Item 11 - Correspondence

From: Donald E. Chamberlin
To: MCP-Chair
Subject: PWPA material #1 re Item 11 Reflection Park agenda for 12-15-2022
Date: Wednesday, December 14, 2022 11:40:58 AM
Attachments: 30-Day Mortality re Chemotherapy.xlsx
PWPA Composite Reference List 3-22-2022.docx

Please see the attached files.

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Scepura Studies - Bibliography

ref	source	authors	title	Country: US	Country: Non-US	where done	cancer type	treatment: palliative	treatment: curative	study dates	total patients	30-day mortality %	Chemo regime	Remarks
1	J Oncol Pharm Pract. 2021:10781552211016086. Epub 2021/05/16. doi: 10.1177/10781552211016086. PubMed PMID: 33990165. https://pubmed.ncbi.nlm.nih.gov/33990165/?otool=mdufdrlib	Zimbwa et al	Retrospective analysis of mortality within 30 days of systemic anticancer therapy and comparison with a previous audit at an Australian Regional Cancer Centre.		1	Regional Cancer Center Australia	solid tumors & haematology			Jan 2016 - Jul 2020	1,709	7.0%		deaths within 14 days of SACT = 3.3%. Mean time to death = 15.5 days.
2	BMC Cancer. 2021; 21(1):41. Epub 2021/01/09. doi: 10.1186/s12885-020-07756-7. Pubmed PMID:33413223; PubMed Central PMCID: PMCPMC7791857 https://pubmed.ncbi.nim.nih.gov/33413223/?otool=mdufdrlib	Zhou et al	High-grade postoperative complications affect survival outcomes of patients with colorectal Cancer peritoneal metastases treated bith Cytoreductive surgery and Hyperthermic intraperitoneal chemotherapy		1	China National Cancer Center, Huanxing Cancer Hospital, China	colorectal with peritoneal metasteses			June 2017 - June 2019	86			`30-DAY MORTALITY NOT SPECIFIED; No mortality during post-operative period; medial survival of all patients was 25 months.
3	https://pubmed.ncbi.nlm.nih.gov/33758663/?otool=mdufdrlib	Tashkandi et al	Mortality and morbidity of curative and palliative anticancer treatments during the COVID-19 pandemic: A multicenter population-based retrospective study.		1	5 large cancer centers in Saudi Arabia		1	1	1 Mar - 30 Jun 2020	2,504	5.1%		
4	JAMA Netw Open. 2021;4(11):e2134330. Epub 2021/11/13. doi: 10.1001/jamanetworkopen.2021.34330. PubMed PMID: 34767021; PubMed Central PMCID: PMCPMC8590166; https:/pubmed.ncbi.nim.nih.gov/34767021/?otool=mdufdrlib **//have full study//**	Schmidt et al	Association Between Androgen Deprivation Therapy and Mortality Among Patients With Prostate Cancer and COVID-19.	1		Vanderbilt Univ Med Ctr, Nashville TN.]	prostate			3/17/2020 - 2/11/2021	**1,106**		androgen deprivation therapy	determine if ADT therapy is associated with decreased rate of 30-day mortality from SARS Cov-19 among patients with prostate cancer. CONCLUSION: ADT not associated with decreased 30-day mortality.
5	BMC Cancer. 2021;21(1):274. Epub 2021/03/17. doi: 10.1186/s12885-021-07992-5. PubMed PMID: 33722202; PubMed Central PMCID: PMCPMC7958422. https://pubmed.ncbi.nlm.nih.gov/33722202/?otool=mdufdrlib	Oselin et al	Intensity of end-of-life health care and mortality after systemic anti-cancer treatment in patients with advanced lung cancer.		1	Estonia	advanced lung			2015-2017		**14.7%**		**6.7% died within 14 days of SACT.**

6	Am J Hematol. 2021;96(3):282-91. Epub 2020/12/03. doi: 10.1002/ajh.26061. PubMed PMID: 33264443; PubMed Central PMCID: PMCPMC8128145. https://pubmed.ncbi.nlm.nih.gov/33264443/?otool=mdufdrlib	Maiti et al	**Venetoclax with decitabine vs intensive chemotherapy in acute myeloid leukemia: A propensity score matched analysis stratified by risk of treatment-related mortality.**	1	**MD Anderson Cancer Center, Houston, Texas,**	acute myeloid leukemia	May 2000 - July 208	85	**24.0%**	intensive chemotherapy (unspecified)	**Venetoclax w/decitabine: 30-day mortality = 1%; standard IC: 30-day mortality = 24%. 85 in DEC10-VEN cohort match to 85 of 405 in IC cohort.**
7	Future Sci OA. 2021;7(7):Fso709. Epub 2021/07/15. doi: 10.2144/fsoa-2021-0008. PubMed PMID: 34258022; PubMed Central PMCID: PMCPMC8256323. https://pubmed.ncbi.nlm.nih.gov/34258022/?otool=mdufdrlib	Ferro et al	Neutrophil percentage-to-albumin ratio predicts mortality in bladder cancer patients treated with neoadjuvant chemotherapy followed by radical cystectomy.	1	Romania	muscle-invasive bladder cancer, non-metastatic		213			**30-day mortality not given**
8	J Infect Chemother. 2021;27(4):568-72. Epub 2021/01/22. doi: 10.1016/j.jiac.2020.11.011. PubMed PMID: 33472747. https://pubmed.ncbi.nlm.nih.gov/33472747/?otool=mdufdrlib	Eidenschink et al	Opioid use prior to admission for chemotherapy induced febrile neutropenia is associated with increased documented infection, sepsis, and death. **// Have Full Study //**	1	North Dakota	**febrile neutropenia (leukemia)** + others (incl breast, connec-tive tissue, ENT, genitourinary, GI, lung, lymphomas, leukemias)		481			274 patients w/opioid prescriptions within 10 days of hospital; 207 patients without opioid prescriptions for >1 yr pre-hospitalization. CONCLUSION: Opioid increases by 2.3X the odds of death/hospice w/in 30 days of [post chemo] discharge.
9	Lung Cancer. 2021;153:150-7. Epub 2021/02/03. doi: 10.1016/j.lungcan.2021.01.018. PubMed PMID: 33529989. https://pubmed.ncbi.nlm.nih.gov/33529989/?otool=mdufdrlib	Eichhorn et al	Neoadjuvant anti-programmed death-1 immunotherapy by pembrolizumab in resectable non-small cell lung cancer: First clinical experience.	1	Heidelberg, Germany	lung (non-small cell)		15	0.0%	neoadjuvant pembrolizumab (KEYTRUDA)	13 patients with adenocarcinoma; 2 patients with squamouis cell carcinoma; CONCLUSION: neoadjuvant pembrolizumab is feasible therapy, assoc w/tollerable toxicity and did not comromise tumor resection. Overall postoperative morbidity was 7%.
10	//SEE Source E above.//										
11	J Cancer. 2021;12(18):5494-505. Epub 2021/08/19. doi: 10.7150/jca.50802. PubMed PMID: 34405012; PubMed Central PMCID: PMCPMC8364636. https://pubmed.ncbi.nlm.nih.gov/34405012/?otool=mdufdrlib	Chen S. et al	A practical update on the epidemiology and risk factors for the emergence and mortality of bloodstream infections from real-world data of 3014 hematological malignancy patients receiving chemotherapy.	1	China	hematologic malignancies	2013-2016	3,014			**after chemo, 725 patients (24.1%) had blood stream infections.** Gram-neg bacteria were 64.7% of the 744 isolated strains. Most common isolates were klebsiella pneumoniae (19.2%. 95.1% of the multi-drug-resistant strainswere extended spectrum beta-lactamase-producing strains. CONCLUSION: G- bacteria were the predominant microflora and **antibiotic resistance levels of the pathogens detected were high, especially for MDR stgrains. Mortality of BSI patients was high in this large cohort.**

12	Br J Cancer. 2021;125(5):658-71. Epub 2021/06/18. doi: 10.1038/s41416-021-01452-4. PubMed PMID: 34135471; PubMed Central PMCID: PMCPMC8206183. https://pubmed.ncbi.nlm.nih.gov/34135471/?otool=mdufdrlib	Assaad et al	Mortality of patients with solid and haematological cancers presenting with symptoms of COVID-19 with vs without detectable SARS-COV-2: a French nationwide prospective cohort study.		1	France (23 cancer centers)	solid or haematological tumors			1 Mar - 1 May 2020	1,162	**28.8%**		**cohort = patients suspected of having COVID-19. CT scan identified 425 Covid+ and 737 Covid- patients. 28-day mortality occurred in 116 (27.8%) Covid+ patients and 118 (16.3%) Covid- patients.**
13	Ann Surg Oncol. 2020;27(3):783-92. Epub 2019/10/30. doi: 10.1245/s10434-019-07964-x. PubMed PMID: 31659645. https://pubmed.ncbi.nlm.nih.gov/31659645/?otool=mdufdrlib	Wiseman et al	Predictors of Anastomotic Failure After Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy: Does Technique Matter?	1		**12 major academic medical institutions in multiple US metro areas.**	bowel	1	1	2000-2017	1,020	**9.0%**	hyperthermic intraperitoneal chemotherapy	30-day mortality with AF = 9%, without Anastomotic Failure = 1%
14	Cancer Manag Res. 2020;12:12301-8. Epub 2020/12/10. doi: 10.2147/cmar.S277924. PubMed PMID: 33293858; PubMed Central PMCID: PMCPMC7718861. https://pubmed.ncbi.nlm.nih.gov/33293858/?otool=mdufdrlib	Tashkandi et al	Thirty-Day Mortality After Curative and Palliative Anti-Cancer Treatment: Data Interpretation and Lessons for Clinical Implementation.		1	2 large cancer centers in Saudi Arabia	solid and hematological malignancies; 66.5% of patients had breast and gastrointestinal cancers.	1	1	1 Dec 2019 - Feb 29 2020	1,694	3.5%		
15	BMC Cancer. 2020;20(1):867. Epub 2020/09/11. doi: 10.1186/s12885-020-07375-2. PubMed PMID: 32907555; PubMed Central PMCID: PMCPMC7488043. https://pubmed.ncbi.nlm.nih.gov/32907555/?otool=mdufdrlib	Taniguchi et al	Antithrombin use and mortality in patients with stage IV solid tumor-associated disseminated intravascular coagulation: a nationwide observational study in Japan.		1	Japan	Stage IV terminal-stage solid tumors			Jul 2010 - Mar 2018	919	**30.3%**	antithrombin agents to treat disseminated intravascular coagulation	**28-day in-hospital mortality was 30.3% for the antithrombin group vs 28.9% for the 3676 no-antithrombin control group. Total cohort was 25,299 patients.**
16	. Int J Clin Oncol. 2020;25(4):541-51. Epub 2019/12/08. doi: 10.1007/s10147-019-01579-8. PubMed PMID: 31811602. https://pubmed.ncbi.nlm.nih.gov/31811602/?otool=mdufdrlib	Sugiyama et al	Prognostic significance of hyponatremia induced by systemic chemotherapy in a hospital-based propensity score-matched analysis		1	japan	malignancy in various organs			Jan 2011 - Jul 2017	2,129		various systemic	Nagoya City University Hospotal; within 30 days of starting chemo, 4.4% of patients developed severe hyponatremia. Platinum-containing regimens induced more severe hyponatremia.
17	Cancer Med. 2020;9(8):2742-51. Epub 2020/02/26. doi: 10.1002/cam4.2912. PubMed PMID: 32096915; PubMed Central PMCID: PMCPMC7163083. https://pubmed.ncbi.nlm.nih.gov/32096915/?otool=mdufdrlib	Melchior et al	Treatment times in breast cancer patients receiving neoadjuvant vs adjuvant chemotherapy: Is efficiency a benefit of preoperative chemotherapy? **//have full study//**	1		Fox Chase Cancer Center, Philadelphia PA	breast			2004-2015	155,606	**0.04%**	Neoadjuvant vs Adjuvant chemotherapy	patients with stage I-III breast cancer: 28,241 women received neoadjuvant chemo and 127,365 women received adjuivant chemo. 30-day mortality was 0.04% for NAC and 0.01% for AC.

18	Breast J. 2020;26(5):952-9. Epub 2019/10/12. doi: 10.1111/tbj.13652. PubMed PMID: 31602749. https://pubmed.ncbi.nlm.nih.gov/31602749/?otool=mdufdrlib	Li S, et al	Delayed adjuvant hormonal therapy and its impact on mortality in women with breast cancer	1	Beth Israel Deaconess, Harvard Med. Sch., Boston MA	hormone-sensitive breast cancer			2010-2015			**hormonal therapy only; Patients receiving chemotherapy were excluded**	Delayed initiation of hormone therapy is associated with a survival disadvantage.
19	Ann Hematol. 2020;99(8):1925-32. Epub 2020/06/22. doi: 10.1007/s00277-020-04144-w. PubMed PMID: 32564194. https://pubmed.ncbi.nlm.nih.gov/32564194/?otool=mdufdrlib	Kara Ali et al	An eleven-year cohort of bloodstream infections in 552 febrile neutropenic patients: resistance profiles of Gram-negative bacteria as a predictor of mortality.	1	Istanbul Univ., Turkey	acute myeloid leukemia			2006-2015	522			35% of the 522 patients with Blood Stream Infections had acute myeloid leukemia. 1016 organisms were isolated: Gram negative (G-) organisms accounted for 42.4% of the episodes, **Among G-, Enterobacteriaceae were 86%, E. coli at 34% extended-spectrum Beta-lactamases and Klebsiella spp at 48.3% ESBL; 20% of the Klebsiella spp had carbapenemase activity, and 5% colistin-resistant Klebsiella spp. 26.5k% of Psuedomonas spp and 60.7% of Acinetobacter spp has carbapenemase activity. [i.e., they are antibiotic-resistant]** **The tremendous rise in G- [antibiotic] resistance rates is dreadfully related to increasing mortality.**
20	Lung Cancer. 2020;141:44-55. Epub 2020/01/20. doi: 10.1016/j.lungcan.2019.12.015. PubMed PMID: 31955000. https://pubmed.ncbi.nlm.nih.gov/31955000/?otool=mdufdrlib	Jones GS et al	A systematic review of survival following anti-cancer treatment for small cell lung cancer.	1		small cell lung cancer				160	1.0%	irinotecan + cisplatin (mostly in Asian populations) carboplatin + etoposide	30-day mortality was the same for limited and extensive-stage SCLC
21	Int J Cancer. 2020;147(1):152-9. Epub 2019/11/14. doi: 10.1002/ijc.32788. PubMed PMID: 31721193; PubMed Central PMCID: PMCPMC7317578. https://pubmed.ncbi.nlm.nih.gov/31721193/?otool=mdufdrlib	Heeg et al	Association between initiation of adjuvant chemotherapy beyond 30 days after surgery and overall survival among patients with triple-negative breast cancer.	1	Netherlands	triple-negative breast cancer			2006-2014	3,016			Delayed initiation of chemotherapy >30 days after surgery is associated with < overall survival for breast-conserving surgery. There is no difference for patients who underwent mastectomy. 30-day mortality not given
22	Rev Med Chil. 2019;147(7):887-90. Epub 2019/12/21. doi: 10.4067/s0034-98872019000700887. PubMed PMID: 31859987. https://pubmed.ncbi.nlm.nih.gov/31859987/?otool=mdufdrlib	Pulgar et al	Mortality within 30 days of receiving systemic chemotherapy at a regional oncology unit	1	Chile	multiple	1	1		690	2.5%	ambulatory systemic	**International 30-day mortality standard is 5%**

