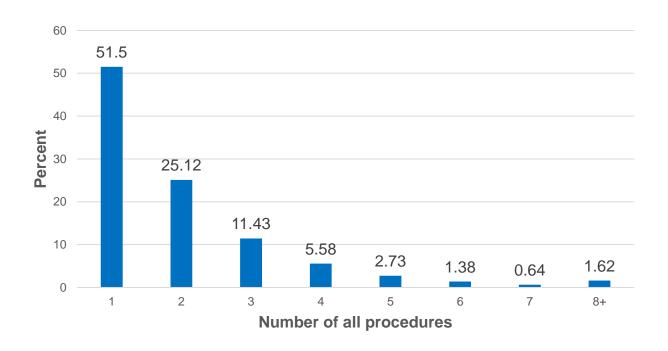


Number of Thoracentesis





Procedures in Ontario MPE patients 2004-2018





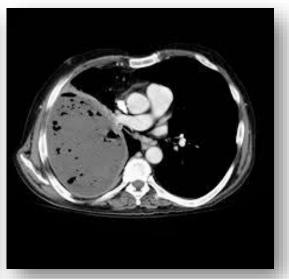


Patients managed with TPC need ongoing outpatient support

Tract metastasis



Empyema: time to empyema 158 days*







The OPTIMUM trial Outpatient IPC management for malignant pleural effusion was not superior to inpatient chest drain and talc pleurodesis in improving quality of life after 30 days Participants: 142 patients with malignant pleural effusion Intervention: Outpatient IPC ± talc pleurodesis Control: Inpatient chest drain + talc pleurodesis Primary outcome: Global health status at 30 days post-intervention (EORTC QLQ-C30)

Chest drain: 30/56 patients

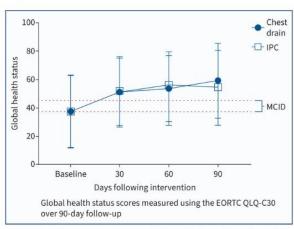
had a significant (>8 points)

improvement in global

health status at 30 days



Results: Primary outcome data were available in 58 IPC and 56 chest drain participants



Day 30 mean intergroup difference in baseline-adjusted global health status of 2.06 (95% CI -5.86-9.99); p=0.61



IPC: 33/58 patients had

a significant (>8 points)

improvement in global

health status at 30 days

Take home: Management choice should be based on patient preferences, acceptability of risk, social circumstances and treatment accessibility





TPC vs Talc in MPE management

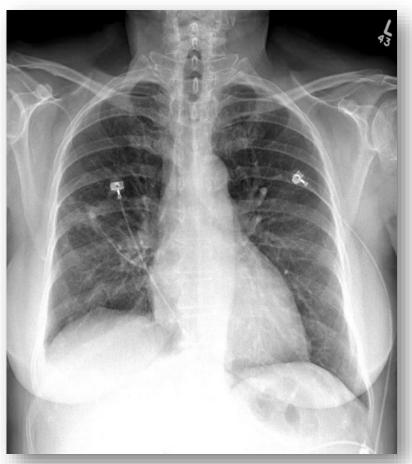
Study	ι	.os	Hospital admissions (effusion related)		Additi proced		Adverse	events
	TPC	TP	TPC	TP	TPC	TP	TPC	TP
TIME2 Davies 2012	0 IQR 0-1	4 IQR 2-6			6%	22%	40%	13%
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Boshuiz en 2017	0	5	1	1.5	15%	35%	19%	16%



Malignant pleural effusion

- 10-12% of Ontario Cancer patients
- Median length of stay 10 (5-18)
- Hospital readmission rate:
 - 25.6% (95% CI 25.0%- 26.3)
- Readmission mortality rate:
 - 17.3% (95% CI 16.6% 18.1%)









TPC vs Talc in MPE management

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MPE at UHN

- ~ 250 admissions with MPE as primary admission diagnosis
- Annually ~400-570 admissions
 - Effusion as secondary admission diagnosis
- 16.8% mortality
- LOS: 16.5 days
- Cost/admission: \$30,743

