



### National Clinical Guideline

### Diagnosis, staging and Treatment of Gestational Trophoblastic Disease

### Literature Search Strategies

# Diagnosis

Clinical Question	Clinical Question							
Should all women unde trophoblastic disease?		iedical n	nanagement of misc	arriage have histopath	ology of products of conception to	o exclude		
PICO								
Population/Problem	Women	undergo	oing medical manag	ement of miscarriage				
Intervention/Indicat or	Histopat	listopathology of products of conception						
Comparator/Control	-							
Outcome	To ident	ify partic	al or complete molar	pregnancy				
Is the question specific	to any of	the cate	egories below?					
GENDER		GE GROI		DATE OF PUBLICATIO	Ν			
Male Female ✓	Infant (0 – 23 months) Child (2 – 12 years) Adolescent (13 – 18 years) Adult (19 – 65 years) Aged (> 65 years)			Current year only 0 – 5 years > 5 years ✓				
Question Type								
Therapy/Intervention					Prognosis/Prediction			
Frequency/Rate	Phen	omena	Ot	her:				
Search Strategy								
Primary Database(s) Searched		MEDLIN	NE					
Search Strategy		#	Query		Limiters/Expanders	Results		
		\$15	S9 OR \$13		Limiters - Date of Publication from: 20000101-20131231	55		
		S14	S9 OR \$13			121		
		\$13	S11 OR S12			57		
		\$12	\$7 AND \$10			44		
		\$11	\$5 AND \$10			57		
		\$10	TI "product* of con "product* of conce			718		
		S9	S6 OR S8			74		
		S8	S2 AND S7			65		
		S7	(MH "Hydatidiform	Mole+")		4,471		
		S6	S2 AND S5			74		
		S5	\$3 OR \$4			11,496		
		S4	(MH "Trophoblastic	Neoplasms+")		11,496		

	\$3	(MH "Gestational Trophoblastic Disease+")		10,193
	\$2	(MH "Abortion, Habitual+/PA") OR (MH "Abortion, Spontaneous+/PA") OR (MH "Abortion, Incomplete/PA") OR (MH "Abortion, Missed/PA")		1,166
	S1	TI "product* of conception" OR AB "product* of conception"		718
Other/Secondary Resources Searched	UpTo	Date; Cochrane; RCOG; MD Consult; Trip Datab	pase	
Search Strategy: Other Resources				
Comments				
Date				

Clinical Question								
For women with suspect molar pregnancy?	cted mola	ar pregn	ancy, what diagnostic t	ests should be done to accurately diagnose partial of	or complete			
PICO								
Population/Problem	Women	with sus	spected molar pregnan	су				
Intervention/Indicat or	Diagnos	Diagnostic tests						
Comparator/Control	-							
Outcome	Accurat	tely diag	gnose partial/complete	molar pregnancy - sensitivity and specificity				
Is the question specific GENDER Male Female ✓	to any of the categories below? AGE GROUP DATE OF PUBLICATION Infant (0 – 23 months) Child (2 – 12 years) Current year only Adolescent (13 – 18 years) 0 – 5 years Adult (19 – 65 years) > 5 years ✓ Aged (> 65 years)							
Question Type Therapy/Intervention Frequency/Rate Search Strategy	Aetio			nosis ✓ Prognosis/Prediction er:				
Primary Database(s) Searched		Medlir	ne					
Search Strategy		#	Query	Limiters/Expanders	Results			
		\$3	(MM "Gestational Trophoblastic Disease+/DI")	Limiters - Date of Publication from: 20070101- 20131231; Clinical Queries: Diagnosis - High Sensitivity	181			
		S2	(MM "Gestational Trophoblastic Disease+/DI")	Limiters - Date of Publication from: 20070101- 20131231	181			
		S1	(MM "Gestational Trophoblastic Disease+/DI")		1,053			
Other/Secondary Reso Searched	urces	Cochr	ane (Incl Medline); TRIP	database; UpToDate;Ebsco Discovery federated sec	arch			
Search Strategy: Other Resources								
Comments								
Date								

Clinical Question						
For women where there frame should the pathc	; is suspicion o logy report (r	of partial or complete molar pregnancy who post-evacuation) be available to the clinicia	have an evacuation performed, in n?	ו what time		
PICO						
Population/Problem	Women Wit	h Suspected Partial Or Complete Molar Preg	gnancy			
Intervention/Indicator	Histopathol	ogical review				
Comparator/Control	-					
Outcome	Time to rep	ort to clinicians				
Is the question specific t GENDER	o any of the o		JBLICATION			
Male Female √		AGE GROUP DATE OF PUBLICATION Infant (0 – 23 months) Child (2 – 12 years) Adolescent (13 – 18 years) Adult (19 – 65 years) Aged (> 65 years) AGE GROUP DATE OF PUBLICATION Current year only 0 – 5 years > 5 years ✓				
Question Type			Prognosis (Prodiction			
Therapy/Intervention Frequency/Rate		etiology/Risk Factors Diagnosis ✓ Diagnosis ✓ Diagnosis ✓	Prognosis/Prediction			
Search Strategy						
Primary Database(s) Searched	Medlin	e				
Search Strategy	#	Query	Limiters/Expanders	Results		
	S19	\$15 AND \$18		1		
	\$18	(MH "Delayed Diagnosis")	Limiters - Date of Publication from: 20020101-20121231	1,539		
	S17	\$10 AND \$15	Limiters - Date of Publication from: 20020101-20121231	13		
	S16	\$10 AND \$15		91		
	S15	(MM "Hydatidiform Mole+")		3,353		
	S14	TI Routine pre-evacuation ultrasound diagnosis of		1		
	\$13	\$10 AND \$12		22		
	S12	(MM "Hydatidiform Mole+/DI/PA")		907		
	S11	\$4 AND \$10		3		
	S10	(MH "Time Factors")		954,789		
	S9	"time to treatment" AND (mole OR molar) AND *pathol*		0		
	S8	S4 AND S7		0		
	S7	"time to treatment"		2,099		

	S6	\$4 AND \$5		15
	\$5	TX hour* OR day* OR week* OR time*	Limiters - Clinical Queries: Diagnosis - High Sensitivity	592,857
	S4	S1 OR S2	Limiters - Date of Publication from: 20020101-20131231	349
	\$3	\$1 OR \$2		1,156
	S2	(MM "Gestational Trophoblastic Disease+/PA")		1,156
	S1	(MM "Hydatidiform Mole+/PA")		349
Other/Secondary Resources Searched	Uptoc	date; Cochrane; Rcog; Md Consult; Trip Datab	Dase	
Search Strategy: Other Resources				
Comments				
Date				