23	Gynecol Oncol. 2019;155(1):58-62. Epub 2019/08/14. doi: 10.1016/j.ygyno.2019.08.004. PubMed PMID: 31402165. https://pubmed.ncbi.nlm.nih.gov/31402165/?otool=mdufdrlib	Narasimhulu et al	Using an evidence-based triage algorithm to reduce 90-day mortality after primary debulking surgery for advanced epithelial ovarian cancer.	1		**Mayo Clinic Rochester MN**	stage III-IV advanced epithelialal-ovarian		2012 - Jul 2016	232		neoadjuvant chemo	Use of the Mayo Triage Algorithm is associated with reduced 90-day mortality after primary debulking surgery and improved oncologic outcomes. **30-day mortality not given**	
24	Ann Surg. 2019;270(3):400-13. Epub 2019/07/10. doi: 10.1097/sla.0000000000003468. PubMed PMID: 31283563. https://pubmed.ncbi.nlm.nih.gov/31283563/?otool=mdufdrlib	Macedo et al	Survival Outcomes Associated With Clinical and Pathological Response Following Neoadjuvant FOLFIRINOX or Gemcitabine/Nab-Paclitaxel Chemotherapy in Resected Pancreatic Cancer.	1		multiple US univeristy cancer centers	pancreatic ductal adenocarcinoma (PDAC)	1	2018 or 2019	274	2.2%	neoadjuvant chemotherapy with FOLFIRINOX or gemcitabine/nab-paclitaxel followed by pancreatectomy	CONCLUSION: improved biochemical, pathological and clinical responses associated with NAC FLX or GNP result in improved OS, local recurrence-free survival and metasties free survival in PDAC patients.	
25	Lung Cancer. 2019;134:141-6. Epub 2019/07/20. doi: 10.1016/j.lungcan.2019.06.003. PubMed PMID: 31319972. https://pubmed.ncbi.nlm.nih.gov/31319972/?otool=mdufdrlib	Gibson AJW et al	Factors associated with early mortality in non-small cell lung cancer patients following systemic anti-cancer therapy: A 10 year population-based study.		1	Calgary, Canada	non-small cell lung cancer		2005-2014	1,044	**22.3%**	systemic anti-cancer therapies (SACT)	Risks of early death decreased for never-smokers and those receiving SACT in 2010-2014	
26	JAMA Netw Open. 2019;2(1):e186847. Epub 2019/01/16. doi: 10.1001/jamanetworkopen.2018.6847. PubMed PMID: 30646202; PubMed Central PMCID: PMCPMC6484874. https://pubmed.ncbi.nlm.nih.gov/30646202/?otool=mdufdrlib	Foster JM et al	Morbidity and Mortality Rates Following Cytoreductive Surgery Combined With Hyperthermic Intraperitoneal Chemotherapy [CRS/HIPEC] Compared With Other High-Risk Surgical Oncology Procedures [Whipple].	1		Univ. Nebraska, Omaha NE	liver, pancreas-duodenum, esophagus		1 Jan 2005 - 31 Dec 2015; analysis done in 2018	1822 CRS/HIPEC	2.5%	CRS/HIPEC	**Study cohort was 34,115 patients;** **30-day mortality was 1.1% for CRS/HIPEC vs 2.5% for Whipple**	
27	BMC Palliat Care. 2019;18(1):42. Epub 2019/05/22. doi: 10.1186/s12904-019-0427-4. PubMed PMID: 31109330; PubMed Central PMCID: PMCPMC6528308. https://pubmed.ncbi.nlm.nih.gov/31109330/?otool=mdufdrlib	Florin de Vasconcellos V, et al	Inpatient palliative chemotherapy is associated with high mortality and aggressive end-of-life care in patients with advanced solid tumors and poor performance status		1	Brazil	advanced solid tumors with poor performance status	1		228	44.3%	palliative chemotherapy	30-day mortality from start of palliative chemotherapy	
28	BMJ Support Palliat Care. 2019. Epub 2019/07/06. doi: 10.1136/bmjspcare-2019-001807. PubMed PMID: 31272999. https://pubmed.ncbi.nlm.nih.gov/31272999/?otool=mdufdrlib	Dizdar et al	Cancer chemotherapy: incidence and predictors of 30-day mortality.		1	Turkey	unspecified		2018?	4,560	1.7%	unspecified		

29	Lancet Oncol. 2019;20(7):984-97. Epub 2019/06/09. doi: 10.1016/s1470-2045(19)30150-0. PubMed PMID: 31175001. https://pubmed.ncbi.nlm.nih.gov/31175001/?otool=mdufdrlib	Cortes JE et al	Quizartinib versus salvage chemotherapy in relapsed or refractory FLT3-ITD acute myeloid leukaemia (QuANTUM-R): a multicentre, randomised, controlled, open-label, phase 3 trial.	1	152 hospitals and cancer centers in 19 countiies	acute myeloid leukemia	7 May 2014 - 13 Seo 2917	367		single-agent quizartinib vs salvage chemotherapy: cytarabine, mitoxantrone, etoposide, cytarabine, fludarabine, idarubicin	245 patients quizartinib 122 patients other chemo; most frequent adverse effects were febrile neutropenia and sepsis/septic shock. **30-day mortality not given**; but overall survival rate for quizartinib was median 6.2 mos vs 4.7 mos for other cehmo, but quizartin ib had m ore non-haemotological adverse effects than std chemo.
30	J Intensive Care Med. 2019;34(9):732-9. Epub 2017/06/06. doi: 10.1177/0885066617711894. PubMed PMID: 28578599. https://pubmed.ncbi.nlm.nih.gov/28578599/?otool=mdufdrlib	Calderon-Pelayo et al	Influence of Chemotherapy Within 30 Days Before ICU Admission on Mortality in Critically Ill Medical Patients With Cancer	1	Spain single institution study in an ICU of a tertiary univeristy hospital.		2005-2014	248	56.6%		cohort = 248 patients with cancer admitted to IC for non-surgical problems; 76 had received chemotherapy in one month before admission
31	Gynecol Oncol. 2019;154(3):622-30. Epub 2019/07/28. doi: 10.1016/j.ygyno.2019.07.011. PubMed PMID: 31349996. https://pubmed.ncbi.nlm.nih.gov/31349996/?otool=mdufdrlib	Bartels et al	A meta-analysis of morbidity and mortality in primary cytoreductive surgery compared to neoadjuvant chemotherapy in advanced ovarian malignancy.	1	Dublin, Ireland	advanced ovarian		3,759		neoadjuvant chemotherapy	The aim of this meta-analysis is to review the morbidity and mortality associated with primary cytoreductive surgery (PCS) compared to neoadjuvant chemotherapy and interval cytoreductive surgery (NACT + ICS) for advanced ovarian cancer. CONCLUSION: NACT+ICS < mortality and > cytoreduction vs PCS, with no survival benefit.
32	Asia Pac J Clin Oncol. 2018;14(2):e193-e202. Epub 2017/07/12. doi: 10.1111/ajco.12723. PubMed PMID: 28695617. https://pubmed.ncbi.nlm.nih.gov/28695617/?otool=mdufdrlib	Wong YET et al	Morbidity and mortality of elderly patients following cytoreductive surgery and Hyperthermic Intraperitoneal Chemotherapy (HIPEC).	1	Asia-Pacific region; single institution		Apr 2001 - Jul 2015	177	0.0%		Comparison between non-elderly (<= age 65) and elderly (< age 65) patients with peritoneal metasteses undergoing Cytoreductive surgery (CRS) + Hyperthermfic Interaperitoneal Cemotgherapy (HIPEC). 18 elderly and 159 non-elderly patients. CONCLUSION: there is no difference in 30-day mortality between the two groups
33	Pediatr Blood Cancer. 2018;65(4). Epub 2017/12/30. doi: 10.1002/pbc.26934. PubMed PMID: 29286576. https://pubmed.ncbi.nlm.nih.gov/29286576/?otool=mdufdrlib	Scalabre et al	Cytoreductive surgery and hyperthermic intraperitoneal perfusion with chemotherapy in children with peritoneal tumor spread: A French nationwide study over 14 years.	1	France	pediatric peritoneal tumors; peritoneal mesothelioma, desmoplastic small round cell tumors, pseudopapillary pancreatic, & other histologic types	2001-2015.	22		Cytoreductive surgery + hyperthermic peritoneal perfusion with chemotherapy (CRS+HIPEC)	Conclusion: patients with mesothelioma had significantly better overall survival rates than other histologic types. 30-day mortality not given.

34	J Thorac Oncol. 2018;13(4):543-9. Epub 2018/02/08. doi: 10.1016/j.jtho.2018.01.010. PubMed PMID: 29410127. https://pubmed.ncbi.nlm.nih.gov/29410127/?otool=mdufdrlib	Morgansztern et al	Early Mortality in Patients Undergoing Adjuvant Chemotherapy for Non-Small Cell Lung Cancer.	1	St. Louis, Missouri	non-small cell lung cancer		2004-2102	19,691	0.7%		30-day mortality from start of chemotherapy. CONCLUSION: early mortality with use of adjuvant chemotherapy after complete resection of NSCLC is a clinical concern. Risk is > in patients > 70 yrs old, with higher comorbidity scores and prolonged postoperative length of stay.
35	Prospective analysis of 30-day mortality following palliative chemotherapy at a tertiary cancer centre.	McCracken et al	Prospective analysis of 30-day mortality following palliative chemotherapy at a tertiary cancer centre. **// have full study//**	1	Australian Tertiary Cancer Centre - Sunshsine Hospital Day unit		1	1 yr period	314	6.6%		Worldwide 30-day mortality rates btgw 8.1% and 43%; previous Australian sudits btw 3.4% and 18%. 30-day mortality from start of chemo.
36	Ann Thorac Surg. 2018;105(4):1008-16. Epub 2018/02/18. doi: 10.1016/j.athoracsur.2017.10.056. PubMed PMID: 29453000. https://pubmed.ncbi.nlm.nih.gov/29453000/?otool=mdufdrlib	Krantz SB et al	Neoadjuvant Chemoradiation Shows No Survival Advantage to Chemotherapy Alone in Stage IIIA Patients.	1	Illinois	Stage IIIA operable non-small cell lung cancer		2006-2012	1,936	2.9%		Compares outcomes for neoadjuvant chemoradiotherapy 9NCRT) with neoadjuvant chemotherapy (NCT) alone. 30 day mortality for NCT = 1.3%; 30-day mortality for Ncrt = 2.9%
37	Cancer. 2018;124(24):4685-91. Epub 2018/09/29. doi: 10.1002/cncr.31760. PubMed PMID: 30264853. https://pubmed.ncbi.nlm.nih.gov/30264853/?otool=mdufdrlib	Kehl KL, et al	Hospitalization by cytotoxic chemotherapy regimen among older women with stage IV breast cancer.	1	**Dana-Farber in Boston MA; MD Anderson in Houston TX**	stage IV de novo breast cancer	1	2010-2013	693	19.0%	10 most common:	Primary outcome criterfia: hospitalization or death in <= 30 days of starting chemo. **RESULTS: Significant vcariation in outcome by chem regimen vs capecitabine: H/D rates higher with cyclophosphamide+docetaxel, cyclophosphamide++doxorubicin, docetaxel, and gemcitabine.**
38	Eur J Cancer. 2018;103:176-83. Epub 2018/09/28. doi: 10.1016/j.ejca.2018.07.133. PubMed PMID: 30261439. https://pubmed.ncbi.nlm.nih.gov/30261439/?otool=mdufdrlib	Jones GS et al	Factors influencing treatment selection and 30-day mortality after chemotherapy for people with small-cell lung cancer: An analysis of national audit data.	1	England	small cell lung cancer		(<=2018)	2,235	**7.8%**		
39	Cancer. 2018;124(9):1938-45. Epub 2018/02/17. doi: 10.1002/cncr.31296. PubMed PMID: 29451695; PubMed Central PMCID: PMCPMC6911353. https://pubmed.ncbi.nlm.nih.gov/29451695/?otool=mdufdrlib	Ho G, et al	Decreased early mortality associated with the treatment of acute myeloid leukemia at National Cancer Institute-designated cancer centers in California.	1	California at a a National Cancer Center Institute-designated Cancer Center	acute myueloid lukemia		1999-2014	1,726			Results: treatment at a NCI-CC is associated with lower early mortality (<= 60 days from diagnosis). **30-day mortality not specified.**
40	SEE Source D above.	Elfiky AA, et al										

41	Lancet Oncol. 2018;19(2):216-28. Epub 2018/01/18. doi: 10.1016/s1470-2045(18)30010-x. PubMed PMID: 29339097. https://pubmed.ncbi.nlm.nih.gov/29339097/?otool=mdufdrlib	DiNardo et al	Safety and preliminary efficacy of venetoclax with decitabine or azacitidine in elderly patients with previously untreated acute myeloid leukaemia: a non-randomised, open-label, phase 1b study.		1	**UC Davis and Stanford Univeristy, CA.**	acute myueloid lukemia in elderly patients			2014-2016	57	7.0%	venetgoclax/decitabine; venetoclax/azacitidine; venetoclas/decitabine with posaconazole.	multiple study sub-groups and dosages.
42	Ann Oncol. 2018;29(6):1437-44. Epub 2018/04/05. doi: 10.1093/annonc/mdy103. PubMed PMID: 29617710; PubMed Central PMCID: PMCPMC6354674. https://pubmed.ncbi.nlm.nih.gov/29617710/?otool=mdufdrlib	Derosa et al	Negative association of antibiotics on clinical activity of immune checkpoint inhibitors in patients with advanced renal cell and non-small-cell lung cancer.	1	1	Multiple sites, France, Canada, **& Sloan-Kettering in the US.**	kidney(advanced renal cell - RCC) and non-small cell lung cancer (NSCLC)						immune checkpoint inhibitors (ICI) in cancer	study of patients who received antibiotics within 30 days of receiving ICI agents. CONCLUSION: antibiotics are associated with reduced clinical benefit from ICI in RCC and NSCLC
43	ERJ Open Res. 2018;4(4). Epub 2018/11/09. doi: 10.1183/23120541.00030-2018. PubMed PMID: 30406123; PubMed Central PMCID: PMCPMC6215912 https://pubmed.ncbi.nlm.nih.gov/30406123/?otool=mdufdrlib	Burgers et al	30-day mortality after the start of systemic anticancer therapy for lung cancer: is it really a useful performance indicator?		1	Netherlands	unresectable stage II and IV lung cancer			2010-2015	26,277	6.2%	systemic anti-cancer therapy administered in 77 hospitals.	Other (not specified) studies: 30-day mortality rate = 5-10%; CONCLUSION: In Netherlands, 30-day mortality was comprable to earlier reports; 30-day mortality is not a meaningful indicator to monitor quality of care
44	JAMA Netw Open. 2018;1(6):e183023. Epub 2019/01/16. doi: 10.1001/jamanetworkopen.2018.3023. PubMed PMID: 30646220; PubMed Central PMCID: PMCPMC6324452 Conquer Cancer Foundation. https://pubmed.ncbi.nlm.nih.gov/30646220/?otool=mdufdrlib	Brooks GA et al	Hospitalization and Survival of Medicare Patients Treated With Carboplatin Plus Paclitaxel or Pemetrexed for Metastatic, Nonsquamous, Non-Small Cell Lung Cancer.	1		**Dartmouth College, Geisel School of Medicine, New Hampshire; Dana-Farber Cancer Institute, Boston MA.**	Metastatic non-squamous non-small cell lung cancer				3,310		carboplatin + paclitaxel vs. carbotplatin + pemetrexed with and without bevacisumab	Primary outcome measured was 30-day hospitalization within 30 days or chemo start. **30-day mortality not given.**
45	Intern Med J. 2018;48(4):403-8. Epub 2017/09/06. doi: 10.1111/imj.13618. PubMed PMID: 28872748. https://pubmed.ncbi.nlm.nih.gov/28872748/?otool=mdufdrlib	Ang E et al	Thirty-day mortality after systemic anticancer treatment as a real-world, quality-of-care indicator: the Northland experience.		1	Whangarei Base Hospital, Northland Region, New Zealand			1	1 Jan 2012 - 31 Dec 2016	1,103	5.17%	Systemic anti-cancer therapy (SACT)	patients who died within 30 days of last SACT treatment. CONCLUSION: WBH rates were comparable to studies from larger institutions.
46	N Z Med J. 2017;130(1460):63-72. Epub 2017/08/11. PubMed PMID: 28796772. https://pubmed.ncbi.nlm.nih.gov/28796772/?otool=mdufdrlib	Wilson M eet al	Mortality within 30 days of systemic anticancer therapy at a tertiary cancer centre: assessing the safety and quality of clinical care.		1	Auckland city Hospital, New Zealand			1	Oct 2014 - Sept 2015	1,965	2.2%	SACT (chemotheraby or biologic agents)	deaths within 30 days of SACT. CONCLUSION: ACH/NZ 30-day mortality rate compares favourably to international benchmarks of 5% and has improved slightly since an earlier study Oct 2008-Sep 2009. (2.2% now vs 2.8% then).