>\$ 7,685,750 /year





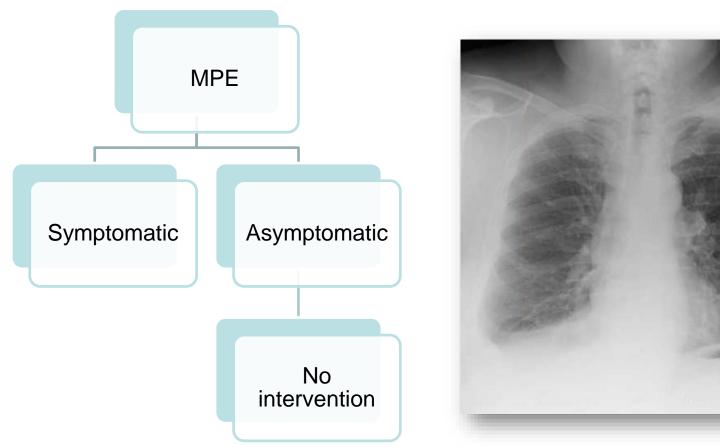


MPE - management goals

- Improve patient's quality of life
 - Improve pleural effusion-related symptoms
 - Reduce number of pleural based procedures
 - Reduce number of days spent in hospital
- Reduce health care costs



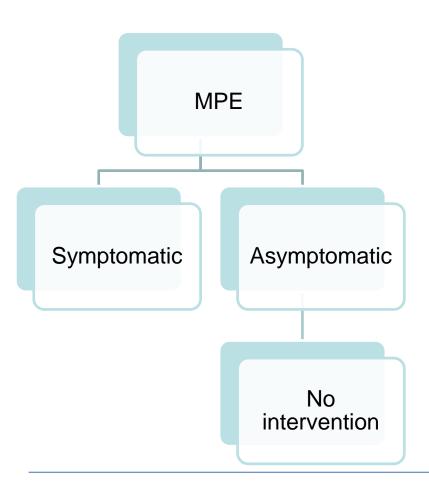










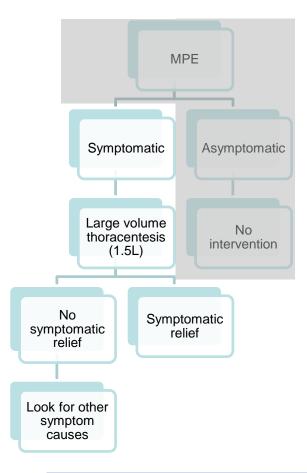


- no drainage unless:
 - confirmation of diagnosis needed
 - suspicion of infection
 - ? chylothorax
 - Organ dysfunction



Toronto General Hospital





- Disease progression
 - Parenchymal
 - airway obstruction
 - Lymphangitic carcinomatosis
- Treatment complications
 - Pneumonitis
 - Fibrosis
- Other
 - Pneumonia
 - Venous thromboembolism
 - AECOPD/asthma/ILD
 - Pericardial effusion
 - Ascites
 - Anemia

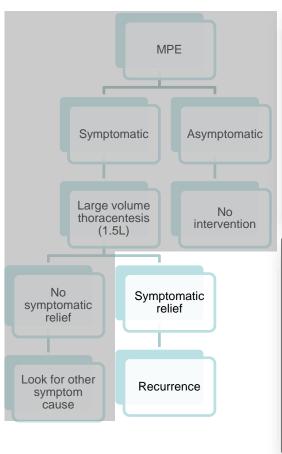




Am J Respir Crit Care Med. 2018;(198):839-849.