Clinical Question						
imum outcome?	tional	trophol	blastic disease should mo	anagement be centralised to c	a specialised centre(s) to	o ensure
PICO						
Population/Problem	Wom	ıen witł	h confirmed GTD			
Intervention/Indicat	Regis	stration	and central advice			
Comparator/Contr	-					
Outcome	- - -	early c improv protoc	outcomes appropriate managemer ved overall survival col-driven systemic therap			
Is the question specific						
GENDER		GE GR	200P ) – 23 months)	DATE OF PUBLICATION	ON	
Male Female √	C A A	Child (2 dolesc dult (19	- 12 years) cent (13 – 18 years) 9 – 65 years) > 65 years)	Current year only 0 – 5 years > 5 years ✓		
Question Type						
Therapy/Intervention	Aet	iology/	/Risk Factors	Diagnosis 🗸	Prognosis/Prediction	
Frequency/Rate	Phe	enomer	na	Other:		
Search Strategy Primary Database(s) S searched		Medlir	ne			
Search Strategy	Г	#				
4		#	Query		Limiters/Expanders	Results
		# \$14	S1 AND S13		Limiters/Expanders	Results147
				:are+")	Limiters/Expanders	
		S14	\$1 AND \$13	Care+")	Limiters/Expanders	147
		S14 S13	S1 AND S13 (MH "Quality of Health C		Limiters/Expanders	4,505,550
		<ul><li>S14</li><li>S13</li><li>S12</li></ul>	S1 AND S13 (MH "Quality of Health C S1 AND S11		Limiters/Expanders	147 4,505,550 0
		<ul><li>\$14</li><li>\$13</li><li>\$12</li><li>\$11</li></ul>	S1 AND S13 (MH "Quality of Health C S1 AND S11 (MH "Oncology Service,	Hospital/OG/ST/TD/EC")	Limiters/Expanders	147 4,505,550 0 523
		<ul><li>\$14</li><li>\$13</li><li>\$12</li><li>\$11</li><li>\$10</li></ul>	S1 AND S13 (MH "Quality of Health C S1 AND S11 (MH "Oncology Service, S1 AND S9	Hospital/OG/ST/TD/EC")	Limiters/Expanders	147       4,505,550       0       523       3
		<ul><li>S14</li><li>S13</li><li>S12</li><li>S11</li><li>S10</li><li>S9</li></ul>	S1 AND S13 (MH "Quality of Health C S1 AND S11 (MH "Oncology Service, S1 AND S9 (MH "Academic Medico	Hospital/OG/ST/TD/EC")	Limiters/Expanders	147         4,505,550         0         523         3         65,856
		S14         S13         S12         S11         S10         S9         S8	S1 AND S13 (MH "Quality of Health C S1 AND S11 (MH "Oncology Service, S1 AND S9 (MH "Academic Medico S3 OR S5 OR S7 S1 AND S6	Hospital/OG/ST/TD/EC") al Centers+") ent (Health Care)+") OR (MH	Limiters/Expanders	147         4,505,550         0         523         3         65,856         49
		S14         S13         S12         S11         S10         S9         S8         S7	S1 AND S13 (MH "Quality of Health C S1 AND S11 (MH "Oncology Service, S1 AND S9 (MH "Academic Medico S3 OR S5 OR S7 S1 AND S6 (MH "Outcome Assessme	Hospital/OG/ST/TD/EC") al Centers+") ent (Health Care)+") OR (MH	Limiters/Expanders  Limite	147         4,505,550         0         523         3         65,856         49         44
		S14         S13         S12         S11         S10         S9         S8         S7         S6	S1 AND S13 (MH "Quality of Health C S1 AND S11 (MH "Oncology Service, S1 AND S9 (MH "Academic Medico S3 OR S5 OR S7 S1 AND S6 (MH "Outcome Assessme come and Process Asses	Hospital/OG/ST/TD/EC") al Centers+") ent (Health Care)+") OR (MH ssment (Health Care)+")	Limiters/Expanders         Imiters/Expanders         Imiters         Imiters         Imiter	147         4,505,550         0         523         3         65,856         49         44         631,762
		S14         S13         S12         S11         S10         S9         S8         S7         S6         S5	S1 AND S13 (MH "Quality of Health C S1 AND S11 (MH "Oncology Service, S1 AND S9 (MH "Academic Medico S3 OR S5 OR S7 S1 AND S6 (MH "Outcome Assessme toone and Process Asses S1 AND S4	Hospital/OG/ST/TD/EC") al Centers+") ent (Health Care)+") OR (MH ssment (Health Care)+")	Limiters/Expanders         Imiters/Expanders         Imiters         Imiters         Imiter	147         4,505,550         0         523         3         65,856         49         44         631,762         3
		S14         S13         S12         S11         S10         S9         S8         S7         S6         S5         S4	S1 AND S13 (MH "Quality of Health C S1 AND S11 (MH "Oncology Service, S1 AND S9 (MH "Academic Medico S3 OR S5 OR S7 S1 AND S6 (MH "Outcome Assessme tcome and Process Asses S1 AND S4 (MH "Referral and Consu	Hospital/OG/ST/TD/EC") al Centers+") ent (Health Care)+") OR (MH ssment (Health Care)+") ultation+")	Limiters/Expanders         Imiters/Expanders         Imiters         Imiters         Imiters         Imiters         Imiters         Imiters	147         4,505,550         0         523         3         65,856         49         44         631,762         3         52,940

	20070101-20121231
Other/Secondary Resources Searched	Cochrane (incl. in Medline); TRIP Database; UpToDate; Ebsco Discovery federated search; NICE; ncer Guideline Resource Centre
Search Strategy: Other resources	
Comments	
Date	

Clinical Question							
				t clinical and human chor up and require no further	rionic gonadotropin monit r therapy or monitoring?	oring protocol	
PICO							
Population/Problem	Worr	nen with p	partial or complete mole	ar pregnancy			
Intervention/Indicat or	Moni	Aonitoring investigation – hCG levels					
Comparator/Control	-						
Outcome	Do n	ot require	e further therapy or mon	itoring			
Is the question specific	to any						
GENDER Male Female ✓		AGE GROUPDATE OF PUBLICATIONInfant (0 – 23 months)Current year onlyChild (2 – 12 years)Current year onlyAdolescent (13 – 18 years)0 – 5 yearsAdult (19 – 65 years)> 5 years ✓Aged (> 65 years)> 5					
Question Type							
Therapy/Intervention				iagnosis ✓ F ther:	Prognosis/Prediction		
Frequency/Rate Search Strategy		henomeno					
Primary Database(s) Searched		Medline	e				
Search Strategy		#	Query		Limiters/Expanders	Results	
		S17	S14 OR S16			47	
l		S16	\$4 AND \$11 AND \$15			7	
I		\$15	(MH "Risk Assessment-	+")		157,209	
		S14	S9 OR S13			45	
		\$13	\$10 AND \$11		Limiters - Date of Publication from: 20020101-20121231	25	
l		\$12	\$10 AND \$11			69	
		S11	(MH "Neoplasm Recu	urrence, Local")		76,002	
		S10	(MM "Hydatidiform M	lole+")		3,337	
		59	S5 OR S7		Limiters - Date of Publication from: 20070101-20121231	22	
		S8	S5 OR S7			85	
		S7	S5 AND S6			2	
		S6	SU monitor*			164,341	
			1		1		

	S4	(MM "Gestational Trophoblastic Disease+")	7,508
	\$3	S1 AND S2	33,214
	S2	( TI mole* OR molar* OR "gestational trophoblastic" ) OR ( AB mole* OR molar* OR "gestational trophoblastic" )	1,292,273
Other/Secondary Resources Searched	Coch	rane (incl. in Medline); TRIP Database; UpToDate; Ebsco Discover	ry federated search
Search Strategy: Other Resources			
Comments			
Date			