47	N Z Med J. 2017;130(1459):33-42. Epub 2017/07/21. PubMed PMID: 28727692. https://pubmed.ncbi.nlm.nih.gov/28727692/?otool=mdufdrlib	Ly NJ et al	Short-term outcomes following cytoreductive surgery and heated intra-peritoneal chemotherapy [CRS + IPC] at Waikato.		1	Waikato, Hamilton New Zealand	peritoneal with pseudomyxoma peritonei	1	1		68	1.4%		major complication rate with CRS+IPC = 24%; 76% of patients had pseudomyxoma peritonei.
48	Gland Surg. 2017;6(1):14-26. Epub 2017/02/18. doi: 10.21037/gs.2016.08.04. PubMed PMID: 28210548; PubMed Central PMCID: PMCPMC5293640. https://pubmed.ncbi.nlm.nih.gov/28210548/?otool=mdufdrlib	Landercasper et al	Does neoadjuvant chemotherapy [NAC] affect morbidity, mortality, reoperations, or readmissions in patients undergoing lumpectomy or mastectomy for breast cancer?	1		**Gunderson Medical Foundation and Health System, LaCrosse WI**	breast			2005-2012	30,309		Neoadjuvant chemotherapy (NAC)	NAC variable eliminated from the National Surgical Quality Improvemet Program database after 2012. Primary outcome measured was combined Morbidity/Mortality (M&M). 30-day mortality alone not given. RECOMMENDATION: NSQIP should reinstate NAC variable. **NAC was associated with > M&M inlumpectomy patients 2010-2012.**
49	Strahlenther Onkol. 2017;193(8):673-6. Epub 2017/07/02. doi: 10.1007/s00066-017-1170-5. PubMed PMID: 28667470. https://pubmed.ncbi.nlm.nih.gov/28667470/?otool=mdufdrlib	Gruber I., et al	[30-day mortality after systemic anticancer treatment : Population-based observational study on breast and lung cancer].		1	ENGLAND	breast & lung								**Article published in German. PDF available for $39.95.**
50	Lancet Oncol. 2017;18(11):1532-42. Epub 2017/10/17. doi: 10.1016/s1470-2045(17)30605-8. PubMed PMID: 29033099. https://pubmed.ncbi.nlm.nih.gov/29033099/?otool=mdufdrlib	Beer TM et al	Custirsen (OGX-011) combined with cabazitaxel and prednisone versus cabazitaxel and prednisone alone in patients with metastatic castration-resistant prostate cancer previously treated with docetaxel (AFFINITY): a randomised, open-label, international, phase 3 trial.		1	95 cancer treatment centres in 8 countries	metastatic castration-resistant prostate cancer			9 Sep 2012 - 29 Sep 2014	635	6.9%	Custirsen (OGX011) + cabazitaxel + prednisone	No survival benefit noted from the addition of Custirsen to the treatment regime.
51	Ann Hematol. 2017;96(9):1449-56. Epub 2017/06/10. doi: 10.1007/s00277-017-3042-6. PubMed PMID: 28597167. https://pubmed.ncbi.nlm.nih.gov/28597167/?otool=mdufdrlib	Abla O. , et al	Predictors of thrombohemorrhagic early death in children and adolescents with t(15;17)-positive acute promyelocytic leukemia treated with ATRA and chemotherapy.	1	1	multiple countries, incl US	acute promyeolocytic leukemia				683	4.7%	All-Trans Retinoic Acid (ATRA) + chemotherapy	
52	Lancet Oncol. 2016;17(9):1203-16. Epub 2016/09/07. doi: 10.1016/s1470-2045(16)30383-7. PubMed PMID: 27599138; PubMed Central PMCID: PMCPMC5027226. https://pubmed.ncbi.nlm.nih.gov/27599138/?otool=mdufdrlib	Wallington et al	30-day mortality after systemic anticancer treatment for breast and lung cancer in England: a population-based, observational study. **//also have full study//**		1	England multiple sites	breast, lung	1	1	1 Jan - 31 Dec 2014	32,862	BC 2.5% NSCLC 7.8% all LC 8.5%	systemic anti-cancer treatment (SACT)	Study of patients receiving SACT; 30-day mortality after receiving SACT. 2 breast cancer patients, 9634 NSCLC patients; **Certain subgroups (unspecified) are at a substantially increased risk of early and 30-day mortality. Exact figures not given in the abstract.** *Full study Fig 1: BC 28,364 patients, 700 deaths = 3% NSCLC 11,199 patients, 867 deaths = 7.8%; all LC: 15045 patients not excluded, 1274 deaths = 8.5%*

53	J Clin Oncol. 2016;34(11):1217-22. Epub 2016/02/24. doi: 10.1200/jco.2015.62.9683. PubMed PMID: 26903574; PubMed Central PMCID: PMCPMC4872322 online at www.jco.org	Low CA, et al	Depressive Symptoms in Patients Scheduled for Hyperthermic Intraperitoneal Chemotherapy With Cytoreductive Surgery: Prospective Associations With Morbidity and Mortality.	1		University of Pittsburgh, PA	colorectal and GI		2012?	98		HIPEC + CRS	Study measures 30-day morbidity and readmission and overall survival rates, but **not specifically 30-day mortality.** By the time the analysis was completed (medial follow-up = 49 months), 76% of patients had died, with a **median OS time of 11 months.**
54	Leuk Res. 2015;39(2):204-10. Epub 2015/01/03. doi: 10.1016/j.leukres.2014.11.031. PubMed PMID: 25554239. https://pubmed.ncbi.nlm.nih.gov/25554239/?otool=mdufdrlib	Roberts DA, et al	Low efficacy and high mortality associated with clofarabine treatment of relapsed/refractory acute myeloid leukemia and myelodysplastic syndromes	1		**Beth Israel Deaconess Medical Center, Dana-Farber Cancer Institute, Brigham and Women's Hospital, Boston MA**	acute myeloid leukemia and myelodysplastic syndromes			84	21.0%	clofarbamine alone vs with cytarabine	**CONCLUSION: Clofaraine's efficacy in real-world setting appears to be less than in clinical trials, and is a ssociated with a high early mortality rate.**
55	Asian Pac J Cancer Prev. 2015;16(4):1449-53. Epub 2015/03/07. doi: 10.7314/apjcp.2015.16.4.1449. PubMed PMID: 25743814. https://pubmed.ncbi.nlm.nih.gov/25743814/?otool=mdufdrlib	Phya VC, et al	Capecitabine pattern of usage, rate of febrile neutropaenia and treatment related death in asian cancer patients in clinical practice		1	Univeristy of Malaya Medical Centre.	multiple, colorectal predominating, followed by breast	1	1 Jan 2009 - 31 June 2010 [sic]	274	5.1%	oral capacitabine as replacement for 5-flouroracil; also XELOX and ECX	Study on risk of febrile neutropenia and treatment-related death. Most chemo in palliative setting, followed by adjuvant. Overal FN rate was 2.2% and opverall TRD rate was 5.1%
56	Eur J Surg Oncol. 2015;41(7):920-6. Epub 2015/04/25. doi: 10.1016/j.ejso.2015.03.226. PubMed PMID: 25908010. https://pubmed.ncbi.nlm.nih.gov/25908010/?otool=mdufdrlib	Klevebro et al	Morbidity and mortality after surgery for cancer of the oesophagus and gastro-oesophageal junction: A randomized clinical trial of neoadjuvant chemotherapy vs. neoadjuvant chemoradiation.		1	7 centers in Sweden and Norway	esophageal			155	**0.0%**	neoadjuvant chemotherapy vs. neoadjuvant chemoradiotherapy. 3 cycles of cisplatin/5-flourouracil for all patients, plus 40 Gy concomitant radiation for NCRT	severity of complications was greater after NCRT.
57	Eur J Cancer. 2015;51(2):233-40. Epub 2014/12/17. doi: 10.1016/j.ejca.2014.11.011. PubMed PMID: 25500146. https://pubmed.ncbi.nlm.nih.gov/25500146/?otool=mdufdrlib	Khoja L, et al	Mortality within 30 days following systemic anti-cancer therapy, a review of all cases over a 4 year period in a tertiary cancer centre		1	UK			2009-2013	**31,183**	4.0%	Systemic Anti-Cancer Therapy (SACT)	
58	Ann Surg Oncol. 2015;22(5):1680-5. Epub 2014/08/15. doi: 10.1245/s10434-014-3977-y. PubMed PMID: 25120250. https://pubmed.ncbi.nlm.nih.gov/25120250/?otool=mdufdrlib	Ihemelandu et al	Iterative cytoreductive surgery and hyperthermic intraperitoneal chemotherapy for recurrent or progressive diffuse malignant peritoneal mesothelioma: clinicopathologic characteristics and survival outcome. **// have full study//**	1		Washington Cancer Institute, Washington DC	difuse malignant peritoneal mesothelioma		1989-2012	205	**0.0%**	CRS + HIPEC	**No 30-day mortality following iterative procedures.**

59	J Clin Neurosci. 2015;22(6):998-1001. Epub 2015/03/15. doi: 10.1016/j.jocn.2015.01.005. PubMed PMID: 25769250. https://pubmed.ncbi.nlm.nih.gov/25769250/?otool=mdufdrlib	Hein PN, et al	Influence on morbidity and mortality of neoadjuvant radiation and chemotherapy among cranial malignancy patients in the postoperative setting.	1	NY University & Columbia Univ., NY NY	metastatic brain tumors		2006-2012	1,044		neoadjuvant chemotherapy; neoadjuvant radiotherapy, vs no chemo or radiation.	**neoadjuvant chemotherapy was associated with a 2.4X increase in risk of 30-day mortality vs no chemotherapy. Specific numbers not given.** Neoadjuvant radiotherapy was not associated with an inbcerease in 30-day morbidity or mortality, and therefore may be safer
60	Ann Surg Oncol. 2015;22(5):1645-50. Epub 2014/08/15. doi: 10.1245/s10434-014-3976-z. PubMed PMID: 25120249; PubMed Central PMCID: PMCPMC4329108. https://pubmed.ncbi.nlm.nih.gov/25120249/?otool=mdufdrlib	Doud AN, et al	Impact of distal pancreatectomy on outcomes of peritoneal surface disease treated with cytoreductive surgery and hyperthermic intraperitoneal chemotherapy. **// have full study //**	1	**Wake-Forest Univ**, Winston-Salem NC	peritoneal surface disease		1991-2013	1,019	3.2%	CRS/HIPEC	upper left quadrant peritoneal surface disease may require distal pancreatectomy (DP) to achive completge cytoreduction. Low Grade Appendiceal (LDA) cancer is a frequent complication 30-day mortality was 2.6% of 63 patients with DP, and 3.2% of patients without DP.
61	Clin Oncol (R Coll Radiol). 2014;26(4):236. Epub 2014/01/21. doi: 10.1016/j.clon.2013.12.005. PubMed PMID: 24439656. https://pubmed.ncbi.nlm.nih.gov/24439656/?otool=mdufdrlib	Silverman R, et al	Benchmarking 30 day mortality after palliative chemotherapy for solid tumours.	1	Nottingham University, UK	solid tumors	1					**No abstract available**
62	BMC Infect Dis. 2014;14:286. Epub 2014/06/03. doi: 10.1186/1471-2334-14-286. PubMed PMID: 24884397; PubMed Central PMCID: PMCPMC4039648. https://pubmed.ncbi.nlm.nih.gov/24884397/?otool=mdufdrlib	Rosa RG, et al	Association between adherence to an antimicrobial stewardship program [ASP]and mortality among hospitalised cancer patients with febrile neutropaenia: a prospective cohort study.	1	tertiery hospital in Brazil	febrile neutropenia (FM) in hospitalised hematology patients (leukemia)		Oct 2009 - Aug 2011	169		not specified	Study to assess the association between adherence to an antimicrobial stewardship program (ASP) and lower mortality among hospitalized cancer patients with FN. **28-day mortality was lower in patients adhering to an ASP.**
63	Asian Pac J Cancer Prev. 2014;15(23):10263-6. Epub 2015/01/06. doi: 10.7314/apjcp.2014.15.23.10263. PubMed PMID: 25556458. https://pubmed.ncbi.nlm.nih.gov/25556458/?otool=mdufdrlib	Phua CE et al	Risk of treatment related death and febrile neutropaenia with first line palliative chemotherapy for de novo metastatic breast cancer in clinical practice in a middle resource country.	1	University of Malaya Medical Centgre	metastatic breast cancer	1	1 Jan 2002 - 31 Dec 2011	186	3.2%	5-flourouracil + epirubicin + cyclophosphamide	Treatment-related death is death within 30 days of last chemo, as a consequence of chemo. Median survival (MS) for the entire cohort was 19 mos; for multiple metastatic sites 18 mos; for liver only 24 mos, for lung only 19 mos, for bone only 24 mos for brain only 8 mos.
64	Br J Surg. 2014;101(4):321-38. Epub 2014/02/05. doi: 10.1002/bjs.9418. PubMed PMID: 24493117. https://pubmed.ncbi.nlm.nih.gov/24493117/?otool=mdufdrlib	Kumagai et al	Meta-analysis of postoperative morbidity and perioperative mortality in patients receiving neoadjuvant chemotherapy or chemoradiotherapy for resectable oesophageal and gastro-oesophageal junctional cancers.	1	Karolinska University Hospital, Stockholm, SWEDEN	oesophageal					neoadjuvant chemotherapy vs. neoadjuvant chemoradiotherapy.	23 relevant studies; CONCLUSION: Neither NAC nor NACR for oesophageal carcinoma increases risk of …perioperative mortality compared with surgery alone. Care should be taken with NACR in oesophageal squamouis cell carcinoma where> risk of postoperative and treatment-related mortality was apparent

65	. Clin Oncol (R Coll Radiol). 2014;26(12):807. Epub 2014/09/30. doi: 10.1016/j.clon.2014.09.005. PubMed PMID: 25262844. https://pubmed.ncbi.nlm.nih.gov/25262844/?otool=mdufdrlib	Boardman A et al	The assessment of deaths after radiotherapy is an essential part of service evaluation—results of a 30 day mortality audit of patient deaths after palliative radiotherapy.		1	Royal Preseon Hospital, University of Manchyester, UK		1				radiotherapy (not chemo)	**abstract not available**
66	J Clin Neurosci. 2014;21(11):1895-900. Epub 2014/07/30. doi: 10.1016/j.jocn.2014.05.010. PubMed PMID: 25065847. https://pubmed.ncbi.nlm.nih.gov/25065847/?otool=mdufdrlib	Abt NB, et al	Concurrent neoadjuvant chemotherapy is an independent risk factor of stroke, all-cause morbidity, and mortality in patients undergoing brain tumor resection.	1		**Johns Hopkins University, Baltimore MD.**	brain		2006-2012	3,812	2.4%	152 patients on neoadjuvant chemotherapy (NC)	Of the 92 patients who died within 30 days, 10 were on NC CONCLUSION: Concurrent NC is associated with > risk of short term stroke with neurological deficit, all-cause morbidity, and mortality in patients undergoing brain tumor resection.
67	Am J Hematol. 2013;88(10):906-9. Epub 2013/07/06. doi: 10.1002/ajh.23530. PubMed PMID: 23828018. https://pubmed.ncbi.nlm.nih.gov/23828018/?otool=mdufdrlib	Wenzell CM et al	Outcomes in obese and overweight acute myeloid leukemia patients receiving chemotherapy dosed according to actual body weight **// have full study //**	1		Cleveland Clinic Cleveland OH	acute myeloid leukemia (excluding acute promyelocytic leukemia)		2002-2009	247	4.4%	anthracycline, cytarabine-based remission induction chemotherapy doses according to body weight	**4.4% 30-day mortality is composite average of: underweight/normal normal weight patients (33%), overweight 33% and obese (34%) at 3.7%, 2.5% and 7.1% respectively.**
68	Ann Surg Oncol. 2013;20(12):3899-904. Epub 2013/06/27. doi: 10.1245/s10434-013-3087-2. PubMed PMID: 23800899; PubMed Central PMCID: PMCPMC3968533. https://pubmed.ncbi.nlm.nih.gov/23800899/?otool=mdufdrlib	Votanopoulos KI, et al	Obesity and peritoneal surface disease: outcomes after cytoreductive surgery with hyperthermic intraperitoneal chemotherapy for appendiceal and colon primary tumors. **//have full study//**	1		Wake-Forest Univ, Winston-Salem NC	appendiceal, colon with peritoneal surface disease			246	2.5%	Cytoreductive surgery + hyperthermic peritoneal perfusion with chemotherapy (CRS+HIPEC)	**37% of US population is obese.** Study of how obesity influences operative and survival outcomes of CRS+HIPEC procedures. **30-day mortality = 1.5% for obese patients and 2.5% for non-obese patients.**
69	Ann Surg Oncol. 2013;20(4):1088-92. Epub 2013/03/05. doi: 10.1245/s10434-012-2787-3. PubMed PMID: 23456381; PubMed Central PMCID: PMCPMC3901309. https://pubmed.ncbi.nlm.nih.gov/23456381/?otool=mdufdrlib	Votanopoulos KI, et al	Cytoreductive surgery with hyperthermic intraperitoneal chemotherapy in peritoneal carcinomatosis from rectal cancer.	1		Wake-Forest Univ, Winston-Salem NC	peritoneal carcinomas [PC] from rectal and colon cancers			217	5.0%	cytoreductive surgery (CS) with hyperthermic intraperitoneal chemotherapy (HIPEC)	13 patients with PC from rectal cancer; 204 patients with PC from colon cancer. **30-day mortality was 5% for colon cancer, and 0% for rectal cancer.**
70	Ann Surg Oncol. 2013;20(11):3497-503. Epub 2013/06/20. doi: 10.1245/s10434-013-3053-z. PubMed PMID: 23780382; PubMed Central PMCID: PMCPMC3881978. https://pubmed.ncbi.nlm.nih.gov/23780382/?otool=mdufdrlib	Votanopoulos KI, et al	Outcomes of Cytoreductive Surgery (CRS) with hyperthermic intraperitoneal chemotherapy (HIPEC) in patients older than 70 years; survival benefit at considerable morbidity and mortality. **// have full study//**	1		Wake-Forest Univ, Winston-Salem NC	appendiceal, mesothelioma, ovarian, colon, gastric		1991-2011	81	13.6%	cytoreductive surgery (CRS)+ hyperthermic intraperitoneal chemotherapy (HIPEC)	CONCLUSION: HIPEC in the elderly is associated with a steep learning curve and considerable morbidity and mortality. However, age alone is not a contraindication for the procedure. Institutional experience and stringent patient selection are key factors for prolonged survival.