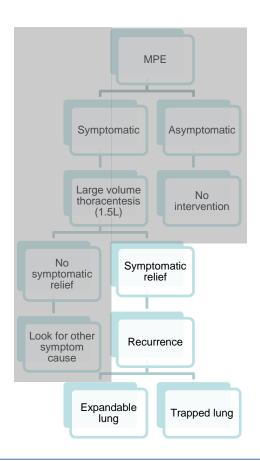




- > 50% effusions recur
- 58% recur rapidly (within 1 month)
- Plans for management at time of first drainage

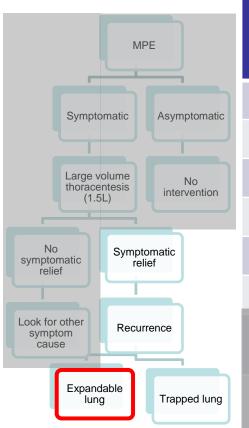
Am J Respir Crit Care Med. 2018;(198):839–849.
Ost et al. CHEST. 2018;153(2):438-52.
Toronto General Hospital





University Health Network





MPE management options	Expandable lung
Thoracentesis	✓
TPC	✓
Pleurodesis	✓
VATS	✓
Chest tube	✓
TPC	✓
Pleuroperitoneal shunt	✓
Decortication/pleu rectomy	√

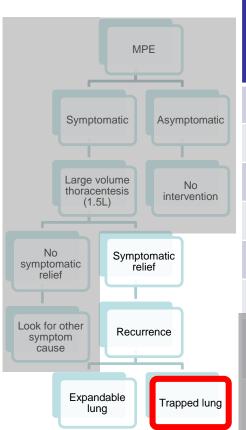




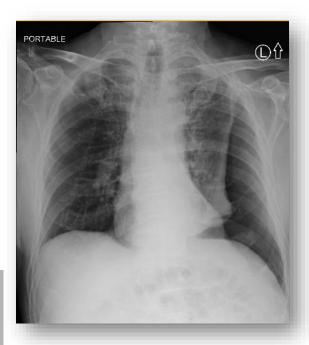
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MPE management options	Trapped lung
Thoracentesis	✓
TPC	✓
Pleurodesis	
VATS	
Chest tube	
TPC	
Pleuroperitoneal shunt	✓
Decortication/pleu	✓



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Advantages and disadvantages of most common MPE management options

	TPC	Pleurodesis
Symptom improvement	Yes	Yes
Pleurodesis success rate	Up to 40%	60-90%
Drainage duration	4 weeks - > 4 y	days
Infection risk	5-10%	< 1%
Ambulatory	Yes	No
Need for outpatient care	YES	NO





Factors to consider while offering definitive management of MPE

Patient factors/wishes

- 86F with MPE and expandable lung, on chemo
 - Slow re-accumulation
 - Mild cognitive impairment
 - Wheelchair bound
 - Delirium with narcotics

Option offered: TPC

- 55F MPE, trapped lung
 - Large MPE
 - Weekly thoracentesis
 - Improvement of dyspnea with drainage
 - Issue: not comfortable with TPC AND with CCAC visits at home

 Option offered: continue with thoracentesis until ready to commit





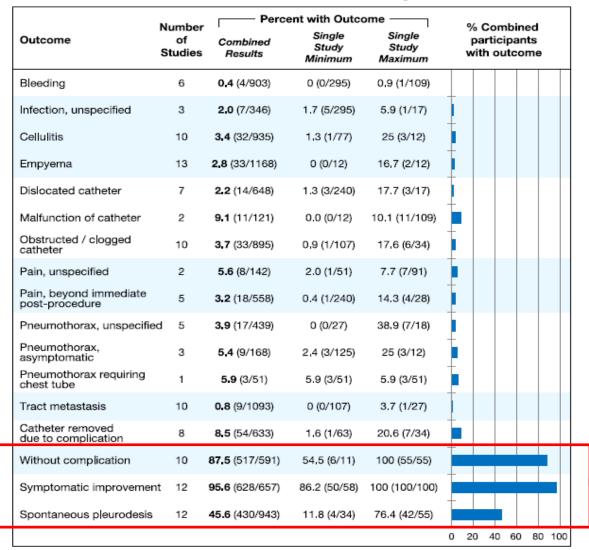
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- Ongoing patient/family/oncology support
 - Catheter-related questions
 - Catheter-related complications
 - Is it time to remove the catheter?