# Staging

Clinical Question								
For women with Gesto	ational Tro	phoblastic Neoplasia (GTN), wl	hat investigat	ions should be done to accurately	/ stage GTN?			
PICO								
Population/Problem	Women	with confirmed GTN						
Intervention/Indicat or	(MRI) bro	hest X-ray (CXR), liver ultrasound (US), transvaginal ultrasound (TVU), Magnetic Resonance Imaging ARI) brain (if Lung metastases), Computed Tomography – Thorax, Abdomen and Pelvis (CT-TAP) (if bnormality on chest x-ray or liver ultrasound)						
Comparator/Contr ol								
Outcome		mine extent of disease mine chemotherapy regimen						
Is the question specific	to any of	the categories below?						
GENDER		AGE GROUP	DATE C	DF PUBLICATION				
Male Female ✓		Infant (0 – 23 months) Child (2 – 12 years) Adolescent (13 – 18 year Adult (19 – 65 years) Aged (> 65 years)	Curren s) 0 – 5 ye > 5 yeo					
Question Type								
Therapy/Intervention Frequency/Rate			Diagnosis Other:	Prognosis/Prediction ${f v}$	1			
Search Strategy Primary Database(s) Searched	Medlin	e						
Search Strategy	#	Query		Limiters/Expanders	Results			
	S21	S9 OR \$15 OR \$18 OR \$19		Limiters - Date of Publication: 20130101-20141231	19			
	S20 S19 S18 S17 S16 S15 S14 S13 S12 S11 S10 S9 S8 S7 S6 S5 S4	S9 OR S15 OR S18 OR S19 S8 AND S17 S8 AND S15 S5 AND S16 (TI x-ray OR ultraso* OR tome imaging) OR (AB x-ray OR ultraso* OR tome tomog* OR imaging) S5 AND S14 S10 OR S11 OR S12 OR S13 MH "Ultrasonography" MH "Positron-Emission Tomog MH "Magnetic Resonance In MM "Diagnostic Imaging" S5 AND S8 S6 OR S7 TI staging OR AB staging MM "Neoplasm Staging" S1 OR S2 OR S3 OR S4 TI gestational N2 trophoblastic gestational N2 trophoblastic	Jitraso* OR graphy" naging" ic OR AB		463 28 9 1,235 1,570,758 358 378,089 62,658 31,985 279,517 16,877 114 55,627 53,753 5,456 9,904 2,048			

	Neoplasms+") S2 (Tl (hydatidiform OR invasive) N2 mole ) OR ( AB (hydatidiform OR invasive)	2,616
	N2 mole ) \$1 (MM "Hydatidiform Mole+")	3,441
Other/Secondary Resources Searched		
Search Strategy: Other Resources	Cochrane (incl. in Medline); TRIP Database; UpToDate; MD Consult; Ebsco Discove	ry federated search
Comments		
Date		

Clinical Question							
For women with gestat	tional trophot	plastic neoplasia (GTN), what risk scoring system sho	uld be used to stage GTN?				
PICO							
Population/Problem	Women wit	h confirmed GTN					
Intervention/Indicat or	Staging syst	Staging system					
Comparator/Control	-						
Outcome	Accurate st	aging of GTN					
Is the question specific	to any of the	categories below?					
GENDER		E GROUP DATE OF PUBLICATION	Ν				
Male Female ✓	Chi Ada Ada	int $(0 - 23 \text{ months})$ Current year onlyId $(2 - 12 \text{ years})$ Current year onlyblescent $(13 - 18 \text{ years})$ $0 - 5 \text{ years}$ ult $(19 - 65 \text{ years})$ > 5 years $\checkmark$ ed (> 65 years)> 10 years)					
Question Type Therapy/Intervention			, ,				
merapy/intervermon	Aetiology/	Risk Factors Diagnosis	Prognosis/Prediction $\checkmark$				
Frequency/Rate	Phenomer	na Other:					
<u>Search Strategy</u> Primary Database(s) Searched	Medline	2					
Search Strategy	#	Query	Limiters/Expanders	Results			
	\$15	\$2 AND \$14		1			
	S14	\$1 AND \$13		23			
	\$13	TI "Charing Cross" OR AB "Charing Cross"		214			
	S12	S6 OR S7	Limiters - Date of Publication from: 20070101-20121231	64			
	S11	\$9 AND \$10		22			
	S10	.AB "International Federation of Obstetrics and Gynecology" OR FIGO	Limiters - Date of Publication from: 20070101-20121231	1,659			
	S9	S6 OR S7		158			
	\$8	S6 AND S7		30			
	S7	\$1 AND \$4		136			
	\$6	\$1 AND \$5		52			
	\$5	TI staging* OR AB staging*		48,027			
	S4	(MH "Neoplasm Staging")		110,181			
	\$3	\$1 AND \$2		6			
	S2	(MM "Neoplasm Staging")		5,005			

	S1     (MM "Gestational Trophoblastic Disease+")     7,515
Other/Secondary Resources Searched	Cochrane (incl. in Medline); TRIP Database; UpToDate; MD Consult; Ebsco Discovery federated search
Search Strategy: Other Resources	
Comments	
Date	

# Treatment

Clinical Question					
	al trophoble	astic neoplasia, wh	at are the clinical indicators	to diagnose GTN warranting	)
chemotherapy?					
PICO					
Population/Problem	Women wi	ith GIN			
Intervention/Indicator	Clinical inc	dicators			
Comparator/Control	-				
Outcome	Commenc	cement of chemot	herapy		
Is the question specific to	any of the c	ategories below?			
GENDER	AGE GRC		DATE OF PUBLICATION		
Male		- 23 months)	Current year only		
Female 🗸	Child (2 – Adolesce	ent (13 – 18 years)	0 – 5 years > 5 years ✓		
		(5)			
	Aged (> a	– 65 years) 65 vears)			
_Question Type	<u> </u>	, ,			
Therapy/Intervention $\checkmark$	Aetiology,	Risk Factors	Diagnosis	Prognosis/Prediction	
Frequency/Rate	Phenomer	na	Other:		
Search Strategy					
Primary Database(s) Searched	Medline				
Search Strategy	#	Query		Limiters/Expanders	Results
	\$12	S4 AND S9		Limiters - Date of Publication: 20070101- 20131231; Review Articles	45
	S11	S4 AND S9		Limiters - Date of Publication: 20070101- 20131231	430
	\$10	S4 AND S9			2,556
	L	1		1	

	58	(TI (etoposide or methotrexate or dactinomycin or actinomycin or cyclophosphamide or vincristine or chlorambucil* or doxorubicin or melphalan or hydroxyurea or Hammond or Goldstein or EMA?CO or EMA-CO or CHAMOCA) ) OR ( AB (etoposide or methotrexate or dactinomycin or actinomycin or cyclophosphamide or vincristine or chlorambucil* or doxorubicin or melphalan or hydroxyurea or Hammond or Goldstein or EMA?CO or EMA-CO or CHAMOCA) )	125,975	
	S7	TI chemotherap* OR AB chemotherap*	259,999	
	S6	(MH "Antineoplastic Combined Chemotherapy Protocols")	98,889	
	S5	(MH "Antineoplastic Agents+")	269,597	
	S4	\$1 OR \$2 OR \$3	11,579	
	\$3	(MM "Gestational Trophoblastic Disease+")	7,565	
	\$2	"gestational trophoblastic" N2 (neoplasm* OR tumor* OR tumour*)	520	
Other/Secondary Resources Searched Search Strategy: Other Resources	UpToDe	ate; Cochrane	· · · · · · · · · · · · · · · · · · ·	
Comments				
Date				