71	Ann Surg Oncol. 2013;20(11):3519-26. Epub 2013/06/12. doi: 10.1245/s10434-013-3049-8. PubMed PMID: 23748607. https://pubmed.ncbi.nlm.nih.gov/23748607/?otool=mdufdrlib	Ihemelandu CU, et al	Predicting postoperative morbidity following cytoreductive surgery with hyperthermic intraperitoneal chemotherapy (CS+HIPEC) with preoperative FACT-C (Functional Assessment of Cancer Therapy) and patient-rated performance status.	1	...	Wake Forest School of Medicine, Winston-Salem NC	peritoneal carcinomatosis			387	**7.7%**	CS+HIPEC	
72	Int J Cancer. 2013;133(8):1859-66. Epub 2013/04/09. doi: 10.1002/ijc.28192. PubMed PMID: 23564267. https://pubmed.ncbi.nlm.nih.gov/23564267/?otool=mdufdrlib	Dassen AE et al	Changes in treatment patterns and their influence on long-term survival in patients with stages I-III gastric cancer in The Netherlands.		1	Netherlands	stage I-III gastric (cardia and non-cardia) cancers		1989-2009			Since 2005 more patients are treated with (neo)adjuvant chemotherapy	**post-operative mortality ranged from 1% - 7% for cardia cancers and from0.4-12.2% for non-cardia cancers.**
73	Ann Oncol. 2013;24(2):420-8. Epub 2012/10/03. doi: 10.1093/annonc/mds336. PubMed PMID: 23028040. https://pubmed.ncbi.nlm.nih.gov/23028040/?otool=mdufdrlib	Aggarwal et al	Relationship among circulating tumor cells, CEA [carcinoembryonic antigen] and overall survival in patients with metastatic colorectal cancer.	1	1	muiltiple global and US universities	metastatic colorectal			217			mortality not discussed.
74	Asia Pac J Clin Oncol. 2012;8(4):325-9. Epub 2012/08/18. doi: 10.1111/j.1743-7563.2011.01498.x. PubMed PMID: 22897423. https://pubmed.ncbi.nlm.nih.gov/22897423/?otool=mdufdrlib	Yoong et al	Mortality within 30 days of receiving systemic anti-cancer therapy at a regional oncology unit: what have we learned?		1	a regional Victorian oncology center in Ballarat, Australia	epithelial malignancies and hematological malignancies (excluding acute leukemia)	1	1 Jan - 31 Dec 2008	378	3.4%	systemic anti-cancer therapies (SACT)	Benefits of SACT occur at a cost of significant toxicities that can be life-threatening. No published Australian data on SACT mortality outlide clinical trials exist. CONCLUSION: Ballarat outcome data are similar to limited current international data.
75	Can J Anaesth. 2012;59(8):758-65. Epub 2012/05/29. doi: 10.1007/s12630-012-9735-3. PubMed PMID: 22638675. https://pubmed.ncbi.nlm.nih.gov/22638675/?otool=mdufdrlib	Turan A et al	Chemotherapy within 30 days before surgery does not augment postoperative mortality and morbidity. **// have full study //**	1		Cleveland Clinic Cleveland OH				1,348	2.2%	any chemo	US-patients study pub in Canadian Journal of Anaesthesiology
76	Lung Cancer. 2012;76(2):216-21. Epub 2011/11/15. doi: 10.1016/j.lungcan.2011.10.010. PubMed PMID: 22078278. https://pubmed.ncbi.nlm.nih.gov/22078278/?otool=mdufdrlib	Rivera C et al	Are postoperative consequences of neoadjuvant chemotherapy for non-small cell lung cancer more severe in elderly patients?		1	French Society of Thorasic and Cardiovascular Surgerey, Paris, France	non-small-cell lung cancer (NSCLC)		Jan 2005 - Dec 2009	81	4.9%		Study of patients with NSCLC >= age 75; 81 matched-to-control patient pairs found from 1510 patient candidates. 30-day mortality was 2.5% in the under-75 control group. Post-operative morbidity is more important in elderly patients. 30-day mortality difference is not significant.

77	Asian Pac J Cancer Prev. 2012;13(9):4623-6. Epub 2012/11/22. doi: 10.7314/apjcp.2012.13.9.4623. PubMed PMID: 23167391. https://pubmed.ncbi.nlm.nih.gov/23167391/?otool=mdufdrlib	Phua CE et al	Risk of treatment related death and febrile neutropaenia with taxane-based adjuvant chemotherapy for breast cancer in a middle income country outside a clinical trial setting.	1	Univ. Malaysia Medical Centre	early breast, stages I,II, III		2007-2011	209	0.0%	adjuvant taxane-based chemotherapy - 209 patients other chemo - 413 patients	CONCLUSION: adjuvant taxane-0based chemotherapy at UMMC has a FN rate of 10%, but 0% Treatment-Related-Death (derfined as death accuringduring or within 30 days of completing chemo as a consequence of the chemo.
78	Haematologica. 2012;97(2):227-34. Epub 2011/10/14. doi: 10.3324/haematol.2011.047506. PubMed PMID: 21993673; PubMed Central PMCID: PMCPMC3269482. https://pubmed.ncbi.nlm.nih.gov/21993673/?otool=mdufdrlib	Iland H et al	Results of the APML3 trial incorporating all-trans-retinoic acid and idarubicin in both induction and consolidation as initial therapy for patients with acute promyelocytic leukemia.	1	Australia: Australasian Lukaemia and Lymphoma Group	acute promyelocytic leukemia (newly diagnosed)			101	8.0%	all-trans-retinoic acid + idarubicin as anti-leukemic therapy for both induction and consolidation; then ATRA+methotrexate and 6-mercaptopurine for maintenance.	
79	Clin Transl Oncol. 2011;13(6):426-9. Epub 2011/06/18. doi: 10.1007/s12094-011-0677-y. PubMed PMID: 21680304. https://pubmed.ncbi.nlm.nih.gov/21680304/?otool=mdufdrlib	Sánchez-Muñoz A, et al	Limited impact of palliative chemotherapy on survival in advanced solid tumours in patients with poor performance status.	1	Medical Oncology Department, Hospital Universitario Virgen de la Victoria, Málaga, Spain.	advanced solid tumors and poor general status	1		92	49.0%		**only 23% of patients lived longer than 90 days. CONCLUSION: Palliative chemotherapy for patients with AST and ECOG 3-4 scores with short life expectancy provided no benefit for survival.**
80	J Surg Oncol. 2011;104(6):692-8. Epub 2011/06/30. doi: 10.1002/jso.22017. PubMed PMID: 21713780. https://pubmed.ncbi.nlm.nih.gov/21713780/?otool=mdufdrlib	Gill RS et al	Treatment of gastric cancer with peritoneal carcinomatosis by cytoreductive surgery and HIPEC: a systematic review of survival, mortality, and morbidity.	1	Univ. of Alberta, Edmonton, Canada	gastric with peritoneal carcinomas		2000-2010		4.8%	CRS+ HIPEC	gastric cancer with perito0nkeal carcinomas has very poor prognosis. Medial overall survival was 7.9 months.
81	Ann Oncol. 2010;21(2):415-8. Epub 2009/07/28. doi: 10.1093/annonc/mdp330. PubMed PMID: 19633046. https://pubmed.ncbi.nlm.nih.gov/19633046/?otool=mdufdrlib	Mol L, et al	A prospective monitoring of fatal serious adverse events (SAEs) in a Dutch Colorectal Cancer Group (DCCG) phase III trial (CAIRO) in patients with advanced colorectal cancer.	1	Netherlands	advanced colorectal			40		Capecitabine-Irinotecan-Oxaliplatin study	Goal: assess 30-day mortality from last administration of study drugs (excludes disease progression). Initial cohort was 820, of which 40 were selected for detailed review. **CONCLUSION: little agreement between causal relation assessed by local investigator vs independent data monitoring committee. 30-day mortality due to chemo regieme could not be assessed. A quality control program is needed to prevent Major Protocol Violations.**

82	Oncologist. 2009;14(7):752-9. Epub 2009/07/15. doi: 10.1634/theoncologist.2008-0257. PubMed PMID: 19596665. https://pubmed.ncbi.nlm.nih.gov/19596665/?otool=mdufdrlib	Hashimoto K, et al	Factors that affect the duration of the interval between the completion of palliative chemotherapy and death.		1	National Cancer Center Hospital, Tokyo, Japan	breast, gynecological, primary unknown & others	1	2002-2006	255	12.6%		Study to identifyu factors affecting duration of interval between completion of palliative chemo and death. Primary indicators of short survival were males aged <=45 with obvious symptoms and poor Eastern Cooperatve Oncology Group preformance scores, who had not been given info about other palliative care options
83	HPB (Oxford). 2009;11(8):645-55. Epub 2010/05/25. doi: 10.1111/j.1477-2574.2009.00107.x. PubMed PMID: 20495632; PubMed Central PMCID: PMCPMC2799617. https://pubmed.ncbi.nlm.nih.gov/20495632/?otool=mdufdrlib	Fahy BN et al	Chemotherapy within 30 days prior to liver resection does not increase postoperative morbidity or mortality.		1	Methodist Hospital, Houston TX	metastatic liver		2005-2007	184	2.0%		Study of chemo within 30 days prior to liver resection; Total cohort was 2331 patients: 2147 no chemo, 184 chemo. 30-day mortality was 2% for chemo group and 3% for no-chemo grouip.
84	Clin Oncol (R Coll Radiol). 2009;21(9):730. Epub 2009/07/31. doi: 10.1016/j.clon.2009.07.001. PubMed PMID: 19640691. https://pubmed.ncbi.nlm.nih.gov/19640691/?otool=mdufdrlib	Bradshaw A et al	Thirty-day mortality for patients with genitourinary malignancies being treated with chemotherapy.		1	UK							ABSTRACT NOT AVAILABLE. Article published in *Clinical Oncology* (partner with *Royal College of Radiologists*). CO is Published by Elsevier.
85	Ann Surg Oncol. 2008;15(3):754-63. Epub 2007/12/15. doi: 10.1245/s10434-007-9701-4. PubMed PMID: 18080166. https://pubmed.ncbi.nlm.nih.gov/18080166/?otool=mdufdrlib	Gusani NJ et al	Aggressive surgical management of peritoneal carcinomatosis with low mortality in a high-volume tertiary cancer center **//have full study //**		1	in a high-volume regional perfusion program, U. Pittsburg, PA	peritoneal carcinomatosis: appendiceal, colorectal, ovarian, peeritoneal mesothelioma.		Jan 2002 - March 2005	122	1.6%	CRS + HIPEC	in-hospital mortality was 0%. CONCLUSION: in a high volume center with extensive experience treating peritoneal malignancies, perioperative mortality can be lowered to near zero, although morbidity remains high. Appendiceal cancer has better survival, colorectal worse
86	Br J Cancer. 2006;95(12):1632-6. Epub 2006/12/13. doi: 10.1038/sj.bjc.6603498. PubMed PMID: 17160081; PubMed Central PMCID: PMCPMC2360753. https://pubmed.ncbi.nlm.nih.gov/17160081/?otool=mdufdrlib	O'Brien ME, et al	Mortality within 30 days of chemotherapy: a clinical governance benchmarking issue for oncology patients. **//SAME AS REFERENCE B ABOVE//**		1	Royal Marsden Hospital, Sutton, Surrey UK	solid tumours and haemological malignancies, subsets for breast, gastrointestinal malignancy	1	1	Apr - Sep 2005	1,976	**8.1%**	unspecified	161 deaths overall, but only 12 in the subsets for potentially curative chemo for breast and gastrointestinal malignancy had mortality rates of 0.5% and 1.5% respectively.
87	Lasers Surg Med. 2001;29(4):323-7. Epub 2001/12/18. doi: 10.1002/lsm.1124. PubMed PMID: 11746109. https://pubmed.ncbi.nlm.nih.gov/11746109/?otool=mdufdrlib	Maier A., et al	Does new photosensitizer improve photodynamic therapy in advanced esophageal carcinoma?		1	Austria	advanced esophageal			49	0.0%	polyhematoporphyrin (Photosan); 5-aminolaevulinic acid (ALA) + hyperbaric oxygenization.	Study to compare efficacy of ALA vs Photosan for photodynamic therapy (PDT): 22 patients with ALA, 27 with Photosan. CONCLUSION: Photosan is more effective in PDT. Median survival times were 8 mos for ALA vs 9 mos for Photosan.

88	Am J Hematol. 1999;62(3):139-43. Epub 1999/10/28. doi: 10.1002/(sici)1096-8652(199911)62:3<139::aid-ajh2>3.0.co;2-f. PubMed PMID: 10539879. https://pubmed.ncbi.nlm.nih.gov/10539879/?otool=mdufdrlib	Ruiz-Arguelles, et al	All trans-retinoic acid decreases early mortality in patients with promyelocytic leukemia and can be given entirely on an outpatient basis.		1	Centro de Hematología y Medicina Interna de Puebla, Mexico	acute promyleocytic leukemia				43	44.0%	all-trans-retinoic acid (ATRA) - 27 patients; conventional chemo - 16 patients; & all patients got myelosuppressive chemo after initial treatment.	**5-day mortality: 0% for ATRA, and 44% for conventional chemo; 28-day mortality was 4% for ATRA and 44% for conventional chemo.** 13 ATRA patients were fully outpatient. ***My observation: you're dead pretty fast with conventional chemo. Other survival attributes are much better with ATRA!***
89	Ann Surg Oncol. 1997;4(5):440-5. Epub 1997/07/01. doi: 10.1007/bf02305559. PubMed PMID: 9259973. https://pubmed.ncbi.nlm.nih.gov/9259973/?otool=mdufdrlib	Taber SW, et al	Mortality, major amputation rates, and leukopenia after isolated limb perfusion with phenylalanine mustard for the treatment of melanoma. **// have full study //**	1	1	treatment at several centers worldwide; study done at Univ. of Louisville School of Medicine, KY	cutaneous melanmoma			1980-1995	>2000	0.6%	isolated perfusion with phenylalanine mustard alone or combined with other agents.	13 global studies: Death often resulted from cardiopulmonary complications or overwhelming sepsis from leukopenia. Leukopenia was caused by leakage of chemotherapeutic agents into systemic circulation
A	Cancer Reports: 2018:1:e1135 https://doi.org/10.1002 cnr 2.1135	McCracken et al	Prospective Analysis of 30-day Mortality following palliative chemotherapy at a tertiary cancer centre		1	Victoria, Australia		1		Dec 2014 - Dec 2015	314	**6.6%**		**retrospective audits worldwide put 30-day mortality figure 8.1-43%; prev Australian audits at 3.4-18%**
AA97	Cancer 2006 May; 106(10):2258-66	Kuderer, et al	Mortality, morbidity and cost associated with febrile neutropenia in adult cancer patients	1		data from 115 U.S. medical centers; study by Wilmont Cancer Center and Dept of Medicine, Univ.of Rochester NY	febrile neutropenia in adult cancer patients			1995-2000	**41,799**	9.5%		**Mortality for patients: OVERALL IN-HOSPITAL MORTALITY WAS 9.5% no major comorbidities = 2.6%; o major comorbidity = 10.3%; >1 major comorbidity = >=21.4%** median time to death was 17 days; **81 of the 161 deaths occurred in hospital;** 12 of the 161 patient deaths were receiving potentially curative chemo; 30-day mortalityt for breast cancer 0.5%; and 1.5% for for gastrointestinal cancer.
B	British Journal of Cancer (2006) 95 1632-1636; doi: 10.1038/sj.bjc6603498	O'Brien et al	Mortality within 30 days of Chemotherapy: a clinical governance benchmarking issue for oncology Patients **//SAME AS REFERENCE 86 BELOW//**		1	UK	multiple	1	1	Apr-Sep 2005	1,976	**8.1%**		
C	NZMJ 11 Aug 2017, vol 130 No 1460, ISSN 1175-8716	Wilson et al	Mortality within 30 days of systemic anticancer therapy at a tertiary cancer centre: assessing the safety and quality of clinical care		1	Auckland NZ	multiple	1	1	Oct 2014 - Sep 2015	1,965	2.2%		59.6% of deaths occurred in-hospital; comparison to other areas: Ballarat Aus - 3.4%; Royal Marsden UK 8.1%; Christie UK 4%
D	JAMA Network Open. 2018; 1(3):e180926. doi:10.1001/jamanetworkopen.2018.09026	Ellfiky et al	Development abd Application of a Machine Learning Approach to Assess Short-term Mortality Risk Among Patients with Cancer starting chemotherapy	1		**Dana-Farber/Brigham and Women's Cancer Center, Boston MA**	multiple - most common = breast, colorectal, lung			1 Jan 2004 - 31 Dec 2014	26,946	2.1%	most common = carboplatin and paclitaxel, gemcitabine hydrochloride, albumin-bound paclitaxel	**30-day mortality from start of chemo**; highest-risk decile = 22.6%; lowest risk = 0%
E	Leukemia & Lymphoma, 62:8, 1949-1957, DOI: 10.1080/10428194.2021.1894651 https://doi.org/1080/10428194.2021.1894651	Dhakal et al	Early mortality and overall survival in acute promyelocytic leukemia: do real-world data match results of the clinical trials **//have .docx abstract//**	1		Univ. Nebraska, Omaha NE Puyallup WA; Yale Univ. New Haven CT; Cleveland Clinic Weston FL	acute promyeolocytic leukemia			2004-2015	7,190	**12.0%**		30-day mortality by age group: 6% at <18; 6% at 19-40; 10%@41-60; 21% at >60; **this largest APL database study to date demonstrates that early mortality from APL remains high in real-world practices in the US despite recent advances in clinical trials in last 10 years.**

F	https://doi.org 10.1016/j.athoracsur.2019.10.057	Horne et al	Drivers of 30- and 90-day Postoperative Death after Neoadjuvant Chemoradiation for Esophageal Cancer	1		Allegheny Health Ntwk Cancer Institute, Pittsburgh PA; City of Hope Hospital, Duarte CA; Hillman Cancer Centeer U.Pittsburgh Med Ctr.	esophageal			2004-2014	7,691	2.9%	neoadjuvant chemoradiotherapy and esophagectomy 75% of patients received <= 50.4Gy radiation dose	Patients with adenocarcinomas experienced lower rates of 30 and 90-day mortality vs patients with squamous cell carcinomas.
G	Indian Journal of Medical and Paediatric Oncology, Jan-Mar 2015, Vol 36 Issue 1 doi: 10.4103/0971-5851.151792	Karim et al	Time from last chemotherapy to death and its correlation with end of life care in a feferral hospital		1	King Faisal Specialist Hospital, Riyadh, Saudia Arabia; National Cancer Institute, Cairo, Egypt	multiple	1	1	Jan 2010 - Jan 2012				**many patients in Saudi Arabia die in the hospital.** Lack of structured hospice system. adult patients who received chemo and died in hospital in <= 60 days = 41. TOTAL COHORT NOT GIVEN.