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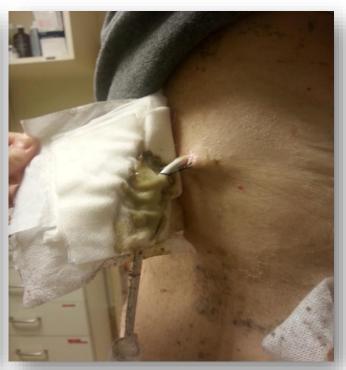




Patients managed with TPC need ongoing outpatient support











Patients managed with TPC need ongoing outpatient support

Tract metastasis



Empyema









Is ongoing support needed for patients managed with TPC?

- Ongoing patient/family/oncology support
 - Catheter-related questions
 - Catheter-related complications
 - Is it time to remove the catheter?
- Ongoing community nursing support
 - Diminishing comfort level of the nursing staff in managing indwelling devices
- Longer survival of patients with MPE (?more time at risk for complications/catheter-related issues)





Rapid Assessment of Complex Pleural Effusion (RACE) program

- RACE Program introduced in 2012
- · Goal:
 - Prompt access to definitive management of MPE for the UHN patients
 - Improving QOL for patients with MPE
 - Reducing ER/ hospital/ambulatory visits related to MPE
 - Reducing health care costs related to MPE care
 - Clinical research for continued quality improvement in MPE care





- The RACE program is a part of the Department of Thoracic Surgery
- We offer:
 - Prompt assessment of UHN MPE patients interested in definitive MPE management
 - Patent centered definitive MPE management
 - Long-term follow-up of MPE patients managed with TPC
 - Shift inpatient management of MPEs to an ambulatory setting













Services RACE at present does not provide:

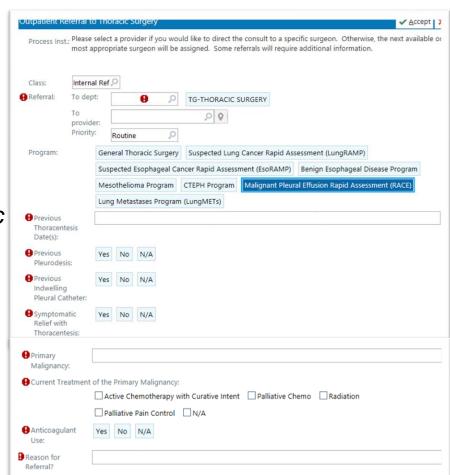
- Ongoing management of Non-Malignant Pleural Effusions
- Ongoing therapeutic thoracentesis for MPE patients not pursuing definitive management
- Support for indwelling devices inserted outside of the RACE program
- Replace services of ER/Urgent care for patients in acute distress





Out-Patient RACE Referrals via EPIC

- Go to "Add Orders"
- Type "Outpatient Referral to Thoracic Surgery" or "REF13"
- Select "RACE program" as subcategory
- Fill out requested patient information

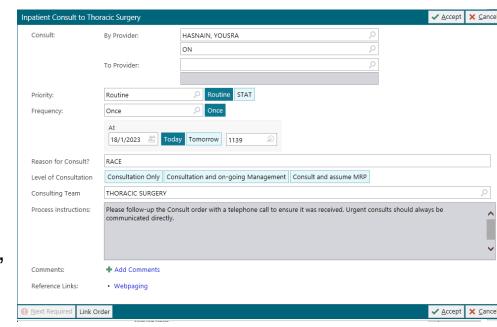






In-Patient RACE Referrals via EPIC

- Go to "Inpatient Orders"
- Type "Inpatient Consult to Thoracic Surgery" or type "CON73"
- In the free text for reason for referral, type in "RACE consultation"













RACE Team
Division of Thoracic Surgery
Division of Respirology
Toronto General Hospital
University Health Network

Thank you