Clinical Question						
For patients with low-risk	(FIGO 0- <i>6</i>	6) GTN, what is the optimal first-line chemo	therapy regimen?			
_PICO						
Population/Problem	Wor	Women with GTN				
Intervention/Indicator	- M	emotherapy regimens lethotrexate / Folinic Acid ctinomycin D				
Comparator/Control	-					
Outcome	Rec Met Side Toxi					
Is the question specific to GENDER	o any of th	he categories below? AGE GROUP	DATE OF PUBLICATION	1		
Male Female √		Infant (0 – 23 months) Child (2 – 12 years) Adolescent (13 – 18 years) Adult (19 – 65 years) Aged (> 65 years)	Current year only 0 – 5 years ✓ > 5 years			
Question Type			· - · · · · · · ·			
Therapy/Intervention√ Frequency/Rate		Aetiology/Risk Factors Diagr Phenomena Othe	-			
Search Strategy			···			
Primary Database(s) Searched	Medline					
Search Strategy	#	Query	Limiters/Expanders	Results		
	\$15	\$5 AND \$10	Limiters - Date of Publication: 20120101-20131231; Review Articles	62		
	S14	\$5 AND \$10	Limiters - Review Articles	770		
	\$13	\$5 AND \$10	Limiters - Date of Publication: 20120101-20131231; Publication Type: Clinical Trial, Clinical Trial, Phase I, Clinical Trial, Phase II, Clinical Trial, Phase III, Clinical Trial, Phase IV, Controlled Clinical Trial, Multicenter Study, Randomized Controlled Trial	5		
	\$12	\$5 AND \$10	Limiters - Publication Type: Clinical Trial, Clinical Trial, Phase I, Clinical Trial, Phase II, Clinical Trial, Phase III, Clinical Trial, Phase IV, Controlled Clinical Trial, Multicenter Study, Randomized Controlled Trial	101		
	S11	\$5 AND \$10		4,231		

]	S10	S6 OR S7 OR S8 OR S9		634,335
	\$9	(etoposide or methotrexate or dactinomycin or actinomycin or cyclophosphamide or vincristine or chlorambucil* or doxorubicin or melphalan or hydroxyurea or Hammond or Goldstein or EMA?CO or EMA-CO or CHAMOCA)		212,216
	\$8	chemotherap*		316,118
	S7	(MH "Antineoplastic Combined Chemotherapy Protocols")		98,936
	S6	(MH "Antineoplastic Agents+")		269,772
	\$5	S1 OR S2 OR S3 OR S4		33,189
	S4	((hydatidiform or invasive) and mole*)		24,412
	\$3	(GTT or GTD or GTN)		3,360
	\$2	("gestational trophoblastic" N2 (neoplasm* or tumor* or tumour* or disease*))		1,819
	S1	(MH "Gestational Trophoblastic Disease+")	-	10,221
Other/Secondary Resources Searched	UPTODA	ATE; COCHRANE; NCI		
Search Strategy: Other Resources				
Comments				
Date				