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Waiting on additional information from author:

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Added 3/24/22: Beak Consultants Ltd., Soil and Groundwater Quality Study of the Mount Pleasant Cemetery, July 1992. Available from the Toronto, Ontario, Canada central Library.

From: Donald E. Chamberlin
To: MCP-Chair
Subject: PWPA materials #2 re Item 11 Reflection Park Agenda for 12-15-2022
Date: Wednesday, December 14, 2022 11:45:52 AM
Attachments: Okeefe - Copy of NIOSH 2014 Hazardous Drugs w Excretion Data 2022Mar23-1.xlsx

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Please see the attached file re NIOSH hazardous chemotherapy chemicals.

Donald E. Chamberlin, Representative
Patuxent Watershed Protective Association
PO BOX 512
Burtonsville MD 20811
301-421-9013

NIOSH 2014 Hazardous Drug List (184 Drugs) - Analysis of Excretion and Method of Action

Awaiting final list for 2020 (https://www.cdc.gov/niosh/docket/review/docket233c/pdfs/DRAFT-NIOSH-Hazardous-Drugs-List-2020.pdf)
NCCN Drugs for Use in Cancer (226 drugs,
Antineoplastic NOTon NCCN List/no longer in use

NIOSH 2014 Hazardous Drugs	Reason for listing	AHFS Pharmacologic-therapeutic classification	Excretion		Maximum Recommended Dose		Total max Recommend Dose Male (80 Kg Avg)		Est Maximum Daily Conc in Human Bodily Waste(mg/L, ppm)		Notes
			Top % low = <3%	Days							
Abacavir	FDA Pregnancy Category C; malignant tumors observed in male and female mice and rats; genotoxic in in vivo micronucleus test.	8:18.08.20 nucleoside and reverse transcriptase inhibitors	low								anti-viral for the treatment of HIV-1 infection
Abiraterone	FDA Pregnancy Category X	10:00 Antineoplastic agents	77%	1	1000	mg/day	1000	mg	770	mg/L	CYP17 enzyme inhibitor
Acitretin	Black Box warning on adverse reproductive effects; FDA Pregnancy Category X	88:04 Vitamin A	0%								Retinoid
Ado-trastuzumab emtansine	Conjugated monoclonal antibody; FDA Pregnancy Category D	10:00 Antineoplastic agents	0%								Antibody drug conjugate
Alefacept	Increased frequency of malignancies observed in treated patients; FDA Pregnancy Category B	84:92 Skin and mucous membrane agents, miscellaneous	No longer on market								
Alitretinoin	FDA Pregnancy Category D	84:92 Skin and mucous membrane agents, miscellaneous	0%								
Altretamine	FDA Pregnancy category D	10:00 Antineoplastic agents	low								
Ambrisentan	Black Box warning on adverse reproductive effects; reduced sperm counts in patients; FDA Pregnancy Category X	24:12.92 Vasodilating agents, miscellaneous	ill defined								
Amsacrine	IARC Group 2B	Not in AHFS (antineoplastic agent)									Not available in US
Anastrozole	FDA Pregnancy category X	10:00 Antineoplastic agents	low								
Apomorphine	FDA Pregnancy Category C; genotoxic in several in vitro assays.	28:36.20.08 Nonergot-derivative dopamine receptor agonists	low								Treatment for Parkinson's disease
Arsenic trioxide/Trisenox	IARC Group 1 carcinogen**; FDA Pregnancy Category D	10:00 Antineoplastic agents	15%	1	15	mg/kg	1200	mg	180	mg/L	Restricted use; DNA fragmentation
Azacitidine	IARC Group 2A carcinogen; FDA Pregnancy Category D	10:00 Antineoplastic agents	low								Little effect on normal cells at low doses
Azathioprine	IARC Group 1 carcinogen**; FDA Pregnancy Category D***	92:44 Immunosuppressant agents	0%								Retinoid
Bacillus Calmette-Guerin (BCG)†	See special handling requirements**; FDA Pregnancy Category C	80:12 Vaccines	low								
Bendamustine HCl	FDA Pregnancy Category D	10:00 Antineoplastic agents	low								
Bexarotene	FDA Pregnancy Category X	10:00 Antineoplastic agents	low								Retinoid
Bicalutamide	FDA Pregnancy Category X	10:00 Antineoplastic agents	low								Androgen receptor inhibitor
Bleomycin	IARC Group 2B; FDA Preg-nancy Category D	10:00 Antineoplastic agents	70%	1	50	units (mg)/	4000	mg	2800	mg/L	Damages DNA and RNA synthesis
Bortezomib	FDA Pregnancy Category D	10:00 Antineoplastic agents	low								
Bosentan	Black Box warning on adverse reproductive effects; FDA Pregnancy Category X	24:12.92 Vasodilating agents, miscellaneous	low								
Brentuximab vedotin	Conjugated monoclonal antibody; FDA Pregnancy Category D	10:00 Antineoplastic agents	low								Antibody drug conjugate
Busulfan	IARC Group 1 carcinogen; FDA Pregnancy Category D	10:00 Antineoplastic agents	low								Not widely used due to toxicity
Cabazitaxel	FDA Pregnancy Category D	10:00 Antineoplastic agents	2%								Microtubule inhibitor
Cabergoline	Inhibition of conception and embryo fetal effects at doses below recommended human dose; FDA Pregnancy Category B	28:36.20.04 Ergot-derivative dopamine receptor agonists	low								
Capecitabine	Metabolized to 5-fluoro-uracil; FDA Pregnancy Cate-gory D	10:00 Antineoplastic agents	low								Converts to 5FU inside cells
Carbamazepine	Black Box warning for aplastic anemia; congenital malformations in offspring of mothers who took drug; rapid transplacental passage; FDA Pregnancy Category D	28:12.92 Anticonvulsants, miscellaneous	low								Can transfer to breast milk
Carboplatin	FDA Pregnancy Category D	10:00 Antineoplastic agents	71%	1	12	mg/kg	960	mg	682	mg/L	Crosslinks DNA in chromosomes
Carmustine	IARC Group 2A carcinogen; FDA Pregnancy Category D	10:00 Antineoplastic agents	0%								
Cetrorelix acetate	FDA Pregnancy Category X	92:40 Gonadotropin-releasing hormone antagonists	4%	1	3	mg	3	mg	0.12	mg/L	Inhibitor of gonadotropin secretion
Chlorambucil	IARC Group 1 carcinogen; FDA Pregnancy Category D	10:00 Antineoplastic agents	low								
Chloramphenicol	IARC Group 2A carcinogen; FDA Pregnancy Category C	8:12.08 Chloramphenicols	12%	1	100	mg/kg	8000	mg	960	mg/L	Antibiotic for acute setting
Choriogonadotropin alfa	FDA pregnancy Category C; may cause fetal harm when administered to a pregnant woman.	68:18 Gonadotropins	hCG								Identical to hormone measured in pregnancy test
Cidofovir	FDA Pregnancy Category C	8:18.32 Nucleosides and nucleotides	100%	1	5	mg/kg	400	mg	400	mg/L	Anti-viral (CMV)
Cisplatin	IARC Group 2A carcinogen; FDA Pregnancy Category D	10:00 Antineoplastic agents	17%	1	3.3	mg/Kg	264	mg	45	mg/L	Crosslinks DNA in chromosomes
Cladribine	FDA Pregnancy Category D	10:00 Antineoplastic agents	18%	1	0.09	mg/kg	7.2	mg	1.3	mg/L	Internal nucleotide toxin; Requires continuous infusion to maintain dosage
Clofarabine	FDA Pregnancy Category D	10:00 Antineoplastic agents	60%	1	1.73	mg/kg	138.7	mg	83	mg/L	Inhibits DNA synthesis. Used in pediatric ALL as third round of treatment
Clonazepam	Increased risk of congenital abnormalities when taken in first trimester; FDA Pregnancy Category D	28:12.08 Benzodiazepines	low								
Colchicine	FDA Pregnancy Category C; published animal reproduc-tion and development studies indicate it causes embryofetal toxicity, teratogenicity, and altered postnatal develop-ment at exposures within or above the clinical therapeutic range	92:16 Antigout agents	20%	1	1.2	mg/day	1.2	mg	0.24	mg/L	Gout, anti-neutrophil
Crizotinib	FDA Pregnancy Category D	10:00 Antineoplastic agents	55%	2	500	mg/day	500	mg	138	mg/L	Kinase inhibitor
Cyclophosphamide	IARC Group 1 carcinogen; FDA Pregnancy Category D	10:00 Antineoplastic agents	25%	1	50	mg/kg	4000	mg	1000	mg/L	Crosslinks DNA in chromosomes
Cyclosporin	IARC Group 1 carcinogen; FDA pregnancy Category C	92:44 Immunosuppressive agents	low								
Cytarabine	FDA Pregnancy Category D	10:00 Antineoplastic agents	low								

Dacarbazine	FDA Pregnancy Category C	10:00 Antineoplastic agents	40%	1	4.5	mg/kg	360	mg	144	mg/L	Alkylates DNA
Dactinomycin, Actinomycin	FDA Pregnancy Category D	10:00 Antineoplastic agents	30%	7	50	ug/Kg	4	mg	0.17	mg/L	Damages DNA and RNA synthesis
Dasatinib	FDA Pregnancy Category D	10:00 Antineoplastic agents	19%	10	100	mg	100	mg	1.9	mg/L	Kinase inhibitor
Daunorubicin HCl	IARC Group 2B, AKA dauno-mycin; FDA Pregnancy Category D	10:00 Antineoplastic agents	65%	3	1.5	mg/kg	120	mg	26	mg/L	Directly causes DNA damage; Blocks DNA repair (anti-topoisomerase II)
Decitabine	FDA Pregnancy Category D	10:00 Antineoplastic agents	low								
Deferiprone	Genotoxic *in vitro* and *in vivo* ; FDA Pregnancy Category D	64:00 Heavy metal antagonists	25%	1	99	mg/kg	7920	mg	1980	mg/L	Iron chelator
Degarelix	FDA Pregnancy Category X	10:00 Antineoplastic agents	low								Blocks testosterone release
Dexrazoxane	FDA Pregnancy Category C; secondary malignancies observed in patients treated long term with Razoxane (a racemic mixture containing dexrazane); genotoxic in vitro and in vivo; in labo-ratory studies, testicular atrophy observed at or below the human dose	92:56 protective agents	42%	1	20	mg/kg	1600	mg	672	mg/L	Intracellular chelating agent; excretion of metabolites and primary drug not studied
Diethylstilbestrol (DES)	IARC Group 1 carcinogen; FDA Pregnancy Category X	Not in AHFS (nonsteroidal synthetic estrogen)	Removed from market								
Dinoprostone	Hazardous only for women in late pregnancy; FDA Pregnancy Category C	76:00 Oxytocics	Naturally-occurring biomolecule								Induces labor
Divalproex	Black Box warning for tera-togenicity; FDA Pregnancy Category D; tumors seen in laboratory studies at doses below MRHD	28:12:92 anticonvulsants, miscellaneous	3.00%								Believed it increases brain concentrations of gamma-aminobutyric acid
Docetaxel	FDA Pregnancy Category D	10:00 Antineoplastic agents	8%	2	3.3	mg/kg	267	mg	11	mg/L	Microtubular inhibitor
Doxorubicin	IARC Group 2A carcinogen; FDA Pregnancy Category D	10:00 Antineoplastic agents	55%	5	2.5	mg/kg	200	mg	22	mg/L	Directly causes DNA damage; Blocks DNA repair (anti-topoisomerase II)
Dronedarone HCl	Teratogenic in laboratory studies at ½ MRHD; FDA Pregnancy Category X	24:04.04 Antiarrythmics	0%								Antiarrhythmic drug
Dutasteride	Women warned not to handle; FDA Pregnancy Category X	92:08 5-alpha reductase inhibitors	5%	weeks	0.5	mg	0.5	mg			Benign prostatic hyperplasia
Entecavir	FDA Pregnancy Category C	8:18.32 Nucleosides and nucleotides	73%	10+	0.5	mg	0.5	mg	0.037	mg/L	Chronic hepatitis B, no embryofetal toxicity observed
Epirubicin	FDA Pregnancy Category D	10:00 Antineoplastic agents	55%	4	40	mg/kg	3200	mg	440	mg/L	Directly causes DNA damage; Blocks DNA repair (anti-topoisomerase II)
Ergonovine/methylergonovine	Use is contraindicated during pregnancy because of its uterotonic effects; FDA Pregnancy Category C	76:00 Oxytocics	low		0.2	mg					Control of postpartum hemorrhage
Eribulin	FDA Pregnancy Category D	10:00 Antineoplastic agents	91%	4	0.05	mg/kg	4	mg	1	mg/L	Microtubule inhibitor
Erlotinib	FDA Pregnancy Category D	10:00 Antineoplastic agents	2%								Kinase inhibitor
Estradiol	Black Box warning for malig-nant neoplasms; increased risk of endometrial cancer, breast cancer, and ovarian cancer; in laboratory studies, increased frequency of carci-nomas of the breast, uterus, cervix, vagina, testis, and liver; present in breast milk; FDA Pregnancy Category X	68:16.04 Estrogens	Natural Estrogen profile								Endocrine hormone
Estramustine phosphate	FDA Pregnancy Category X	10:00 Antineoplastic agents	Natural Estrogen profile								Combines estrodiol and mustagen
Estrogen-progestin combinations	IARC Group 1 carcinogen; FDA Pregnancy Category X	68:12 Contraceptives	Natural estrogen-progestin profile								Endocrine hormone
Estrogens, conjugated	Black Box warning for endo-metrial cancer and cardiovascular risks; long-term use in women and laboratory studies increases frequency of several cancers; FDA Pregnancy Category X	68:16.04 Estrogens	Natural Estrogen profile								Endocrine hormone
Estrogens, esterified	Black Box warning for endometrial cancer and cardiovascular risks: FDA Pregnancy Category X	68:16.04 Estrogens	Natural Estrogen profile								Endocrine hormone
Estropipate	Black Box warning for endometrial carcinoma in post-menopausal women and use during pregnancy; FDA Pregnancy Category X	68:16.04 Estrogens	Natural Estrogen profile								Endocrine hormone
Etoposide	IARC Group 1 carcinogen; FDA Pregnancy Category D	10:00 Antineoplastic agents	45%	5	3.3	mg/Kg	264	mg	24	mg/L	Directly causes DNA damage; Blocks DNA repair (anti-topoisomerase II)
Everolimus	FDA Pregnancy Category D	10:00 Antineoplastic agents	0%								Kinase inhibitor
Exemestane	FDA Pregnancy Category X	10:00 Antineoplastic agents	low								Blocks estrogen
Finasteride	Women should not handle crushed or broken finasteride tablets when they are pregnant or may potentially be pregnant due to potential risk to a male fetus; FDA Pregnancy Category X	92:08 5-alpha reductase inhibitors	low								Benign prostatic hyperplasia
Fingolimod	FDA Pregnancy Category C; in laboratory studies, increased malformations and embryo-fetal deaths at less than the RHD; malignant lymphomas observed in male and female mice.	92:20 biologic response modifiers	3%								Sphingosine 1-phosphate receptor modulator
Floxuridine	FDA Pregnancy Category D	10:00 Antineoplastic agents	20%	1	0.6	mg/kg	48	mg	9.6	mg/L	Inhibits DNA and RNA synthesis 5FU prodrug
Fluconazole	FDA Pregnancy Category C; case reports describe con-genital anomalies in infants exposed in utero to maternal fluconazole (400–800 mg/day) during most or all of the first trimester, similar to those seen in animal studies	8:18.08 azoles	80%	3	400	mg	400	mg	107	mg/L	Highly selective inhibitor of fungal enzyme
Fludarabine	FDA Pregnancy Category D	10:00 Antineoplastic agents	60%	1	0.83	mg/kg	66.4	mg	40	mg/L	Inhibits DNA synthesis.
Fluorouracil	FDA Pregnancy Category D	10:00 Antineoplastic agents	20%	1	12	mg/kg	960	mg	192	mg/L	Inhibits DNA and RNA synthesis.
Fluoxymesterone	Tumors in mice and rats and possibly humans; FDA Pregnancy Category X	68:08 Androgens	5%	1	10	mg	10	mg	0.5	mg/L	Oral testosterone
Flutamide	Indicated only for men; FDA Pregnancy Category D	10:00 Antineoplastic agents	low		125	mg					Anti-androgen
Fosphenytoin	Metabolized to phenytoin; FDA Pregnancy Category D	28:12.12 hydantoins	0%								Anticonvulsant
Fulvestrant	FDA Pregnancy Category D	10:00 Antineoplastic agents	low								Estrogen receptor antagonist