For women with high-risk (FIGO 27) GTN, what is the optimal first-line chemotherapy regimen?         Propulation/Problem       Women with STN         Intervention/Indicator       Chemotherapy regimens         -       EV/CM         Comparator/Control       -         -       EV/CM         Outcome       System survival Recurrence         Activation specific to any of thre categories below?       DATE OF PUBLICATION         GENDER       ACE GROUP       DATE OF PUBLICATION         Male       Activation (D - 23 months) Child (2 - 12 years)       Current year only         Actual (19 - 45 years)       > 5 years ×       Actual (19 - 45 years)         Actual (19 - 45 years)       > 5 years ×       Actual (19 - 45 years)         Search Strategy       Phenomena       Other       Search Strategy         Primary Database(s)       State Strategories Data       Emitters - Date of Publication: 2012010- 20131231; Review Articles       62         Search Strategy       State Strategories Data       Emitters - Date of Publication Type: Chineal Trial, Phase Unificanter Study, Randomized Control of Trial, Phase II, Cinical Trial, Phase IV, Control Phas	Clinical Question				
Population/Problem       Women with GTN         Intervention/Indicator       Chemotherapy regimens - EMA-CQ         Intervention/Indicator       EP/EAA chemotherapy         Comparator//Control	For women with high-risk	(FIGO ≥7	) GTN, what is the optimal first-line	e chemotherapy regimen?	
Intervention/Indicator       Chemotherapy regimens - EMA-CQ - EP/EMA chemotherapy - TE/TP chemotherapy         Comparator/Control       -         Outcome       S-year survival Recurrence Metastases         Is the duestion specific to any of the categorifes below?         GENDER       AGE GROUP         Addetscere       DATE OF PUBLICATION Infant (0 - 23 months) Child (2 - 12 years)         Cuestion specific to any of the categorifes below?         GenDER       AGE GROUP         Addetscere (13 - 18 years)       0 - 5 years ✓         Addetscere (13 - 18 years)       0 - 5 years ✓         Addetscere (13 - 18 years)       0 - 5 years ✓         Addetscere (13 - 18 years)       0 - 5 years ✓         Addetscere (13 - 18 years)       0 - 5 years ✓         Addetscere (13 - 18 years)       0 - 5 years ✓         Addetscere (13 - 18 years)       0 - 5 years ✓         Addetscere (13 - 18 years)       0 - 5 years ✓         Phenomena       Other:       Search Strategy         Primary Database(s)       Sits       SS AND S10         Sits       SS AND S10       Limiters - Review Articles       770         Sita       SS AND S10       Limiters - Review Articles       5         Sita       SS AND S10       Limiters - Publication: 2012010-1; 20131231; Review A	PICO				
Intervention/Indicator       -       EWA-CO       -         -       EWA-CO       -       -         Comparator/Control       -       -       -         Outcome       S-year survival Recurrence Metastases       -       -       -         Is the question spacific to only of the categories below?       -       -       -         GENDER       ACE GROUP       DATE OF PUBLICATION Infant 10 – 23 months)       Current year only 0 – 5 years ✓         Male       Acting 12 - 22 words)       Current year only 0 – 5 years ✓       -       -         Female ✓       Acting 12 - 82 words)       0 – 5 years ✓       -       -         Question type       -       -       -       -       -         Primary Database(s)       -       -       -       -       -       -         Searched Strategy       Medine       -	Population/Problem	Wome	n with GTN		
System survival Recurrence Metastases         System survival Recurrence           Is the question specific to any of the categories below?         DATE OF PUBLICATION Infant (0 – 23 months) Child (2 – 12 years) Adde Child (2 – 12 years) Adde (1 – 23 months) Child (2 – 12 years) Addut (1 – 65 years) Addut (1 – 65 years) Addut (1 – 65 years) Aged (> 65 years)         DATE OF PUBLICATION Unrent year only 0 – 5 years ✓ 0 – 5 years ✓ 0 – 5 years ✓ 0 – 5 years           Question Type         Intercept/Intervention ✓ Requency/Rate Phenomena         Aetilology/Risk Factors         Diagnosis         Prognosis/Prediction           Primary Database(s) Search Strategy         Medline         Initiers/Expanders         Results           Starts Strategy         Initiers - Date of Publication: 20120101- 20131231; Review Articles         62           Start Strategy         Start Startego         2012         54           Start Strategy         Start Startego         62           Start Strategy         Startego         62           Start Strategy         Startego         62           Start Stratego         Startego         770           Start Stratego         Startego         5           Start Stratego         Startego         770           Start Startego         Startego         770           Start Startego         Startego         5           Startego         St	Intervention/Indicator	- E/ - El	MA-CO P/EMA chemotherapy		
Outcome       Recurrence Metastases         Is the question specific to ony of the categories below?       DATE OF PUBLICATION         GENDER       AGE GROUP       DATE OF PUBLICATION         Male       Child (2 – 12 years)       Current year only         Female ✓       Adolescent (13 – 18 years)       O – 5 years ✓         Addel (1P – 65 years)       Date of PublicAtion       Results         Guestion Type       Diagnosis       Prognosis/Prediction         Therapy/Intervention ✓       Aetiology/Risk Factors       Diagnosis       Prognosis/Prediction         Searched       Medine       Imiters/Expanders       Results         Searched       Imiters - Date of Publication: 20120101- 20131231; Review Articles       62         Stat       S5 AND S10       Limiters - Date of Publication: 20120101- 20131231; Publication Type: Clinical Trial, Phase IV, Controlled Clinical Trial, Phase II, Clinical Trial, Phase IV, Controlled Clinical Trial, Phase IV, Controlled Clinical Trial, Phase II, Clinical Trial, P	Comparator/Control	-			
GENDER     AGE GROUP     DATE OF PUBLICATION       Male     Infant (0 – 23 months) Child (2 – 12 years) Adolescent (13 – 18 years) Adolescent (13 – 18 years) Adol (19 – 65 years)     Current year only 0 – 5 years ✓       Search Strategy     Medline       Primary Database(s) Search Strategy     Medline       Search Strategy     Query     Limiters/Expanders     Results       Sits     S5 AND S10     Limiters - Patient Victoria (170, Phase I), Clinical Trial, Phase II, Clinical Trial, Phase II, Clinical Trial, Phase III, Clinical Trial, Phase IIIIII, Phase IIIIIIIIIIIIIIIIIIIIIIIIIIIIIIIIIIII		Recurre Metast	ence rases		
Male FemaleLinfant [0 - 23 months] Child [2 - 12 years]Current year only 0 - 5 years $\checkmark$ > 5 yearsQuestion Type Therapy/InterventionAetiology/Risk Factors PhenomenaDiagnosis Other:Prognosis/PredictionSearch StrategyPrimary Database(s) SearchedMeedlineMeedlineResultsSearch StrategyMeedlineImiters/ExpandersResultsSearchedStrategyImiters - Date of Publication: 2012010- 20131231; Review Articles770StatisticStatistic770StatisticStatistic770StatisticStatistics770StatisticStatisticsStatisticsStatisticStatisticsStatisticsStatisticStatisticsStatisticsStatisticStatisticsStatisticsStatisticStatisticsStatisticsStatisticStatisticsStatisticsStatisticStatisticsStatisticsStatisticStatisticsStatisticsStatisticStatisticsStatisticsStatisticStatisticsStatisticsStatisticStatisticsStatisticsStatisticStatisticsStatisticsStatisticStatisticsStatisticsStatisticStatisticsStatisticsStatisticsStatisticsStatisticsStatisticsStatisticsStatisticsStatisticsStatisticsStatisticsStatisticsStatisticsStatisticsStat		any of t			
Therapy/Intervention       Aetiology/Risk Factors       Diagnosis       Prognosis/Prediction         Frequency/Rate       Phenomena       Other:         Search Strategy       Medline         Search Strategy       Medline         Search Strategy       Imiters/Expanders       Results         \$15       S5 AND \$10       Limiters - Date of Publication: 20120101- 20131231; Review Articles       62         \$14       \$5 AND \$10       Limiters - Review Articles       770         \$13       \$5 AND \$10       Limiters - Date of Publication: 20120101- 20131231; Publication Type: Clinical Trial, Phase II, Clinical Trial, Phase II, Clinical Trial, Phase III, Clinical Trial, Phase II, Clinical Tr	Male Female ✓		Infant (0 – 23 months) Child (2 – 12 years) Adolescent (13 – 18 years) Adult (19 – 65 years)	Current year only $0-5$ years $\checkmark$	
Frequency/Rate       Phenomena       Other:         Search Strategy       Medline         Search Strategy       Medline         Search Strategy       Query       Limiters/Expanders       Results         \$search Strategy       \$15       \$5 AND \$10       Limiters - Date of Publication: 20120101- 20131231; Review Articles       62         \$14       \$5 AND \$10       Limiters - Review Articles       770         \$13       \$5 AND \$10       Limiters - Date of Publication: 20120101- 20131231; Publication Type: Clinical Trial, Phase IV, Controlled Clinical Trial, Phase III, Clinical Trial, Phase IV, Controlled Clinical Trial, Phase IV, Controll		Ae	atiology/Risk Eactors	Diagnosis Prognosis/Prediction	
Search Strategy           Primary Database(s) Searched         Medline           Search Strategy         Query         Limiters/Expanders         Results           \$15         \$5 AND \$10         Limiters - Date of Publication: 20120101- 20131231; Review Articles         62           \$14         \$5 AND \$10         Limiters - Review Articles         770           \$13         \$5 AND \$10         Limiters - Date of Publication: 20120101- 20131231; Publication Type: Clinical Trial, Clinical Trial, Phase I, Clinical Trial, Clinical Trial, Phase I, Clinical Trial, Multicenter Study, Randomized         5           \$12         \$5 AND \$10         Limiters - Publication Type: Clinical Trial, Clinical Trial, Phase I, Clinical Trial, Phase I, Clinical Trial, Phase II, Clinical Trial, Phase IV, Controlled Clinical Trial, Phase IV, Controled Clinical				•	
Searched       Ouery       Limiters/Expanders       Results         Search Strategy       S5 AND S10       Limiters - Date of Publication: 20120101- 20131231; Review Articles       62         S14       S5 AND S10       Limiters - Review Articles       770         S14       S5 AND S10       Limiters - Date of Publication: 20120101- 20131231; Publication Type: Clinical Trial, Clinical Trial, Phase II, Clinical Trial, Phase II, Clinical Trial, Phase II, Clinical Trial, Phase IV, Controlled Clinical Trial					
CoueryLimiters/ExpandersResults\$15\$5 AND \$10Limiters - Date of Publication: 20120101- 20131231; Review Articles62\$14\$5 AND \$10Limiters - Review Articles770\$13\$5 AND \$10Limiters - Date of Publication: 20120101- 20131231; Publication Type: Clinical Trial, Phase IV, Controlled		Medlir	ne		
\$15\$5 AND \$1020131231; Review Articles62\$14\$5 AND \$10Limiters - Review Articles770\$13\$5 AND \$10Limiters - Date of Publication: 20120101- 20131231; Publication Type: Clinical Trial, Clinical Trial, Phase II, Clinical Trial, Phase5\$13\$5 AND \$10Limiters - Publication Type: Clinical Trial, Phase IV, Controlled Clinical Trial, Multicenter Study, Randomized5\$12\$5 AND \$10Limiters - Publication Type: Clinical Trial, Phase IV, Controlled Clinical Trial, Phase IV, Controlled Clinical Trial, Phase IV, Controlled Clinical Trial, Phase IV, Controlled Clinical Trial, Phase II, Clinical Trial, Phase II, Clinical Trial, Phase IV, Controlled Clinical Trial, Phase II, Clinical Trial, Phase IV, Controlled Clinical Trial, Phase IV, Controlled Clinical Trial, Phase II, Clinical Trial, Phase III Clinical Trial, Pha	Search Strategy		Query	Limiters/Expanders	Results
S14S5 AND S10770S13S5 AND S10Limiters - Date of Publication: 20120101- 20131231; Publication Type: Clinical Trial, Clinical Trial, Phase I, Clinical Trial, Phase II, Clinical Trial, Phase III, Clinical Trial, Phase IV, Controlled Clinical Trial, Multicenter Study, Randomized Controlled Trial5S12S5 AND S10Limiters - Publication Type: Clinical Trial, Clinical Trial, Phase II, Clinical Trial, Phase IV, Controlled Trial5S12S5 AND S10Limiters - Publication Type: Clinical Trial, Phase IV, Controlled Clinical Trial, Phase IV, Controlle		\$15	\$5 AND \$10		62
\$13\$5 AND \$1020131231; Publication Type: Clinical Trial, Clinical Trial, Phase II, Clinical Trial, Phase II, Clinical Trial, Phase III, Clinical Trial, Phase IV, Controlled Clinical Trial, Multicenter Study, Randomized Controlled Trial5\$12\$5 AND \$10Limiters - Publication Type: Clinical Trial, Clinical Trial, Phase IV, Controlled Clinical Trial, Phase IV, Controlled Trial101		S14	\$5 AND \$10	Limiters - Review Articles	770
S12S5 AND \$10Clinical Trial, Phase II, Clinical Trial, Phase III, Clinical Trial, Phase IV, Controlled Clinical Trial, 101Multicenter Study, Randomized		\$13	\$5 AND \$10	20131231; Publication Type: Clinical Trial, Clinical Trial, Phase I, Clinical Trial, Phase II, Clinical Trial, Phase III, Clinical Trial, Phase IV, Controlled Clinical Trial, Multicenter Study, Randomized	5
		S12	S5 AND \$10	Clinical Trial, Phase I, Clinical Trial, Phase II, Clinical Trial, Phase III, Clinical Trial, Phase IV, Controlled Clinical Trial, Multicenter Study, Randomized	101

F	-	1	
	S10	S6 OR S7 OR S8 OR S9	634,335
	S9	(etoposide or methotrexate or dactinomycin or actinomycin or cyclophosphamide or vincristine or chlorambucil* or doxorubicin or melphalan or hydroxyurea or Hammond or Goldstein or EMA?CO or EMA-CO or CHAMOCA)	212,216
	S8	chemotherap*	316,118
	S7	(MH "Antineoplastic Combined Chemotherapy Protocols")	98,936
	S6	(MH "Antineoplastic Agents+")	269,772
	S5	S1 OR S2 OR S3 OR S4	33,189
	S4	((hydatidiform or invasive) and mole*)	24,412
	\$3	(GTT or GTD or GTN)	3,360
	S2	("gestational trophoblastic" N2 (neoplasm* or tumor* or tumour* or disease*))	1,819
	S1	(MH "Gestational Trophoblastic	10,221
Other/Secondary Resources Searched	UpToE	Date; cochrane; NCI	
Search Strategy: Other Resources			
Comments			
Date			

Clinical Question	Clinical Question						
For women with low-risk gestational trophoblastic neoplasia undergoing chemotherapy (first-course), what is the recommended course of action for observing and managing bleeding?							
PICO							
Population/Problem	Wome	Vomen with GTN undergoing chemotherapy					
Intervention/Indicator	Obser	vation & management of bleeding	)				
Comparator/Control	-						
Outcome	Optim	um management					
Is the question specific t	o any of	the categories below?					
GENDER		AGE GROUP	DATE OF PUBLICATION				
Male Female ✓		Infant (0 – 23 months) Child (2 – 12 years) Adolescent (13 – 18 years) Adult (19 – 65 years) Aged (> 65 years)	Current year only 0 – 5 years > 5 years ✓				
Question Type							
Therapy/Intervention $\checkmark$	/	Aetiology/Risk Factors	Diagnosis Prognosis/Prediction				
Frequency/Rate	F	Phenomena	Other:				
Search Strategy							
Primary Database(s) Searched	Medlir	ne					
Search Strategy	#	Query	Limiters/Expanders	Results			
	\$19	\$11 AND \$14	Limiters - Date of Publication: 20020101- 20131231; Clinical Queries: Therapy - High Sensitivity	43			
	\$18	\$16 AND \$17		4			
	\$17	MM "Uterine Hemorrhage therapy"		453			
	S16	\$11 AND \$14	Limiters - Date of Publication: 20020101- 20131231	84			
	\$15	\$11 AND \$14		110			
	S14	\$12 OR \$13		Display			
	S13	(vagina* N2 (bleed* OR hemorrhag* OR haemorrhag*))	Limiters - Date of Publication: 20020101- 20131231	Display			
	\$12	(MH "Uterine Hemorrhage+")		Display			
	S11	\$5 AND \$10		Display			
	\$10	S6 OR S7 OR S8 OR S9		635,606			
	S9	(etoposide or methotrexate or		212,517			

		dactinomycin or actinomycin or cyclophosphamide or vincristine or chlorambucil* or doxorubicin or melphalan or hydroxyurea or Hammond or Goldstein or EMA?CO or EMA-	
	58	CO or CHAMOCA) chemotherap*	316,767
	S7	(MH "Antineoplastic Combined Chemotherapy Protocols")	99,084
	S6	(MH "Antineoplastic Agents+")	270,378
	\$5	S1 OR S2 OR S3 OR S4	33,265
	S4	((hydatidiform or invasive) and mole*)	24,477
	\$3	(GTT or GTD or GTN)	3,368
	S2	("gestational trophoblastic" N2 (neoplasm* or tumor* or tumour* or disease*))	1,821
	S1	(MH "Gestational Trophoblastic Disease+")	10,226
Other/Secondary Resources Searched	Cochra	ane; UpToDate; eds	· · · · · ·
Search Strategy: Other Resources			
Comments			
Date			