Ganciclovir	FDA Pregnancy Category C	8:18.32 Nucleosides and nucleotides	92%	1	6	mg/kg	480	mg	442	mg/L	Anti-viral (CMV and hepes)
Ganirelix acetate	FDA Pregnancy Category X	92:40 Gonadotropin-releasing hormone antagonists	18%	1	250	ug	250	ug	0.045	mg/L	Managing in vitro egg harvest
Gemcitabine	FDA Pregnancy Category D	10:00 Antineoplastic agents	<10%	7	42	mg/kg	3333	mg	48	mg/L	Nucleoside metabolic inhibitor
Gemtuzumab ozogamicin	FDA Pregnancy Category D	10:00 Antineoplastic agents	0.00%								
Gonadotropin, chorionic	Defects of forelimbs and central nervous system and alterations in sex ratio have been reported in laboratory studies; FDA pregnancy Category C	68:18 Gonadotropins	hCG								Identical to hormone measured in pregnancy test
Goserelin	FDA Pregnancy Category X	10:00 Antineoplastic agents	20%	28	3.6	mg	3.6	mg	0.03	mg/L	Inhibitor of pituitary gonadotropin secretion
Hydroxyurea	Special warning handling bottles/capsules; FDA Pregnancy Category D	10:00 Antineoplastic agents	low								
Icatibant	FDA Pregnancy Category C; in laboratory studies, premature birth and abortion rates increased at a dose that was less than 1/40th the MRHD and delayed parturition and fetal death occurred at 0.5 and 2-fold, respectively, the MRHD	92:32 complement inhibitors	<10%	1	90	mg	90	mg	9	mg/L	Bradykinin B2 receptor antagonist
Idarubicin	FDA Pregnancy Category D	10:00 Antineoplastic agents	20%	8	0.4	mg/kg	32	mg	0.80	mg/L	Directly causes DNA damage; Blocks DNA repair (anti-topoisomerase II)
Ifosfamide	FDA Pregnancy Category D	10:00 Antineoplastic agents	18%	1	40	mg/kg	3200	mg	576.00	mg/L	Crosslinks DNA in chromosomes
Imatinib mesylate	FDA Pregnancy Category D	10:00 Antineoplastic agents	25%	2	800	mg	800	mg	100	mg/L	Kinase inhibitor (Gleevec)
Irinotecan HCl	FDA Pregnancy Category D	10:00 Antineoplastic agents	50%	2	11.7	mg/kg	936	mg	234.00	mg/L	Crosslinks DNA in chromosomes
Ixabepilone	FDA Pregnancy Category D	10:00 Antineoplastic agents	7%	7	1.3	mg/kg	107	mg	1.1	mg/L	Microtubular inhibitor
Leflunomide	Teratogenic in laboratory studies at 1/10 HD; marked postnatal survival at 1/100 HD; FDA Pregnancy Category X; severe liver injury reported in patients; carcinogenicity observed at doses below HD	92:36 Disease-modifying antirheumatic agents	low								Pyrimidine synthesis inhibitor
Lenalidomide	Analog of thalidomide; FDA Black box warnings for limb abnormalaties; pregnancy Category X; in laboratory studies, caused thalidomide-type limb defects in monkey offspring	92:20 Biologic response modifiers	82%	1	25	mg	25	mg	20.5	mg/L	Thalidomide analogue; under a special restricted distribution program
Letrozole	FDA pregnancy Category X	10:00 Antineoplastic agents	6%	4	25	mg	25	mg	0.38	mg/L	Inhibits the conversion of androgens to estrogens
Leuprolide acetate	FDA Pregnancy Category X	10:00 Antineoplastic agents	<5%	1	1	mg	1	mg	0.05	mg/L	Inhibitor of gonadotropin secretion
Liraglutide recombinant	FDA Pregnancy Category C; Black Box warning for thyroid C-cell tumors, with supporting evidence in laboratory studies; also in labo-ratory studies, teratogenic at or below the MRHD.	68:20.06 incretin mimetics	0%								glucagon-like peptide-1 (GLP-1) receptor agonist
Lomustine	IARC Group 2A carcinogen; FDA Pregnancy Category D	10:00 Antineoplastic agents	0%								
Mechlorethamine	FDA Pregnancy Category D	10:00 Antineoplastic agents	0%								
Medroxyprogesterone acetate	IARC Group 2B; FDA Pregnancy Category X	68:32 Progestins	Natural progsterogen profile								Endocrine hormone
Megestrol	FDA Pregnancy Category X	10:00 Antineoplastic agents	86%	10	1600	mg	1600	mg	1376	mg	palliative treatment of advanced carcinoma of the breast or endometrium
Melphalan	IARC Group 1 carcinogen; FDA Pregnancy Category D	10:00 Antineoplastic agents	20%	1	6	mg	6	mg	1.2	mg/L	Mustagen analog, palliative treatment; requires large dose
Menotropins	FDA Pregnancy Category X	68:18 Gonadotropins	Isolated from women's urine								Development of multiple follicles, IVF
Mercaptopurine	FDA Pregnancy Category D	10:00 Antineoplastic agents	Genetic based variable								Nucleotide analog
Methotrexate	FDA Pregnancy Category X	10:00 Antineoplastic agents	90%	1	15	mg/kg	1200	mg	1080.00	mg/L	Inhibits DNA synthesis and repair
Methyltestosterone	FDA Pregnancy Category X	68:08 Androgens	low								Testosterone analog
Mifepristone (RU-486)	When given to pregnant women results in termination of pregnancy; FDA Pregnancy Category X	76:00 Oxytocics	83%	1	600	mg	600	mg	498	mg/L	Cortisol receptor blocker
Misoprostol	FDA Pregnancy Category X	56:28.28 prostaglandins	Natural prostaglandin profile								Synthetic prostaglandin E analog
Mitomycin	IARC Group 2B; FDA Preg-nancy Category D	10:00 Antineoplastic agents	10%	1	0.67	mg/kg	53.6	mg	5.36	mg/L	Inhibits DNA synthesis and repair
Mitotane	FDA Pregnancy Category D	10:00 Antineoplastic agents	0%								
Mitoxantrone HCl	IARC Group 2B; FDA Preg-nancy Category D	10:00 Antineoplastic agents	24%	5	0.47	mg/kg	37.6	mg	1.80	mg/L	Cause DNA breaks and crosslinking
Mycophenolate mofetil	Black Box warning for embryo fetal toxicity, malignancies and serious infections; Increased risk of first- trimester pregnancy loss and increased risk of congenital malformations; FDA Pregnancy Category D; Special warning: tablets should not be crushed and capsules should not be opened or crushed. Avoid inhalation or direct contact with skin or mucous membranes of the powder contained in capsules and oral suspension (before or after constitution). If such contact occurs, wash thoroughly with soap and water; rinse eyes with plain water.	92:44 Immunosuppressive agents	low								immunosuppressive agent
Mycophenolic acid	Black Box warning for first trimester pregnancy loss and an increased risk of con-genital malformations; FDA Pregnancy Category D; Black Box warning for lymphomas and other malignancies; genotoxic *in vitro* and *in vivo*	92:44 Immunosuppressive agents	low								immunosuppressive agent
Nafarelin	Note: Given only as nasal spray; no potential for occupational exposure; FDA Pregnancy Category X	68:18 Gonadotropins	low								Decreased secretion of gonadal steroids; block early puberty
Nelarabine	FDA Pregnancy Category D	10:00 Antineoplastic agents	10%	1	50	mg/kg	4000	mg	400	mg/L	Nucleoside metabolic inhibitor; 3rd round of treatment
Nevirapine	FDA Pregnancy Category B; in laboratory studies, hepa-tocellular adenomas and carcinomas at doses lower than human dose.	8:18.08.16 nonnucleoside reverse transcriptase inhibitors	5%	1	400	mg	400	mg	20		anti-viral for the treatment of HIV-1 infection

Nilotinib	FDA Pregnancy Category D	10:00 Antineoplastic agents	69%	7	400	mg	400	mg	39	mg/L	Kinase inhibitor
Nilutamide	FDA Pregnancy Category D	10:00 Antineoplastic agents	low								Antiandrogen
Oxaliplatin	FDA Pregnancy Category D	10:00 Antineoplastic agents	54%	5	2.8	mg/kg	224	mg	24.19	mg/L	Crosslinks DNA in chromosomes
Oxcarbazepine	Tumors observed in laboratory studies at 1/10 MRHD; FDA Pregnancy Category C	28:12.92 Anticonvulsants, miscellaneous	low								Antiepileptic
Oxytocin	Hazardous only for women in 3rd trimester; FDA Pregnancy Category C	76:00 Oxytocics	0%								Peptide
Paclitaxel	FDA Pregnancy Category D	10:00 Antineoplastic agents	90%	1	5.83	mg/kg	466.4	mg	419.76	mg/L	Interferes with microtubule assembly, proper segregation of chromosomes
Palifermin	FDA Pregnancy Category C; potential for stimulation of tumor growth	84:16 Cell stimulants and proliferants	Natural product								Human Growth Factor, pET21d
Paroxetine	Increased risk of congenital abnormalities when taken in first trimester; complications in pregnancy when taken in third trimester; FDA Pregnancy Category D	28:16.04.20 Selective serotonin uptake inhibitors	low								Psychotropic
Pazopanib HCl		10:00 Antineoplastic agents	low		800	mg					Kinase inhibitor
Pemetrexed	FDA Pregnancy Category D	10:00 Antineoplastic agents	90%	1	17	mg/kg	1333	mg	1200	mg/L	Folate analog metabolic inhibitor
Pentetate calcium trisodium	Severe teratogenic effects in laboratory studies in dogs: supplied in ampule which can lead to occupational exposure; FDA Pregnancy Category C	Not in AHFS	99%	1	1000	mg	1000	mg	1000	mg/L	Metal chelator, used for radioactive contamination
Pentostatin	FDA Pregnancy Category D	10:00 Antineoplastic agents	90%	1	0.13	mg/Kg	11	mg	9.6	mg/L	Inhibitor of the enzyme adenosine deaminase
Phenoxybenzamine HCl	IARC Group 2B; FDA Pregnancy Category C	12:16.04.04 Non-selective alpha-adrenergic blocking agents	low								Alpha-receptor-blocking agent, anti-hypertensive
Phenytoin	IARC 2B; FDA Pregnancy Category D	28:12.12 hydantoins	low		300	mg	300	mg			Antiepileptic
Pipobroman	FDA Pregnancy Category D	Not in AHFS (antineoplastic agent)	Not on US market								Not available in US
Plerixafor	Teratogenic in laboratory studies; FDA Pregnancy Cate-gory D	20:16 Hematopoietic agents	0%								Hematopoietic stem cell mobilizer
Pralatrexate	FDA Pregnancy Category D	10:00 Antineoplastic agents	34%	2	1	mg/kg	80	mg	13.6	mg/L	Folate analog metabolic inhibitor
Procarbazine	IARC Group 2A carcinogen; FDA Pregnancy Category D	10:00 Antineoplastic agents	0.00%								
Progesterone	IARC Group 2B	68:32 Progestins	Natural progsterogen profile								Endocrine hormone
Progestins	FDA Pregnancy Category X	68:12 Contraceptives	Natural progsterogen profile								Endocrine hormone
Propylthiouracil	IARC 2B; FDA Pregnancy Category D	68:36.08 antithyroid agents	35%	1	150	mg	150	mg	53	mg/L	Inhibits synthesis of thyroid hormones
Raloxifene	Abortion and developmental abnormalities seen at low doses in laboratory studies; evidence of tumors at low doses in laboratory studies; FDA Pregnancy Category X	68:16.12 Estrogen agonists-antagonists	low								Selective estrogen receptor modulator
Rasagiline mesylate	FDA Pregnancy Category C	28:36 Antiparkinsonian agents	low								Selective, irreversible MAO-B inhibitor, Parkinsons
Ribavirin	Teratogenic and embryotoxic effects in several laboratory studies; contraindicated in women who are pregnant and in the male partners of women who are pregnant; FDA Pregnancy Category X	8:18.32 Nucleosides and nucleotides	17%	1	0.05	ug/Kg	0.004	mg	0.00068	mg/L	Nucleoside analogue ; treatment of Chronic Hepatitis C
Risperidone	Evidence of tumors at low doses in laboratory studies; may be prolactin-mediated; FDA Pregnancy Category C	28:16.08.04 Atypical antipsychotics	30%	7	8	mg	8	mg	0.34	mg/L	Antipsychotic, rate of excretion varies with genetics
Romidepsin	FDA Pregnancy Category D	10:00 Antineoplastic agents	<5%	1	0.47	mg/kg	37	mg	1.9	mg/L	Histone deacetylase (HDAC) inhibitor
Sirolimus	AKA rapamycin; increased risk of lymphomas and other malignancies; embryotoxic and fetotoxic at 0.2 HD; FDA Pregnancy Category C	92:44 Immunosuppressive agents	low								Immunosuppressive agent
Sorafenib	FDA Pregnancy Category D	10:00 Antineoplastic agents	51%	14	400	mg	400	mg	14.6	mg/L	Kinase inhibitor
Spironolactone	FDA Pregnancy Category C; black box warning for tumorogenicity in laboratory studies.	24:32.20 mineralocorticoid receptor antagonists	low								Diuretic, antihypertensive drug
Streptozocin	IARC Group 2B; FDA Preg-nancy Category D	10:00 Antineoplastic agents	low								DNA synthesis inhibitor
Sunitinib malate	FDA Pregnancy Category D	10:00 Antineoplastic agents	75%	14	50	mg	50	mg	2.7	mg/L	Kinase inhibitor
Tacrolimus	Increased risk of lymphomas and other malignancies; reproductive effects seen in laboratory studies below the MRHD; excreted in breast milk; FDA Pregnancy Category C	92:44 Immunosuppressive agents	low								Calcineurin-inhibitor immunosuppressant
Tamoxifen	IARC Group 1 carcinogen; FDA Pregnancy Category D	10:00 Antineoplastic agents	30%	14	40	mg	40	mg	0.86	mg/L	Antiestrogen
Telavancin	Black Box warning for potential risk to fetus and adverse reproductive outcomes; reduced fetal weights and increased rates of digit and limb malformations in three species at clinical doses; FDA Pregnancy Category C	8:12.28.16 Glycopeptides	76%	9	10	mg/kg	800	mg	68	mg/L	Antibiotic (IV)
Temozolomide	FDA Pregnancy Category D	10:00 Antineoplastic agents	18%	7	5	mg/kg	400	mg	10	mg/L	Alkylation of DNA
Temsirolimus	FDA Pregnancy Category D	10:00 Antineoplastic agents	low								Kinase inhibitor
Teniposide	IARC Group 2A carcinogen; FDA Pregnancy Category D	10:00 Antineoplastic agents	12%	5	8.33	mg/kg	666.4	mg	15.99	mg/L	Cause DNA breaks and crosslinking. No longer recommended
Testosterone	Children should avoid contact with unwashed or unclothed application sites on skin; FDA Pregnancy Category X	68:08 Androgens	Natural testosterone profile								Endocrine hormone
Thalidomide	FDA Pregnancy Category X	92:20 Biologic response modifiers	0%								
Thioguanine	FDA Pregnancy Category D	10:00 Antineoplastic agents	low								Purine analogues
Thiotepa	IARC Group 1 carcinogen; FDA Pregnancy Category D	10:00 Antineoplastic agents	low								
Topiramate	FDA Pregnancy Category D	28:12.92 anticonvulsants, miscellaneous	70%	3	400	mg	400	mg	93	mg/L	Anticonvulsant
Topotecan	FDA Pregnancy Category D	10:00 Antineoplastic agents	75%	9	0.05	mg/kg	4	mg	0.33	mg/L	Topoisomerase inhibitor resulting in DNA mutations
Toremifene citrate	FDA Pregnancy Category D	10:00 Antineoplastic agents	low								Antiestrogenic
Tretinoin	Black Box warning for severe birth defects; Special FDA dis-tribution system; FDA Pregnancy Category X	84:16 Cell stimulants and proliferants	low								Retinoid