Clinical Question							
For women with gestar chemotherapy and fo		noblastic neoplasia, what are the appropriate invest	igations to monitor response to				
PICO							
Population/Problem	Women	Women with GTN					
Intervention/Indicat or	hCG leve	els					
Comparator/Control	-						
Outcome	Response	e to chemotherapy and follow-up					
Is the question specific	to any of t	he categories below?					
GENDER			F PUBLICATION				
Male Female ✓		Infant (0 – 23 months)CurrentChild (2 – 12 years)CurrentAdolescent (13 – 18 years)0 – 5 years)Adult (19 – 65 years)> 5 years)Aged (> 65 years)					
Question Type							
Therapy/Intervention ✔ Frequency/Rate		etiology/Risk Factors Diagnosis P nenomena Other:	rognosis/Prediction				
	FI	lenomend Olher.		_			
Search Strategy							
Primary Database(s) Searched	Medline						
Search Strategy	#	Query	Limiters/Expanders	Results			
	\$19	\$14 not \$15	Limiters - Date of Publication: 20070101- 20131231	97			
	\$18	\$16 AND \$17		13			
	\$17	(MM "Chorionic Gonadotropin, beta Subunit, Human")		1,077			
	S16	\$14 not s15		168			
	S15	\$11 AND \$12	Limiters - Date of Publication: 20020101- 20131231; Publication Type: Case Reports	100			
	\$14	\$11 AND \$12	Limiters - Date of Publication: 20020101- 20131231	268			
	\$13	\$11 AND \$12		654			
	\$12	(MM "Chorionic Gonadotropin, beta Subunit, Human") OR "hcg"		21,068			
	S11	\$5 AND \$10		4,260			

	\$10	S6 OR S7 OR S8 OR S9	637,625
	\$9	(etoposide or methotrexate or dactinomycin or actinomycin or cyclophosphamide or vincristine or chlorambucil* or doxorubicin or melphalan or hydroxyurea or Hammond or Goldstein or EMA?CO or EMA-CO or CHAMOCA)	212,945
	S8	chemotherap*	317,852
	S7	(MH "Antineoplastic Combined Chemotherapy Protocols")	99,380
	S6	(MH "Antineoplastic Agents+")	271,393
	\$5	\$1 OR \$2 OR \$3 OR \$4	33,387
	S4	((hydatidiform or invasive) and mole*)	24,585
	\$3	(GTT or GTD or GTN)	3,378
	S2	("gestational trophoblastic" N2 (neoplasm* or tumor* or tumour* or disease*))	1,825
	S1	(MH "Gestational Trophoblastic Disease+")	10,239
Other/Secondary Resou Searched	irces	Uptodate; Cochrane	
Search Strategy: Other F	Resources	S	
Comments			
Date			

Clinical Question				
For women with low-risk ge chemotherapy?	station	al trophoblastic neoplasia what a	re the indicators to determine switching treatmen	ts from first-lin
PICO				
Population/Problem	Wome	en with low-risk GTN undergoing fi	rst-line chemotherapy	
Intervention/Indicator	Indico - plate - toxic	eau in hCG		
Comparator/Control				
Outcome		n from first-line treatment		
Is the question specific to a	ny of th	ne categories below?		
GENDER AGE GROUP Infant (0 – 23 m	onths)		DATE OF PUBLICATION	
Male Child (2 – 12 ye Adolescent (13 Adult (19 – 65 y Aged (> 65 yea	ars) – 18 ye ears)	ears)	Current year only 0 – 5 years > 5 years ✓	
Question Type Therapy/Intervention 🗸	Aatiol	ogy/Risk Factors Diagnosis	Prognosis/Prediction	
Frequency/Rate	Pheno	•••••••		
Search Strategy				
Primary Database(s) Searched	Medli	ne		
Search Strategy	#	Query	Limiters/Expanders	Results
	S23	\$11 AND \$12	Limiters - Date of Publication: 20020101-20131231; Clinical Queries: Prognosis - Best Balance	25
	S22	\$11 AND \$12	Limiters - Clinical Queries: Prognosis - Best Balance	34
	S21	\$13 AND \$20		3
	S20	MM "Drug Resistance, Neoplasm	u	10,046
	\$19	\$13 AND \$18		32
	\$18	AB fail* OR resist*	Limiters - Date of Publication: 20020101-20131231	715,060
	\$17	\$13 AND \$15	Limiters - Date of Publication: 20020101-20131231	28
	S16	\$13 AND \$15		41
	\$15	\$11 AND \$14		604
	S14	( TI "second-line" OR "second line combination ) OR ( AB "second- "second line" OR combination )		635,089

			1	
	\$13	\$11 AND \$12		90
	\$12	( TI "first-line" OR "first line" ) OR ( AB "first- line" OR "first line" )		39,758
	S11	\$5 AND \$10		4,266
	S10	S6 OR S7 OR S8 OR S9		638,286
	S9	(etoposide or methotrexate or dactinomycin or actinomycin or cyclophosphamide or vincristine or chlorambucil* or doxorubicin or melphalan or hydroxyurea or Hammond or Goldstein or EMA?CO or EMA-CO or CHAMOCA)		213,096
	S8	chemotherap*		318,251
	S7	(MH "Antineoplastic Combined Chemotherapy Protocols")		99,445
	S6	(MH "Antineoplastic Agents+")		271,636
	S5	S1 OR S2 OR S3 OR S4		33,433
	S4	((hydatidiform or invasive) and mole*)		24,626
	S3	(GTT or GTD or GTN)		3,381
	S2	("gestational trophoblastic" N2 (neoplasm* or tumor* or tumour* or disease*))		1,828
	S1	(MH "Gestational Trophoblastic Disease+")		10,239
Other/Secondary Resources Searched				
Search Strategy: Other Resources				
Comments				
Date				

# Question 14a

Clinical Question						
For women with low-risk gestational trophoblastic neoplasia who have not responded or have relapsed from single agent treatment (methotrexate or actinomycin D) or have relapsed following normalisation of hCG after completion of single agent treatment, what is the next line treatment?						
_PICO		-				
Population/Problem	Wome	Women with low-risk invasive GTN who have not responded to single agent treatment or relapsed.				
Intervention/Indicator	Next li	ine treatm	ent chemotherapy			
Comparator/Control	-					
Outcome	5-yeai	r survival				
Is the question specific to	any of t	he catego	ories below?			
GENDER		GE GROUI		LICATION		
		fant (0 – 2 hild (2 – 12	,	only		
Male Female ✓			$(13 - 18 \text{ years})$ $0 - 5 \text{ years} \checkmark$			
		dult (19 – 6 ged (> 65				
Question Type		geu (> 00	years			
Therapy/Intervention √	Aetio	ology/Risk	Factors Diagnosis	Prognosis/Prediction		
Frequency/Rate	Pher	nomena	Other:			
Search Strategy						
Primary Database(s) Searc	ched	Medline				
Search Strategy		#	Query	Limiters/Expanders	Results	
		S22	\$19 AND \$20	Limiters - Date of Publication: 20130101- 20141231	9	
		S21	\$19 AND \$20		89	
		S20	TI "Iow\$risk" OR AB "Iow\$risk"		36,813	
		\$19	\$17 OR \$18		916	
		\$18	\$11 AND \$16		201	
		S17	\$11 AND \$15		755	
		S16	(MH "Drug Resistance, Neoplasm")		28,030	
		S15	\$13 OR \$14		823,822	
		S14	( TI "second\$line" OR combination* ) OR ( AB "second\$line" OR combination* )		792,830	
		\$13	TI "first\$line" OR AB "first\$line"		44,876	
		\$12	(TI fail* OR resist* ) OR (AB fail* OR resist* )		1,541,483	
		S11	\$5 AND \$10		4,599	
		S10	S6 OR S7 OR S8 OR S9		681,272	
		S9	(etoposide or methotrexate or dactinomycin or actinomycin or cyclophosphamide or vincristine or chlorambucil* or doxorubicin or melphalan or hydroxyurea or Hammond or Goldstein or EMA?CO or EMA-CO or		222,372	

		CHAMOCA)	
	S8	chemotherap*	341,998
	S7	(MH "Antineoplastic Combined Chemotherapy Protocols")	105,213
	S6	(MH "Antineoplastic Agents+")	291,192
	\$5	S1 OR S2 OR S3 OR S4	36,550
	S4	((hydatidiform or invasive) and mole*)	27,495
	\$3	(GTT or GTD or GTN)	3,565
	S2	("gestational trophoblastic" N2 (neoplasm* or tumor* or tumour* or disease*))	1,914
	S 1	(MH "Gestational Trophoblastic Disease+")	10,418
Other/Secondary Resources Searched	UpToD	ate, Cochrane	
Search Strategy: Other Resources			
Comments			
Date			

# Question 14b

Clinical Question					
For women with high-risk GTN who have not responded or have relapsed from firstline treatment, what is second-line treatment?					id-line treatment?
PICO					
Population/Problem	Wome	Women with high-risk GTN who have not responded to first-line treatment			
Intervention/Indicator	Secor	nd-line trea	atment chemotherapy		
Comparator/Control	-				
Outcome	5-yea	r survival			
Is the question specific to	any of t	he catego	pries below?		
GENDER	AGE GROUP DATE OF PUBLICATION				
Male Female ✓	Infant (0 – 23 months)Current year onlyChild (2 – 12 years)Current year onlyAdolescent (13 – 18 years)0 – 5 years ✓Adult (19 – 65 years)> 5 yearsAged (> 65 years)> 5 years				
Question Type	• 1.				
Therapy/Intervention ✓ Frequency/Rate		ology/Risk nomena	Factors Diagnosis Other:	Prognosis/Predictic	n
_Search Strategy	11101	lomena			
Primary Database(s) Searc	ched	Medline			
Search Strategy		#	Query	Limiters/Expanders	Results
		\$22	\$19 AND \$20	Limiters - Date of Publication: 20130101- 20141231	13
		S21	\$19 AND \$20		155
		S20	TI "high\$risk" OR AB "high\$risk"		173,224
		S19	\$17 OR \$18		916
		\$18	\$11 AND \$16		201
		S17	\$11 AND \$15		755
		S16	(MH "Drug Resistance, Neoplasm")		28,030
		S15	\$13 OR \$14		823,822
		\$14	( TI "second\$line" OR combination* ) OR ( AB "second\$line" OR combination* )		792,830
		\$13	TI "first\$line" OR AB "first\$line"		44,876
		\$12	( TI fail* OR resist* ) OR ( AB fail* OR resist* )		1,541,483
		S11	\$5 AND \$10		4,599
		S10	S6 OR S7 OR S8 OR S9		681,272
		S9	(etoposide or methotrexate or dactinomycin or actinomycin or cyclophosphamide or vincristine or chlorambucil* or doxorubicin or melphalan or hydroxyurea or Hammond or Goldstein or EMA?CO		222,372

		or EMA-CO or CHAMOCA)	
	S8	chemotherap*	341,998
	S7	(MH "Antineoplastic Combined Chemotherapy Protocols")	105,213
	S6	(MH "Antineoplastic Agents+")	291,192
	S5	\$1 OR \$2 OR \$3 OR \$4	36,550
	S4	((hydatidiform or invasive) and mole*)	27,495
	\$3	(GTT or GTD or GTN)	3,565
	\$2	("gestational trophoblastic" N2 (neoplasm* or tumor* or tumour* or disease*))	1,914
	S1	(MH "Gestational Trophoblastic Disease+")	10,418
Other/Secondary Resources Searched	UpToDo	ate, Cochrane	
Search Strategy: Other Resources			
Comments			
Date			

Clinical Question						
For women with GTN, who are acutely ill with liver, brain or lung metastasis at presentation, what is the optimum chemotherapy regimen?						
PICO						
Population/Problem	Wome	Women with GTN who are acutely ill with liver, brain or lung metastases				
Intervention/Indicator			/ treatment options haring Cross protocol)			
Comparator/Control	-					
Outcome	Surviv	al				
Is the question specific to	any of t	the cate	gories below?			
GENDER		GE GRO		TE OF PUBLICATION		
Male Female ✓	Infant (0 – 23 months)Current year onlyChild (2 – 12 years)Current year onlyAdolescent (13 – 18 years)0 – 5 yearsAdult (19 – 65 years)> 5 years ✓Aged (> 65 years)					
Question Type Therapy/Intervention Frequency/Rate		Aetiology/Risk FactorsDiagnosis ✓Prognosis/PredictionPhenomenaOther:				
Search Strategy						
Primary Database(s) Sear	ched	Medlin	e			
Search Strategy			Query	Limiters/Expanders	Results	
		\$22	S15 OR S17 OR S19	Limiters - Date of Publication: 20020101-20131231; Clinical Queries: Therapy - High Sensitivity	19	
		\$21	S15 OR S17 OR S19	Limiters - Date of Publication: 20020101-20131231	38	
		\$20	\$15 OR \$17 OR \$19		181	
		\$19	\$13 AND \$18		28	
		\$18	(MH "Liver Neoplasms+") OR (MH "Liver+")		472,017	
		\$17	\$13 AND \$16		141	
		S16	(MH "Lung+") OR (MH "Lung Neoplasms+")		365,144	
		\$15	\$13 AND \$14		49	
		S14	(MH "Brain+") OR (MH "Brain Neoplasms+")		1,019,886	
		\$13	\$11 AND \$12		587	

	S11	\$5 AND \$10	4,273
	S10	S6 OR S7 OR S8 OR S9	639,111
	59	(etoposide or methotrexate or dactinomycin or actinomycin or cyclophosphamide or vincristine or chlorambucil* or doxorubicin or melphalan or hydroxyurea or Hammond or Goldstein or EMA?CO or EMA-CO or CHAMOCA)	213,349
	S8	chemotherap*	318,895
	S7	(MH "Antineoplastic Combined Chemotherapy Protocols")	99,445
	S6	(MH "Antineoplastic Agents+")	271,636
	S5	\$1 OR \$2 OR \$3 OR \$4	33,511
	S4	((hydatidiform or invasive) and mole*)	24,697
	\$3	(GTT or GTD or GTN)	3,386
	S2	("gestational trophoblastic" N2 (neoplasm* or tumor* or tumour* or disease*))	1,830
	S1	(MH "Gestational Trophoblastic	10,239
Other/Secondary Resources Searched	UpToD	ate, Cochrane	
Search Strategy: Other Resources			
Comments			
Date			