Triptorelin	FDA Pregnancy Category X	10:00 Antineoplastic agents	Peptide								Analog of gonadotropin releasing hormone; testosterone reduction
Trimetrexate	FDA Pregnancy Category D	10:00 antineoplastic agents	30%	2	1.2	mg/kg	96	mg	14.40	mg/L	Non-classical folate inhibitor; treatment of PCP in HIV
Ulipristal	FDA Pregnancy Category X	68:12 contraceptives	Low								Progesterone agonist/antagonist emergency contraceptive

Valganciclovir	FDA Pregnancy Category C	8:18.32 Nucleosides and nucleotides	90%	1	1800	mg	1800	mg	1620	mg/L	Anti-viral (CMV and hepes)
Valproic acid/ divalproex Na	Black Box warning for teratogenicity; congenital malformations including neural tube defects and others; teratogenic in multiple species; FDA Pregnancy Category D	28:12.92 Anticonvulsants, miscellaneous	low								Anticonvulsants
Valrubicin	FDA Pregnancy Category C	10:00 Antineoplastic agents	99%	1	800	mg	800	mg	800	mg/200 ml	Directly causes DNA damage; Blocks DNA repair (anti-topoisomerase II); Dosed directly into bladder
Vandetanib	FDA Pregnancy Category D	10:00 Antineoplastic agents	low								Kinase inhibitor
Vemurafenib	FDA Pregnancy Category D	10:00 Antineoplastic agents	low								Kinase inhibitor
Vigabatrin	Malformations seen in laboratory studies below the MRHD; FDA Pregnancy Category C	28:12.92 Anticonvulsants, miscellaneous	80%	1	150	mg/kg	12000	mg	9600	mg/L	Anti-seizure
Vinblastine sulfate	FDA Pregnancy Category D	10:00 Antineoplastic agents	35%	1	0.62	mg/kg	49.6	mg	17.36	mg/L	Interferes with microtubule assembly, proper segregation of chromosomes
Vincristine sulfate	FDA Pregnancy Category D	10:00 Antineoplastic agents	20%	1	0.05	mg/kg	4	mg	0.80	mg/L	Interferes with microtubule assembly, proper segregation of chromosomes
Vinorelbine tartrate	FDA Pregnancy Category D	10:00 Antineoplastic agents	11%	5	1	mg/kg	80	mg	1.76	mg/L	Interferes with microtubule assembly, proper segregation of chromosomes
Voriconazole	FDA Pregnancy Category D	8:14.08 azoles	2%								Anti-fungal
Vorinostat	FDA Pregnancy Category D	10:00 Antineoplastic agents	low								Inhibits the enzymatic activity of histone deacetylases; reduces abnormal gene expression
Warfarin	FDA Pregnancy Category D	20:12.04.08 coumarin derivatives	low								Vitamin K antagonist
Zidovudine	IARC Group 2B; FDA Pregnancy Category C	8:18:08 Antiretroviral agents	14%	1	600	mg	600	mg	84	mg/L	Antiviral
Ziprasidone HCl	Developmental toxicity, including possible teratogenic effects at doses similar to human therapeutic doses; an increase in the number of pups born dead and a decrease in postnatal survival at less than MRHD; FDA Pregnancy Category C	28:16.08.04 Atypical antipsychotics	low								Antipsychotics
Zoledronic acid	Number of stillbirths increased and survival of neo-nates decreased in laboratory studies at low doses; FDA Pregnancy Category D	92:24 Bone resorption inhibitors	55%	1	5	mg	5	mg	2.75	mg/L	Inhibits osteoclast-mediated bone resorption.
Zonisamide	Teratogenic in multiple animal species; FDA Pregnancy Category C	28:12.92 Anticonvulsants, miscellaneous	22%	10	400	mg	400	mg	8.8	mg/L	Anticonvulsants

From: Donald E. Chamberlin
To: MCP-Chair
Subject: PWPA material #3 re Item 11 Reflection Park Agenda for 12-15-2022
Date: Wednesday, December 14, 2022 12:02:18 PM
Attachments: Vass-The Elusive Post-Mortem Interval - Formula PMI.pdf

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Please see attached file re Vass post-mortem intervals.

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The Elusive Universal Post-Mortem Interval Formula

Arpad A. Vass, Ph.D.

A.A. Vass, The elusive universal post-mortem interval formula, Forensic Sci. Int. 204 (2011) 34-40.

Abstract

The following manuscript details our initial attempt at developing universal post-mortem interval formulas describing human decomposition. These formulas are empirically derived from data collected over the last 20 years from the University of Tennessee's Anthropology Research Facility, in Knoxville, Tennessee, USA. Separate formulas were developed for surface decomposition and burial decomposition, based on temperature, moisture, and the partial pressure of oxygen, three of the four primary drivers for human decomposition. It is hoped that worldwide application of these formulas to environments and situations not readily studied in Tennessee will result in interdisciplinary cooperation between scientists and law enforcement personnel that will allow for future refinements of these models leading to increased accuracy.

Keywords: human decomposition; formula; burials; post-mortem interval

1. Introduction

A decompositional formula for calculating the post-mortem interval (PMI) of human remains has long been sought after, but it has remained elusive due to the myriad of factors associated with human decomposition. As more and more knowledge is gained from experimental studies of decomposing human remains, we come closer to being able to derive a working model that encompasses all the taphonomic parameters which influence decomposition.

There are four widely recognized factors that influence the rate and ultimate completeness of the decompositional process. These are temperature, moisture, pH, and the partial pressure of oxygen [1]. Temperature is influenced by seasons, altitude, latitude, burial depth, presence of water, air movement, vegetation, wrappings or clothing, etc. Temperature and the rate of decomposition are linked by Van't Hoff's Law, also called the law of ten or Q10, which states that the speed of chemical reactions (enzymatic or catalytic decomposition, etc.) increases two or more times with each 10^{o} C rise in temperature. The presence of water (from rainfall, humidity, bodies of water, or the body itself) also has profound effects on the rate of decomposition. Important attributes associated with water include: a) a high specific heat that stabilizes temperatures; b) buffering capacity that moderates the effects of local pH changes; c) sources of H^{+} required for numerous biochemical reactions; d) its effect as a diluent; and e) its ability to act as a solvent for polar molecules. pH (acidity/alkalinity) is yet another parameter that affects intracellular chemical reactions and the catalytic ability of enzymes. Proteolysis (aerobic surface decomposition) typically forms alkaline environments [2] (well over pH 9.0 on the surface) whereas anaerobic burials tend to be acidic due to bacterial fermentation and the liberation of organic acids. These large changes in pH affect not only the microbial flora, but also the growth of vegetation and chemical reactions as well. The fourth most widely recognized factor associated with decomposition is the partial pressure of oxygen which, like temperature, is

influenced by burial depth, submersion in water, and high altitudes in addition to the presence or formation of adipocere (grave wax) [3,4]. A lack of oxygen surrounding the body tends to slow decomposition due to retardation of oxidative processes. Typically water and soil are oxygen deficient, lowering the reduction/oxidation (redox) potential, slowing down the entire process by favoring anaerobic degradation. Dryer soils, if aerated, tend to have a higher redox potential, speeding up decomposition in shallow burials depending, of course, on the soil type.

Other factors that come into play during the decomposition of human remains also affect the rate at which the process proceeds. These include the presence or absence of clothing or wrappings, injuries, carnivore activity, insect activity and insect access to the corpse, diseases, percent body fat or body mass, vegetation in the area, introduction of chemicals, and indoors vs. outdoors, to mention just a few. A previous study by Megyesi et. al. [5] developed a total body score method that was then used to predict the PMI, but focused mainly on temperature without taking additional environmental variables into account. Additionally, a more useful method compiled by Dr. Ed Friedlander and based on Dr. Henssge's formulas for very early PMIs is available on the World-wide Web [6].

2. Materials and Methods

Over the last 20 years we have been studying human decomposition at the University of Tennessee's Anthropology Research Facility (ARF). This facility is located in a secluded, open-wooded area in Knoxville, TN, USA, and is dedicated to the study of the decomposition of human remains in a natural environment. This 1+ acre facility is surrounded by a chain-link fence to restrict large carnivores and is under 24 hr surveillance to prevent unauthorized intrusions. The bodies used at this facility are predominately donations to the Forensic Anthropology Center. Individuals either voluntarily donate their remains to the center for

research purposes or are donated by family members. Following death, corpses are stored in morgue coolers or come directly from funeral homes prior to the onset of any decay study. Information concerning the race, age, gender, and cause of death are recorded for all individuals, if available.

Data concerning climatic conditions (temperature, humidity, and rainfall) were collected utilizing an electronic weather station (VWR Scientific) located in the research facility. The state of decomposition was also typically recorded as decomposition progressed. Underground thermocouples were used to measure the temperature in burial vaults, and soil moisture content was determined by gram dry weight assays. Soil samples were collected to determine the amount of moisture present. The samples were placed in pre-weighed glass scintillation vials, weighed, frozen and then lyophilized for 24 h. After the water was completely removed, the vials were again weighed using a Sartorius balance (Baxter. Model PT600), and the dry weights recorded. Alternative methods include placing the collected soil samples in an oven (>100^{o}C overnight) and weighing the sample before and after drying [2]. The soil type for the facility has been classified as a fine, mixed, thermic Typic Paleudalf according to U.S. Soil Taxonomy (Soil Survey Staff) [7].

3. Results and Discussion

We have been very fortunate to have observed hundreds of human decompositional events covering a multitude of scenarios and circumstances, both on the surface and in burial situations. In addition, significant numbers of forensic cases have been evaluated providing a large database from which visual and empirical data were collected. These large databases have allowed us to begin developing the elusive formula describing human decomposition. Many PMI methods exist with various associated error estimations. These include entomology based

methods, visual methods (such as *livor* or *rigor mortis*), organic chemical methods (volatile fatty acids, bone citrate, vitreous humor, lactic acid, DNA degradation, etc), inorganic methods, botanical and others (clothing decomposition, bone scattering, *algor mortis*, gastric contents, etc.) [8-25]. The more accurate the method, the longer and more complicated the laboratory analyses become, potentially taking months to complete and have been known to significantly delay criminal investigations. Law enforcement therefore has a need for a rapid and reliable "rule of thumb" methodology to estimate the PMI at the site where a corpse is discovered, especially for older (> 24 - 48 hours) decompositional events. The formulas describing human PMIs presented in this paper are intended to provide law enforcement with an easily obtainable, rapid and fairly accurate PMI estimate. This "rough" estimate is what is required by investigators to begin their investigation as soon as possible while waiting for the detailed laboratory analysis of evidence collected at the site of discovery which will provide the PMI estimate used in any future legal proceedings.

The formulas we have developed to date rely on two very important aspects of human decomposition.: 1) the taphonomic factors temperature, moisture, and the partial pressure of oxygen, in that perceived order, have the greatest influence on the decomposition process, and 2) soft tissue decomposition ends at 1285 +/- 110 Accumulated Degree Days (ADDs) [2, 26] which are an accumulation of average daily temperatures (in Celsius) over time.

The following formulas consist of two parts: 1) an estimation of the amount of decomposition which has occurred (numerator), and 2) the calculated effect of the environment on decomposition (denominator).

1. FORMULA I (PMI $_{Aerobic}$) – Describes above ground (aerobic) human decomposition and is used to estimate the post-mortem interval. Result is in DAYS.

$$PMI_{Aerobic} = \frac{1285 * (decomposition/100)}{0.0103 * temperature * humidity}$$

where:

1285 is a constant, representing the empirically determined ADD value at which volatile fatty acid (VFA) liberation from soft tissue ceases.

decomposition is a single value, or range, between 1 and 100, representing the best estimation of the extent of total body soft tissue decomposition.

0.0103 is a constant, representing an empirically determined measure of the effect of moisture on decompositional rates.

temperature is the value in degrees Celsius (C) of either the average temperature at the site on the day the corpse was discovered or the average temperature over a period of time.

humidity is a value between 1 and 100, representing either the average humidity at the site on the day the corpse was discovered or the average humidity over a period of time.

Formula I Requirements:

- Corpse found above ground (aerobic decomposition)
- Corpse must be in pre-skeletonization phase ($\leq$ 1285 ADD)
    - [Soft tissue present - if mummified, the tissue must be soft and pliable]
- Corpse must be at least one day old
- Corpse should be fairly intact (damage from large carnivores, dismemberment, etc. could affect the results)
- Must estimate the percentage of soft tissue decomposition that has occurred
- Temperature must be above 0^oC
- Average temperature (C) and humidity ideally should be corrected for the discovery site
- Little to no adipocere formation on the corpse

Conditions to note, but not critical in calculation:

- Presentation of the corpse (Stage of decomposition)
- Clothed or loosely wrapped
- Insect access
- Minor soft tissue damage
- The amount of adipocere present under the body

Detailed Explanation of the Formula I terms:

1285 – The decomposition of soft tissue liberates volatile fatty acids (VFAs) [2]. When soft tissue decomposition ends or when the remaining non-nutritive tissue hardens, desiccates and mummifies, VFA production ends. This occurs at approximately 1285 ADDs. This ADD value then corresponds to the cessation of volatile fatty acid (VFA) liberation from soft tissue and signifies the onset of the post-skeletonization phase of decomposition. ADD values less than 1285 indicate that VFAs are still being liberated and the corpse is in the pre-skeletonization phase of decomposition. This formula should only be used if soft tissue remains on the corpse ($\leq$ 1285 ADDs).

Decomposition – This value must be determined by a qualified investigator and is an estimation of how much soft tissue decomposition has occurred. Input from a Medical Examiner or Forensic Anthropologist is recommended. Typically this is in the form of a range (e.g. 40-60%), but can be expressed as a single value if the investigator is confident with their estimation. Example: If a corpse is estimated to be 50% decomposed, then the numerator of Formula I is 1285 (50/100) = 1285(0.5) = 642.5

Historically, decomposition has been described by the use of stages—fresh, bloat, decay and dry [27]. These have always been problematic since there is usually not a clear demarcation between the stages, but rather a blending. The formulas presented in this paper eliminate the need to determine the decompositional stage of the corpse, but since many practicing anthropologists still rely on these stages when assessing remains, Table 1 (based on years of observational data and experience) has been developed as an aid to correlate decompositional stages with a decompositional percentage range. This range would then encompass the boundaries from which the investigator would select the % decomposition required in the

formula calculations. The correlation depends on an assessment of the environmental air temperature (refer to the following section on temperature) with warm defined as > 12^{o}C and cold as < 12^{o}C. This personal definition is somewhat arbitrary, but has its origins in the fact that ~12^{o}C or 53^{o}F is the temperature below which flies, important in human decomposition, typically are not airborne and therefore aren't laying eggs on the corpse [28]. Little to no decomposition occurs at or below 0^{o}C.

0.0103 – When comparing the percentage decomposition to the time-averaged amount of moisture present (either air humidity or soil moisture), the effect of moisture on human decomposition can be represented by a line with a slope of 0.0103. This was empirically derived after observing the effect of humidity on decompositional rates for over a decade. At the Anthropology Research Facility, yearly humidity typically averages 65-75% and this is the most accurate section of the data. In the summer, the average daily humidity can approach 90% and it has been known to drop into the 40% range during the winter months. Humidity ranges below 40% are rarely seen in E. Tennessee and additional data from areas in the world with low humidity is required to confirm that the slope is still linear in this area of the graph. Total body water content for individuals is estimated at 55-65% [29], but many soft tissue components other than fat and lean muscle typically have a water content well over 85%. As these organs decompose, the water they release either surround the body during high humidity (body on the surface) or if the soil moisture is high (burial), or are whisked away from the body during low humidity or if the soil moisture is low. This general trend (as well as the decompositional effect) is similar whether we are discussing environmental humidity or soil moisture allowing us to use the same constant when performing the moisture calculations in the PMI formulas. As moisture (surface or burial) levels rise to over 85%, the rate of decomposition increases, and when

moisture drops below 85%, the rate of decomposition decreases – a phenomenon that is taken into account when performing the formula calculations.

Temperature – This must be in degrees Celsius (C) and can either reflect the average temperature at the scene corresponding to the day the corpse is discovered, or the average temperature at the scene corrected by a several day comparison to the nearest National Weather Service (NWS) station. Since temperature can fluctuate dramatically over time, the investigator may not wish to only use the temperature at the time (or day) of discovery and this decision depends on how quickly a PMI estimate is needed and how accurate the investigator wishes to be. A more accurate estimate can be obtained by taking an average of days, weeks or months of temperature data. One method of determining a rough estimate of how many days of weather data to average is by dividing 1285 by the average temperature on the day on which the corpse was found, thus providing the investigator with a crude estimate of the maximum number of days which has expired since death [2]. For example, if the average environmental temperature is 10^{o}C on the day, and at the site, of discovery, then 1285/10 = 128.5 days. This will provide the investigator with an estimate of approximately how many days of weather data should be collected to obtain a more accurate average temperature (and humidity – see below) estimate over time for the death scene which can then be applied to the PMI formula. (This can be further refined as discussed in the conclusion section of this manuscript).

Approximately 4-5 days of weather data at the site of discovery, compared to the nearest NWS station, is sufficient to arrive at a correction factor which can be applied to all the obtained temperature and/or humidity data.

Figure 1 depicts human decompositional rates based solely on temperature for those individuals found on the surface of the ground (aerobic) [2], but can be misleading if other important parameters are not taken into account.

Humidity – This value is left as a percentage and can reflect the average humidity at the site of discovery on the day the corpse is discovered. A more encompassing average can include a time frame similar to what was determined following the procedure described in the temperature section above.

Forensic Case Example – A partially clothed, forty-two year old man was found in an outdoor urban environment. Cause of death was strangulation. The environment was wet and cold and had been for several months. Initially, three months of temperature and humidity daily averages obtained from the closest NWS Station, 3 miles from the scene, were corrected for temperature differences at the crime scene after a four day comparison between NWS and crime scene data. The corrected average temperature over this time period was 4.5^{o} C and the humidity was on average 87%. The cold temperature had preserved the body well and examination of the corpse indicated that the best estimate for the % decomposition was 20%.

(1285 * 0.20) / (0.0103 * 4.5 * 87) = 257 / 4.03 = 63.8 days

If the % decomposition is difficult to determine accurately, the decomposition estimate could also have been expressed as a range (15-25%), but ultimately depends on the potential accuracy needs of the investigator. This would have resulted in a calculated range of 47.8-79.7 days. After a lengthy investigation, investigators discovered that the victim was killed 65 days prior to discovery. The entomology estimate on this case, used to establish the PMI, indicated a range interval of 3 weeks, which encompassed the correct time frame of when he was killed.

2. FORMULA II (PMI $_{\text{Anaerobic}}$) – Describes human 'burial' decomposition (anaerobic and/or below ground) and is used to estimate the post-mortem interval. Result is in DAYS.

$$\text{PMI}_{\text{Anaerobic}} = \frac{\underline{\textbf{1285 * (decomposition/100) * 4.6 * adipocere}}}{\textbf{0.0103 * temperature * (soil moisture)}}$$

where:

1285 is a constant, representing the empirically determined BADD value (Burial Accumulated Degree Days, [30, 31]) at which volatile fatty acid (VFA) liberation from soft tissue ceases.

decomposition is a value, or range, between 1 and 100, representing the best estimation of the extent of total body soft tissue decomposition.

4.6 is a constant which represents a slowdown in the rate of decomposition due to a lack of oxygen.

adipocere is a multiplicative value based on the % adipocere estimated to be associated with the corpse (refer to Table 2).

0.0103 is a constant, representing an empirically determined measure of the effect of moisture on decompositional rates.

temperature is the value in degrees Celsius (C) of the soil temperature in the grave vault at the time of excavation and at the level of the corpse (or the average temperature over a period of time).

soil moisture is a value between 1 and 100, representing the soil moisture at the site on the day the corpse was discovered (or the average over a period of time).

Formula II Requirements:

- Corpse in anaerobic decomposition (typically buried): depths studied range from 0.46 – 1.07 m (1.5-3.5 ft)
- Corpse must be in pre-skeletonization phase ($\leq$ 1285 BADD).
    - [Soft tissue present - if mummified, the tissue must be soft and pliable]
- Must estimate the percentage of soft-tissue decomposition that has occurred
- Must determine the percentage soil moisture in the grave vault
- Must estimate the percentage of adipocere present on the corpse
- Ground temperature must be above 0^{o}C
- The burial should not be in an area that is highly saturated with water (riverbank, lake bottom, etc.)

Conditions to note, but not critical in calculation:

- Presentation of the corpse (Stage of decomposition)
- Clothed or wrapped
- Insect access
- Minor soft tissue damage

Detailed explanation of the Formula II terms:

1285 – The decomposition of soft tissue liberates volatile fatty acids (VFAs) [2]. When soft tissue decomposition ends or when the remaining non-nutritive tissue hardens, desiccates and mummifies, VFA production ends. This occurs at approximately 1285 BADDs (BADDs are essentially identical to ADDs, but reflect the temperature of the burial vault and not ambient temperature). This BADD value then corresponds to the cessation of volatile fatty acid (VFA) liberation from soft tissue and signifies the onset of the post-skeletonization phase of decomposition. BADD values less than 1285 indicate that VFAs are still being liberated and the corpse is in the pre-skeletonization phase of decomposition. This formula should only be used if soft tissue remains on the corpse ($\leq$ 1285 BADDs) - a time frame which can extend out several years.

Decomposition – This value must be estimated by the investigator and represents an overall rating of how much soft tissue decomposition has occurred. Input from a Medical Examiner or Forensic Anthropologist is recommended. Typically this is in the form of a range (e.g. 40-60%), but can be expressed as a single value if the investigator is confident with their estimation. Example: If a corpse is estimated to be 50% decomposed, then 1285 (50/100) = 1285(0.5) = 642.5

4.6 – Burials (or any decompositional event which is anaerobic) have been estimated to take approximately 8 times longer than aerobic surface decompositional events to attain the same degree of decomposition [32, 33], but can be very misleading if they do not take into account the

percentage of soil moisture. When moisture is taken into account, the decompositional rate delay, or the delay caused by the lack of oxygen in an anaerobic situation when compared to the surface, is 4.6 (not 8), hence this multiplicative factor. This value was determined by comparative experiments (over many years) measuring the decompositional rates of surface vs. buried individuals that have been normalized by temperature and moisture parameters thereby allowing for the estimation of the effects of the partial pressure of oxygen.

Adipocere – This portion of the calculation requires the estimation of the percentage of adipocere that has formed and is insensitive to whether the formation of adipocere is due to binding with sodium or potassium [1]. Once the % adipocere is estimated, the corresponding multiplier from Table 2 is used in the formula calculation. Ranges associated with the % adipocere present can also be applied to this estimation.

The presence of adipocere raises very complicated issues and significantly slows down the rate of decomposition by trapping moisture and further decreasing the partial pressure of oxygen: the more adipocere present the less oxygen available for aerobic microbial degradation of the remaining tissue. In instances where the % adipocere is greater than just small amounts (>~10%), it is believed that (overall) a non-linear adipocere multiplicative factor best describes the decay rate of the buried corpse. Table 2 describes the correlation between the percentage of adipocere present and the associated multiplicative factor. Most of the buried corpses excavated at the Anthropology Research Facility that maintain tissue have been observed to possess a significant amount of adipocere (in the range of 35-90%) associated with their remains. Since considerable adipocere formation is typically present in our observed burials, the multiplicative factor associated with the range of 10-35% adipocere is largely unknown and was given a temporary value of 1 (Table 2). No doubt this will be refined as more data is collected.

Interestingly, visual examination of buried corpses with comparison to those decomposing on the surface indicates that adipocere formation in the 40% - 65% range showed consistently linear decomposition. The adipocere multiplier values were derived by comparative modeling of burials and surface decomposition events with known PMI, correcting for soil moisture and temperature (n=26).

0.0103 – The effect of soil moisture in a burial follows the same pattern as the effect of humidity at the surface (as described previously) therefore the same constant is used in both humidity and soil moisture percentage calculations.

Temperature – This must be in degrees Celsius and should reflect the temperature of the soil in the grave vault at the time of excavation and at the level of the corpse. Ground/soil temperature lags behind surface temperatures, but can be estimated quite accurately if required [30, 31]. Typically a thermometer or thermocouple is placed in the grave vault wall and allowed to equilibrate to assess the soil temperature at the corpse depth and can be compared to surface temperatures. Differences between soil temperatures and surface air temperatures can be used to correct the NWS air temperature data for estimated soil temperature over the length of the projected decompositional process. Occasionally anaerobic conditions around a corpse are created by wrapping the corpse or placing the corpse in a bag or container above ground. In these types of situations, the temperature should reflect that in the enclosed air around the body or in the bag that contains the corpse and this temperature value simply replaces the soil temperature in formula II.

Soil moisture - % soil moisture can be quickly determined using dry weight assays [2]. 5-10 grams of soil are collected at the depth the body is recovered and dried to determine the pre vs. post drying weight of the soil. This reflects the amount of moisture present and can easily be

converted into a percentage by weight. This is usually done in the laboratory and typically delays the result by only one day. Typical percentages of soil moisture at the Anthropology Research Facility range from approximately 40-80% and depend on the amount of rainfall, soil porosity, type of soil, depth of burial, proximity to vegetation, etc. While not recommended, the investigator can use the % air humidity values in place of soil moisture if time is paramount, but should readjust their calculations once the soil moisture has been determined. This value is left as a percentage. Occasionally anaerobic conditions around a corpse are created by wrapping the corpse or placing the corpse in a bag or container above ground. When air humidity is used in these situations, the humidity should reflect that in the enclosed air around the body or in the bag that contains the corpse and this humidity percentage simply replaces the soil moisture percentage in formula II.

Anthropology Research Facility Example – A test subject was buried at the Anthropology Research Facility in the summer of 2007 at a depth of 0.76m (2.5 ft) and excavated 22 months later. The temperature of the soil at the time of excavation was 11.7^{o}C (53^{o}F). Collection of 10 grams of soil, dried in an oven at 100^{o}C overnight, showed that the moisture content of the soil was 64%. Lengthy estimates of soil temperature and estimated soil moisture measurements over time were intentionally not performed. This method is designed to be a rule of thumb so temperatures and moisture levels at the time of discovery were used for this calculation. Visual examination of the corpse showed that only minor amounts of adipocere were present (<10%) and an 85-95% (90%) decomposition estimate was assigned to the remains.

(1285 * 0.90 *4.6 * 1) / (0.0103 * 11.7 * 64) = 5,319.90 / 7.71 = 690 DAYS

690 days is equivalent to 1.9 years or 23 months.

Forensic Case Example #1 – A fully clothed, female homicide victim was found buried in a shallow grave in soil containing fairly high clay content (determined visually). Geophysical tests were used to locate the grave which showed no apparent signs of having been recent (i.e. no significant subsidence was noted at the time of discovery and vegetation had begun to repopulate the area). The temperature of the soil at the time of excavation was 7.2^{o}C (45^{o}F). Collection of 10 grams of soil, dried in an oven at 100^{o}C overnight showed that the moisture content was 57%. Lengthy estimates of soil temperature and estimated soil moisture measurements over time were intentionally not performed. Visual examination of the corpse showed that significant adipocere was present under the remaining clothing and was estimated to be approximately 40%. The percentage of decomposition based on remaining tissue was estimated at 95%.

(1285 * 0.95 *4.6 * 5) / (0.0103 * 7.2 * 57) = 28,077.25 / 4.23 = 6,638 DAYS

6,638 days converts to 18.2 years.

DNA analysis has identified this victim who went missing 18 years ago.

Forensic Case Example #2 - Animals had partially uncovered the remains of a human female in a shallow burial in a dry desert lakebed in the western part of the United States. A small amount of agricultural lime was present in the grave. No clothing was found at the scene. Decomposition was estimated at 50-60% with adipocere formation estimated at 35%. Soil temperature and soil moisture were determined to be 29^{o} C and 15%, respectively. The formula indicated that the length of time the woman was in the grave was 2,177 days or 5.9 years (a range of 5.4 - 6.5 years).

(1285 * 0.55 * 4.6 * 3) / (0.0103 * 29 * 15) = 2,177 days

Subsequent identification of the victim and an eventual confession told investigators that the victim had been buried over 8 years. The error in this estimation is significant. Root causes of

this error are unknown (possible sources include the presence of the lime, the adipocere multiplier is incorrect at that percentage or the estimated % was incorrect, the low soil temperature and humidity parameters are outside the scope of study, etc.), but do illustrate the need for additional input by the forensic and scientific communities so that these models can be adjusted and corrected for varying environments and circumstances not yet evaluated.

Conclusions

These formulas have been found to work well in areas that encompass the mid to eastern section of the United States where humidity, soil moisture, soil type, and vegetation are similar to those studied at the University of Tennessee's Anthropology Research Facility. The surface decomposition formula is the most universal to-date. We have applied this formula to many cases worldwide with remarkable success. Experienced anthropologists, pathologists, Medical Examiners or forensic personnel can estimate the % decomposition to very accurate levels, but this can also be represented in the calculation by ranges if the estimation cannot be made precisely.

To obtain the most accurate PMI estimation it is important that the number of days averaged to obtain the temperature and humidity percentages used in the formulas are in close agreement with the calculated PMI estimate. Since this number is not known until the PMI is calculated, initial humidity and temperature values are first applied for lengths of time that appear logical as described in the text. Once the PMI is calculated using the initial environmental averages, then the total number of days averaged can be adjusted (and the PMI re-calculated) so they will be similar to the calculated PMI result. This iterative process should be repeated until the number of days is within < 1 week of the calculated PMI which ensures that the most relevant humidity and temperature data are being utilized for the calculation.

The most common source of error for this estimation is that the time period has exceeded 1285 ADDs. It is important that the corpse under evaluation is still in the pre-skeletonization phase of decomposition. Mummified tissue, if present, must still be soft and pliable. Additional tests verifying the presence of VFAs can also be performed if a question arises as to the degree of decomposition that has occurred.

Formula II ($PMI_{Anaerobic}$) also works quite well, and significant data from test subjects as well as forensic cases have shown very good correlation between this calculated value and the actual PMI (when known). Soil moisture determinations are easily accomplished, but they tend to slow down the process since samples must be taken back to the laboratory. The soil moisture determination and the lack of oxygen multiplicative factor (4.6) can be replaced by the more antiquated multiplicative factor of 8 if desired. This will tend to overpredict the length of time in moist soils and underpredict in drier soils, but will provide an estimate without additional laboratory analyses if speed is critical. The multiplicative value of 4.6 was empirically derived, yet may change with varying environmental parameters. Additional input from researchers will be required to verify the effectiveness of this formula in different environments.

The inclusion of the adipocere correction factor is currently the weakest aspect of the $PMI_{anaerobic}$ model since not all burials produce adipocere and determining the % adipocere can be difficult. Regardless, the formation of adipocere slows the decompositional process and affects the partial pressure of oxygen as well as the moisture content of the surrounding soil and remaining tissue.

As professionals begin evaluating and utilizing these formulas, we encourage them to provide feedback on the correctness of their calculations when compared to their laboratory based method of choice. This can take the form of tables or simple emails listing specific

taphonomic and case information important to the continual evolution of these formulas, an example of which can be found as Table 3.

Ultimately, it is hoped that these formulas will provide researchers and professionals in the field of forensics or law enforcement a starting point to begin evaluating their efficacy in different environments and under different conditions so that they can be improved and made truly universal. This will not be an easy task and will require cooperation and careful documentation of a number of taphonomic and death scene related factors.

Acknowledgements

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Table 1. Correlation between decompositional stages and degree of decomposition.

Stage	Decomposition range under warm conditions	Decomposition range under cold conditions
Fresh	1 - 10%	1 - 20%
Bloat	11 - 35%	21 - 45%
Decay	36 - 85%	46 – 85%
Dry	86-100%	86-100%

Table 2. Estimated multiplier values for the contribution of % adipocere formation during human burial decomposition.

% Adipocere formation	Multiplier
< 35	1
35	3
40	5
45	5
50	5
55	5
60	5
65	5
70	6
75	7
80	8
85	11
90	14

Table 3. Sample Table of important feedback variables for continued formula development. It is hoped that law enforcement and other professionals will submit information such as this back to the author for inclusion in the database which will then be used to continually improve these formulas.

Submitting Agency:	**Date:**
Surface or burial (depth/soil type)	
Estimated % decomposition	
Estimated % adipocere	
% humidity	On day of discovery
	Average over ( ) days
	Corrected (NWS)
temperature (C) air or soil	On day of discovery
	Average over ( ) days
	Corrected (NWS)
% soil moisture (burial)	
Presentation of the corpse: description of the corpse, soft tissue damage, cause of death, etc.	
Clothed/wrapped	
Unusual circumstances (burned, chemicals, etc.)	
Environment (altitude, latitude, vegetation, terrain, etc)	
Formula calculation	
Laboratory based PMI result	
PMI confirmed?	
Other information	

Figure 1. The effect of temperature on human decompositional rates [2]. Reprinted, with permission, from the *Journal of Forensic Sciences*, Vol. 37. Issue 5, copyright ASTM International, 100 Barr Harbor Drive, West Conshohocken, PA 19428.